Thyroid Function Tests in Thyroid Disorders - a Clinical Approach

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Introduction

Disorders of the thyroid gland are very common in the clinical practice. Investigations regarding various aspects of the thyroid functions have improved in quantity and precision. The clinician is sometimes left in darkness and confusion when interpreting some of these newer investigations in relation to the clinical setting.

This article will review some of the common thyroid disorders that we come across and will guide the physician to come to a reasonable conclusion regarding a diagnosis by making use of the investigations those we have today. This will not include important radiological and histopathological investigations, as these will be discussed in another article

Basic pathophysiology

The thyroid secretes T3 and T4 into the circulation. Iodine from the circulation is taken up into the thyroid follicular gland with the help of sodium iodide symporter. The iodine is oxidized and organified by the thyroid peroxidase enzyme and attached to the tyrosine residues on the thyroglobulin molecule. T3 and T4 are released by hydrolysis of the thyroglobulin molecule. 0.03 % of T3 and 0.3 % of T4 circulates as free form. The rest of the hormone circulates in the blood bound to TBG (70-80%), albumin (10%) and transthyretin. The active form of thyroid hormone is predominantly T3. Majority of T3 (80%) is formed in the periphery by deiodination of T4 by type 2 deiodinase. The thyroid hormones act on nuclear receptors via cAMP mechanism. TSH secreted by the pituitary stimulates the thyroid gland. The hypothalamo-pituitary unit is inhibited by thyroid hormones by a feed back mechanism.

Clinical evaluation of Thyroid diseases

For ease of diagnosis according to symptomatology, diseases of thyroid can be broadly classified according to the functional status. Clinical evaluation should aim at identifying a) the signs and symptoms of thyroid dysfunction (euthyroid, hypothyroid or thyrotoxicosis), b) symptoms of thyroid enlargement and retrosternal extension (goiter, obstructive symptoms) and c) symptoms and signs of extrathyroidal involvement (opthalmopathy, dermopathy etc). Clinical examination of the neck should categorize the goiter into diffuse or nodular goiter.

Table 1.
Classification of Thyroid diseases

I. Diseases associated with thyrotoxicosis

1. Graves' disease
2. Toxic nodular goiter a) Toxic adenoma b) Toxic multinodular goiter
3. Thyroiditis
4. TSH secreting pituitary tumors
5. hCG induced hyperthyroidism e.g. gestational, trophoblastic disease associated
6. Iodine induced hyperthyroidism e.g. iodine, Amiadarone
7. Thyrotoxicosis factita

II. Diseases associated with Hypothyroidism

1. Goitrous hypothyroidism e.g. Hashimoto's thyroiditis, iodine deficiency, lithium
2. Congenital hypothyroidism
3. Atrophic hypothyroidism: e.g. Hashimoto's thyroiditis, post ablative
4. Central hypothyroidism

III. Euthyroid

1. Diffuse nontoxic (simple) goiter.
2. Nodular thyroid disease e.g solitary nodule, multinodular
3. Thyroid neoplasia: e.g. follicular adenoma, thyroid malignancy

The prudent use of clinical examination, biochemical tests and imaging studies (radionuclide, ultrasound, CT scan) along with fine needle aspiration cytology can establish diagnosis in most cases of thyroid diseases. Rational use of relevant investigations will help in arriving at accurate diagnosis at the minimum cost.

Laboratory investigations

The various biochemical tests used in the evaluation of thyroid diseases can be divided into those which tests the thyroid axis (thyroid hormones and TSH), thyroid autoimmunity (thyroid antibodies) and tests that are used in the follow up of thyroid malignancies (thyroglobulin, calcitonin). Tests that evaluate the impact of thyroid hormones on tissues are used only rarely in routine clinical practice.

Tests that assess the state of hypothalamo-pituitary- thyroid axis

TSH (Thyrotropin)

TSH estimation forms the most important part of a thyroid function test. The rate of thyrotropin secretion is exquisitely sensitive to plasma level of free thyroid hormones. The normal range of TSH is between 0.5 and 5 mU/L. This will vary slightly between labs depending on TSH reference preparations and the assay used. TSH assays over time has been classified into "generations" with respect to sensitivity. Each successive generation offers about 10-fold improvement in sensitivity. The lower limits of detectability of these assays are given in the table 2.

Table 2: Generations of TSH assays

Gene-ration	Sensitivity	Methods/ Comments
1	1 mU/L	Radioimmunoassay. Cannot differentiate euthyroid from hyperthyroidism
2	0.1 mU/L	Immunometric assays. Can differentiate euthyroid from hyperthyroid patients
3	0.01mU/L	Immunometric assays. Can differentiate euthyroid from hyperthyroid patients
4	0.001mU/L	Chemiluniscence assays. May be useful to differentiate NTI from hyperthyroidism

A minimally suitable assay should be able to quantitate concentrations of TSH of 0.1 mU/L with a coefficient of variation of less than 20 %, thus falling into second and third generation category. Currently most laboratories use immunometric assay technology. In this assay, a TSH molecule in the test serum is used as a link between a TSH antibody bound to an inert surface (e.g. coated tube) and a second antibody directed against a second TSH epitope that is labeled with a detectable marker. (I^{125} or chemiluminescence). This technique is more specific, sensitive and rapid than radioimmunoassay. Rarely HAMA (Heterophilic antimouse IgG antibodies) present in the sera of patients may substitute for TSH and cause falsely high values.

In patients with thyrotoxicosis, TSH is suppressed. (less than 0.1 mU/L). Patients with TSH values between the lower limit of normal and 0.1 mU/L are relatively asymptomatic (subclinical hyperthyroidism). Patients with primary hypothyroidism have serum TSH concentration that range from minimally elevated to very high values. In patients with central hypothyroidism, TSH can be normal, low (not suppressed) or even elevated. In those patients of central with elevated TSH, the molecules have reduced biological activity.

TRH stimulation test was previously used in clinical practice. Since the advent of sensitive TSH assays, TRH stimulation test has been given up. TRH exaggerates the normal behavior of basal TSH.

Serum Thyroid hormones

Quantitation of the circulating thyroid hormone concentration is essential to confirm that the thyroid status abnormality suggested by an abnormal TSH result is accurate and document its severity. This can be done by quantitating free or total thyroid hormones.

In vitro, the interaction between the thyroid hormone and their binding proteins conforms to a reversible binding equilibrium that can be expressed by conventional equilibrium equations.(Table 3) The free fraction of T4 is inversely proportional to the concentration of unoccupied TBG binding sites. Estimates of free T4 concentration in serum is generated by direct or indirect assay. In normal serum, the free T4 is approximately 0.02 % of total T4 and that of free T3 is 0.3 % of total T3.

Table 3: interaction between thyroid hormone and binding protein

$$T4 + TBG \underset{}{\overset{K}{\longleftrightarrow}} T4.TBG$$

T4 - concentration of free T4

TBG - unoccupied binding protein

K - equilibrium association constant

T4 .TBG - T4 bound to TBG

Because T4 is the major secretory product of the thyroid gland and correlates most closely with serum TSH, in most situations, a serum free T4 along with TSH is all that is required to ascertain the state of thyroid secretion or supply.

A) Free Thyroid hormones

Currently more labs are adapting to free T4 concentration assays for clinical use. However, there is a bewildering array of methods used to quantitate free T4 or T3 in whole serum that involve automation. Many of these commercial FT4 assays give misleading results in patients with abnormal binding proteins. This includes critical illness conditions where there are changes in binding protein concentration, albumin concentration and increase in fatty acids. The clinician should be wary if the FT4 report by any method does not agree with the clinical status and TSH. The methods of free hormone assays are given in table 4

Table 4: Methods of free hormone assays

- Thyroid hormone binding ratio (THBR)
- Equilibrium dialysis
- Ultra filtration
- Free hormone immunoassays
- Analogue tracer methods

B) Total Thyroid hormones

Total T4 assays are subjected to less assay artifacts compared to free T4 assays. However, acquired and hereditary variations in binding protein concentrations can lead to variations in total T4 and T3 levels. Since the hereditary variations in TBG are uncommon, for routine clinical use in stable patients T4 measurements suffice. In most laboratories, these are cheaper compared to free hormones. Total thyroid hormones are assayed by RIA or chemiluminescence. The normal ranges of thyroid hormones are given in table 5.

Serum Thyroglobulin (Tg)

Tg is a 660-kDa glycoprotein produced by the thyroid follicular cells. It contains not only T4 and T3, but also its precursors diiodotyrosine (DIT) and monoiodotyrosine (MIT). The tissue specific origin of Tg has lead to its use as a marker for differentiated (papillary and follicular) thyroid carcinoma (DTC). Serum Tg concentrations vary in response to changes in thyroid volume, thyroid stimulation and thyroid damage.

Tg can be measured in serum. It also can be measured in immunocytochemistry of tissue specimens from neck masses and metastatic lesions. Currently Tg is measured by immunometric assays (IMA) or radioimmunoassay (RIA) techniques. Automated IMA are more commonly used. The sensitivity of current assays is 0.5-1.0 mcg/L. Since there are large variations between different assays, follow up of Tg in patients with DTC should be undertaken with the same assay. The most important limitation of thyroglobulin assays is interference by anti Tg antibodies.

The most important clinical use of Tg measurements is in follow up of DTC. Tg levels do not aid in diagnosis of thyroid carcinomas, because many patients with benign nodules also have high Tg concentration. Reduction of Tg levels after surgery and radioablation is indicative of reduction in tumor load. After surgery and radioactive iodine ablation, patients are monitored indefinitely for recurrent disease using serum Tg measurements in conjunction with imaging. The sensitivity of Tg measurements to detect residual disease is highest in patients with no residual normal thyroid tissue.

Tg is best measured after TSH stimulation. In operated patients with thyroid carcinoma on thyroxine suppression, stopping treatment for 4-6 weeks allows endogenous TSH to rise, thus stimulating Tg release from the residual (or metastatic) tumor. Recombinant human TSH given exogenously can also serve this purpose without discontinuing thyroxine.

Tests for Thyroid autoantibodies

Graves' disease and Hashimoto's disease are well-characterized autoimmune thyroid diseases. Thus antibodies and T cells against one or another thyroid antigen is often present.

Three types of antibodies are used in clinical practice

1. Thyroid peroxidase antibody: this is directed against TPO (thyroid peroxidase), a membrane bound enzyme. This antigen was originally called "microsomal antigen" based on the apparent sub cellular localization of most of the staining by immunofluorescence. AntiTPO antibodies are present in 90-100 % of patients with autoimmune thyroiditis and 75 % of patients with Graves' disease. About 10 % of normal adults and up to 30 % of elderly are anti TPO antibody positive.

2. Thyroglobulin antibodies: Most of the Tg is stored within the thyroid cells, but small amounts are present in circulation. Exposure of the immune system to Tg is responsible for anti Tg antibody production. Anti Tg antibodies are present in 80-90 % of patients with autoimmune thyroiditis, 50 –70 % in Graves' disease, 10 % of normal adults and 15 % of women above 60 years. It is also present in patients with nodular goiter and thyroid carcinoma. The importance of anti Tg antibodies lies in their ability to interfere with Tg assays which are used in follow up of DTC.

3. TSH receptor antibodies (TSHR Ab): TSH R Ab has a direct pathogenetic role in autoimmune thyroid disease. They can act as agonists and activate TSH receptor in Graves' disease. They can also act TSH antagonists in a proportion of patients with chronic autoimmune thyroiditis. TSH R S Ab (TSH receptor stimulating antibodies) causes thyrotoxicosis and goiter in patients with Graves' disease. TSH receptor antibodies are present in 80-95 % of patients with Graves' disease, but extremely rare in normal population.

TSRSAb assays are useful in certain clinical situations

1. Euthyroid patients with ophthalmopathy

2. Nodular variant of Graves' disease.

3. Pregnant women with Graves' disease: if there is high activity of TSHR S Ab in the mother, there is high likelihood of neonatal thyrotoxicosis.

Other antibodies associated with thyroid, directed against Na- I symporter, CA 2 (second colloid antigen), thyroid hormones, Megalin etc have limited clinical use.

Table 5: Normal range of Thyroid hormones

T3: 70-190 ng/dl

T4: 5-11 mcg/dl

FT3: 0.2-0.5 ng/dl

FT4: 0.7-2.1 ng/dl

TSH: 0.5-5.0 mU/L

NB: These ranges vary between laboratories depending on reference preparations and assays.

Rational use of Thyroid function tests

A) Diagnosing Thyroid disease

Initial investigations of any patient with suspected thyroid disease should be an immunometric TSH assay. If the physician has a reasonable suspicion of functional thyroid disease, FT4 or T4 should be included along with TSH. There is rarely a reason to measure total T3 in the initial evaluation unless the patient is taking triiodotyronine. All patients with abnormal TSH (elevated or suppressed) should have a FT4 or T4 measured.

In conditions with elevated TBG (e.g pregnancy, estrogen replacement where total T4 is often elevated) free T4 should be measured rather than total T4. T3 should be measured for confirming diagnosis in certain clinical situations

1. Suspected T3 toxicosis (suspected in a patient with suppressed TSH and normal FT4)

2. In nonthyroidal illness (NTI, Sick euthyroid syndrome): this would show low T3 levels invariably

3. Amiadarone induced thyroid function abnormalities: elevated T4, low/normal T3 and normal TSH.

Despite reaching a diagnosis in the above conditions, treatment seldom changes. Thus T3 measurements have limited role in routine practice. Primary thyroid diseases show concordant changes in FT4 and TSH i.e. as FT4 increases, TSH decreases and vice versa. Discordant thyroid functions are seen in pituitary diseases. (Table 6)

Table 6: Thyroid function tests in different conditions

Disease	FT4	TSH
Primary hypothyroidism	Low	High
Thyrotoxicosis	High	Suppressed
Central Hypothyroidism	Low	Low (normal or high)
TSH producing pituitary adenoma	High	Inappropriately High

Anti TPO antibodies can be used to confirm a diagnosis of autoimmune thyroiditis and postpartum thyroiditis. Patients with subclinical hypothyroidism and positive anti TPO antibody have higher probability of progressing to hypothyroidism compared to those with negative antibody titre. Hence, antibody measurements will form decision-making criteria in patients with subclinical hypothyroidism. Since the sensitivity of anti TPO antibodies is higher than anti Tg antibodies, estimation of anti Tg antibody has limited role in routine clinical practice.

However, quantitation of antibodies against Tg proves to be extremely important in the context of Tg estimations in view of possible interference with assays. The use of Tg in clinical practice is for detection and follows up of DTC. In a rare patient with low uptake thyrotoxicosis in whom exogenous L-T4 intake is suspected, thyroglobulin levels can be used to differentiate it from thyroiditis: low in factitious thyrotoxicosis and elevated in thyroiditis.

B) Monitoring therapy

In patients with primary hypothyroidism, TSH should be the monitoring parameter. In those with central hypothyroidism, thyroxine dose adjustments should be guided by monitoring free T4. In hyperthyroid patients treated with antithyroid drugs, recovery of suppressed TSH takes 6-9 months. Till TSH recovery takes place, monitoring should be undertaken with free T4 measurements. In patients with thyrotoxicosis in pregnancy, free T4 monitoring should be done to keep levels at upper quartile of the normal range.

Confusing Thyroid function tests

At times, interpreting thyroid function tests can turn out to be a nightmare even for the best of physicians. A poorly maintained quality control in the hormone assay laboratory contributes to significant number of these weird thyroid function tests. A few things need to be kept in mind when trying to interpret weird tests

1. Making sure that the test report is correct. This can be done by rechecking the reports in the same lab or different lab/method. Assay artifacts with free T4 can be confirmed with total T4 as these are subjected to less assay errors. Mild elevations of TSH should be rechecked before planning more expensive investigations like scans and considering treatment.

2. Re-examine the patient and look for signs of thyroid disease. If the functional status of the patient (hypo/hyper or reports that show normal TSH with low FT4 levels, drug interference (e.g. phenytoin) and severe systemic illness should be considered. A meticulous clinical history and examination can sort

out a significant proportion of these patients without resorting to an expensive MRI.

Conclusions

Basic understanding of the physiology and pathology of thyroid functions and current knowledge and appropriate use of thyroid investigations helps the physician to make a reasonable diagnosis of a thyroid disorder. It is very important to note that every abnormal result of the thyroid investigation should be correlated with the clinical setting and unnecessary and prolonged treatment should not be undertaken by the treating physician.

Abbrevations

T4: thyroxine
T3: trioidothyronine
Tg: thyroglobulin
TBG: thyroxine binding globulin
TSH: thyroid stimulating hormone
TRH: thyrotropin releasing hormone
FT4: free thyroxine
DTC: differentiated thyroid carcinoma
PO: thyroid peroxidase

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12th Convocation of National Board of Examinations held at Kolkata on 18th February 2006

The 12th convocation of National Board of Examinations was held on Saturday, the 18th February 2006. at Science City Auditorium, Kolkata. Shri Jyoti Basu, Hon'ble, former Chief Minister of West Bengal, was the Chief Guest. Dr.Anbumani Ramadoss, Hon'ble Union Minister of Health and Family Welfare, Govt. of India, delivered the Convocation address.Dr. Surjya Kanta Mishra, Hon'ble Minister of H & F W, Panchayat & Rural Development, Govt. of West Bengal was the Guest of Honour. Prof. A. Rajasekaran, President, National Board of Examinations, presided the function. Nearly 1500 candidates who passed their practical examination in 2005 were conferred with Diplomate National Board. Besides the meritorious students were also given Gold Medal by the Chief Guest.

Dr. Anbumani Ramadoss, complemented the National Board of Examinations for providing opportunities to medical aspirants in post-graduate medical education in different broad and super specialties as well as different postdoctoral Fellowship programmes in various sub-specialties, in the country. He noted that the National Board of Examinations has taken special measures to increase the expertise of medical graduates in the disciplines of Family Medicine. The Family Physician is likely to be more successful in providing comprehensive services to our communities, specially in rural areas. He emphasized that the linkages of National Board of Examinations with several accredited institutions/hospitals should be further strengthened. The Board should ensure that the specialists services through the accredited private hospitals are also provided in the neglected areas, regions of the country, as well as to the poor population. Special incentives may be given to such hospitals. He added that our country is so diverse, geographically & demographically that there are a wide range of health problems. The Government health infrastructure and facilities in the rural areas are not adequate in several states. Here the private and corporate hospitals can also play an important role by providing some technical medical facilities to governmental institutions. The public and private institutions must network and help complement each other in selected health related issues. He congratulated the candidates, their families and wished them all success, a bright and successful career ahead and hoped that their contribution shall go a long way in strengthening the health care delivery in the country.

Imaging of Thyroid

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Introduction

The thyroid gland is located in the lower anterior neck in the infrahyoid compartment. The gland is made up of two lobes located lateral to the trachea joined at the midline by a thin bridge of tissue called isthmus. The pyramidal lobe is an accessory lobe originates from the isthmus or medial aspect of either lobe and extends superiorly along the course of distal thyroglossal duct. Imaging of thyroid gland can be done by USG, CT and MRI which provides anatomical information while nuclear scintrigraphy provides functional information.

Imaging modalities

Ultrasound

Real time ultrasound of the thyroid gland is usually performed with high resolution linear array transducers ranging from 7.5-10 MHz[1]. These allow excellent visualization of both superficial portions of gland and the deep structures posteriorly to the level of spine. Ultrasound is an accurate method to use in calculating thyroid volume. Tissue harmonic imaging techniques are used as an adjunct to conventional sonography to improve lesion detection and characterization .The thyroid gland is the most richly vascularised organ of all superficially located normal structures of the body. As a result colour and power doppler provides useful diagnostic information in thyroid disease. Ultrasound also provides guidance for performing FNA biopsy. Evaluation of retrotracheal and mediastinal regions is difficult by ultrasound because of acoustic shadowing from overlying air or bone[2]. Another limitation is that USG is inferior to CT and MRI in identifying lymphadenopathy [3].

The normal thyroid parenchyma is homogenous in appearance with greater echogenicity than the adjacent strap muscles. It is limited by a thin highly reflective capsule. The dimensions of normal thyroid vary with the size of subject. The anteroposterior thickness is considered the most reliable index of thyroid size. When it is larger than 2cm enlargement can be confidently diagnosed. Arterial and venous branches within the thyroid parenchyma are clearly visible with current high sensitivity colour doppler machines[4]. Normal peak systolic velocities reach 20-40cm/s in the major thyroid arteries and up to 15-30cm/s in the intra parenchymal arteries.

Computed tomography

The thyroid gland is well seen on CT due to its higher attenuation than soft tissue caused by the physiologically high iodine content of the gland. CT is occasionally used to demonstrate the extent of local invasion or local recurrence of thyroid malignancy and to detect the presence of retrosternal and retrotracheal extension of thyroid enlargement. Iodinated contrast may provide additional information about lesion within the thyroid but the contrast will alter radioactive iodine uptake for about six weeks following the study. Nuclear imaging should be performed prior to CT. On non contrast CT , normal thyroid gland has a density of approximately 80-100 HU because of its iodine content. Intravenous injection of iodinated contrast material results in diffuse increase in density of the gland.

Magnetic resonance imaging

MRI is best performed with a dedicated surface coil centered over thyroid gland. MR imaging provides excellent depiction of internal parenchyma of the thyroid gland as well as relationship with adjacent structures in the neck and thoracic inlet. Like CT, MRI is useful in staging of a known thyroid malignant tumor, to identify local invasion , regional lymph node metastases and to detect the recurrence following thyroidectomy. Using dynamic contrast enhancement characteristics thyroid lesions can be classified as benign, indeterminate or malignant. Rapid enhancement is seen in 90% of malignant lesions while steady or gradual enhancement is seen in 70% of benign cases. Normal thyroid gland is homogenously hyperintense to neck musculature on both T1 and T2 weighted images. The gland enhances diffusely and homogeneously following contrast administration.

Plain film

Plain X-ray has a limited role in the thyroid disorders. It may be useful in the assessment of retrosternal extension and tracheal displacement.

Thyroid disorders

Thyroid disorders are further classified into congenital and acquired disorders.

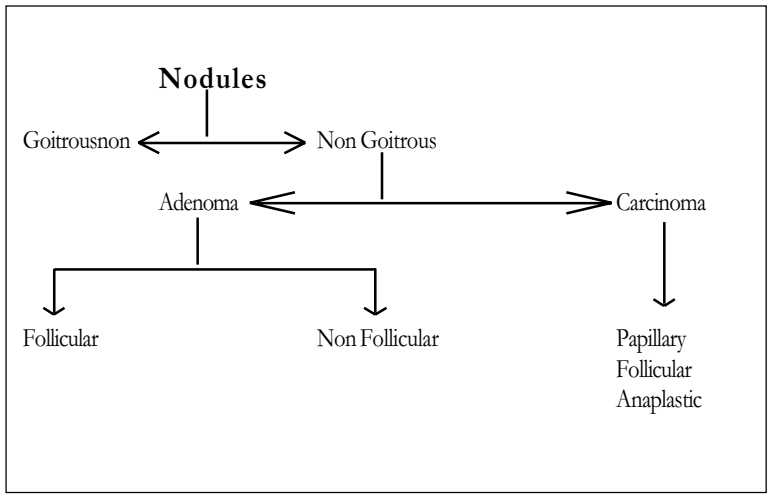
Congenital

Congenital disease of thyroid includes agenesis, hemi-agenesis and varying degrees of hypoplasia and ectopias. Ultrasonography can easily demonstrate all of them except ectopias which are best diagnosed by isotope scan.

Nodular disease of Thyroid

One of the most common clinical problem is patients presenting with a solitary palpable thyroid nodule. The majority of thyroid nodules are benign due to cyst, thyroiditis, adenomas or colloid nodules. Though thyroid carcinoma is uncommon it also very often presents as solitary thyroid nodule[5]. The challenge is to distinguish the few clinically significant malignant nodules from the many benign ones and to identify the patients who are candidates for surgical excision.

Role of Ultrasound in Thyroid nodules



Thyroid nodule is defined as any discrete lesion that is sonographically distinguishable from adjacent parenchyma.

High resolution sonography has four major applications in thyroid disease:

1. Detection of thyroid and other neck masses.

2. Differentiation of benign from malignant masses based on their sonographic appearance

3. Guidance for FNA/biopsy. FNA biopsy is the most effective method for diagnosing malignancy in thyroid nodule.

4. Guidance for percutaneous treatment of non functioning and hyperfunctioning benign thyroid nodules and of lymph node metastasis from thyroid carcinoma.

For the differentiation of benign versus malignant thyroid nodules sonography has sensitivity rates ranging from 63%-94%,specificity from 61%-95% and over all accuracy of about 80%-94%[6].Currently no single sonographic criterion distinguishes benign thyroid nodules from malignant thyroid nodules with complete reliability.

Features almost unique for benign goitrous nodules are

- Completely cystic appearance
- Moving comet tail artifacts
- Widespread cystic changes in isoechoic or highly echogenic nodules.
- Hyperechoic nodules.
- Thin uniform thickness perilesional hypoechoic halo
- Well defined and regular margins
- Perilesional egg shell like or coarse calcification
- Doppler signal of flow around the lesion.

If most of these signs are present in a thyroid nodule the diagnosis of benign disease is highly reliable and no cytological assessment is needed. Conversely the ultrasound signs for malignancy are:

- Hypoechoic nodule
- Irregular margins
- Thick irregular halo
- Doppler signal of flow within the lesion
- Microcalcifiactions
- Hypervascularity
- Invasion of vessels and adjacent structures
- Vessel encasement

The feature with the highest sensitivity is solid composition; however, this feature has a fairly low positive predictive value. The feature with the highest positive predictive value is the presence of microcalcifications. However this feature has low sensitivity. A combination of these features improves the positive predictive value of US to some extent.

The detection of additional occult nodules in patients with clinically solitary lesion though pathognomonic for benign goitre, it does not totally rule out malignancy[7]. In as many as 33%-64% of patients with thyroid cancer at least one associated benign nodule was found either surgically or at ultrasound. When multinodularity is detected each nodule should be carefully studied. If all of them show the same characteristic pattern for goitrous nodules , cytological assessment is not strictly needed and the patient can be followed with periodic scans. Nodules with suspicious ultrasound criteria should under go further assessment with FNA/ biopsy.

Abnormal cervical lymph nodes

US diagnosis of the abnormal lymphnodes depends on the size, shape, vascularity and internal architecture[8]. The US features associated with highest risk of cancer includes heterogenous echotexture, calcifications and cystic areas within the lymph node. A rounded lymph node or one causing a mass effect is also at elevated risk of being malignant. In general, size is a less reliable criterion for malignancy in a lymphnode although chance of malignancy increases as the size of lymphnode increases. Lymphnode should be considered suspicious if it measure more than 7 mm in short axis[8].

Benign neoplasms

Thyroid adenoma

Thyroid adenomas are true neoplasms. They are usually solitary and non functioning. They are usually less than 3 cm in diameter , have well defined margins and may involute, become cystic or may develop internal hemorrhage , necrosis , calcifications or fibrosis[9]. Most thyroid adenomas are hyperechoic or iso echoic with a hypoechoic peripheral halo[10]. On CT scan adenoma may appear solid or cystic when it has degenerated. FNA cannot generally distinguish follicular adenoma from follicular carcinoma as they have similar cytological features. Only histopathological examination can differentiate them based on vascular and capsular invasion.

Malignant neoplasms

Papillary carcinoma

Papillary carcinoma is the most common type of thyroid cancer. It accounts for about 75- 90% of all cases. It most commonly occurs in female adolescents and young adults. Sonographically 90% of papillary carcinoma are hypoechoic. Fine punctate, intralesional microcalcifications are considered characteristic of papillary carcinoma. Typically a centrally vascularised lesion with a chaotic vascular pattern is seen. Cervical lymphnode metastasis seen in upto 50% of cases in the lower deep jugular chain. Metastatic nodes typically show microcalcification and can be cystic.

Medullary, Follicular and Anaplastic carcinomas combined represent only 10%-25% of all thyroid carcinomas.

Incidentally detected nodules

The goal of investigation should be to avoid extensive and costly evaluation in the majority with benign disease, without missing the minority of patients who have clinically significant thyroid cancer. Nodules more than 1.5cm in diameter and having Sonographic feature of malignancy should need FNAC.

USG guided FNA/biopsy

Sonographically guided percutaneous needle biopsy of cervical masses has become an important technique in many clinical situations. It allows continuous real time visualization of the needle, a crucial requirement for the biopsy of small lesions. Palpable thyroid nodules generally undergo biopsy without image guidance. The 25-gauge needles are generally sufficient to yield adequate cytologic specimens; however, in selected cases core biopsy with an 18-to 20-gauge needle may be helpful. Fine-needle aspiration can be done by using nonaspiration-capillary action technique or suction aspiration technique .

Indications for image guided FNA/ biopsy

- Inconclusive physical examination when a nodule is suggested but cannot be palpated with certainty
- Patient who is at high risk for developing thyroid cancer and who has normal gland by physical examination but in whom sonography demonstrates a nodule
- Patients who have had a previous non diagnostic or inconclusive biopsy performed under direct palpation

The diagnostic accuracy is very high, with rates of sensitivity of approximately 85% and specificity 99% in centers with a large experience with these procedures.

Diffuse Thyroid disease

Diagnosis of these conditions is usually made on the basis of clinical and laboratory findings and or occasion by FNA. Sonography is seldom indicated. High-resolution sonography is useful to rule out the possibility of a mass in the large lobe if the underlying diffuse disease causes asymmetric enlargement.

Grave's disease

On US the parenchyma is diffusely hypoechoic and inhomogenous. With colour doppler hypervascular pattern referred to as 'thyroid inferno 'is seen indicating an acute stage of the process. Spectral doppler shows peak systolic velocities to exceed 70 cm/s. There is no correlation between the hyperfunction and the extent of hypervascularity or blood flow velocities. But with doppler analysis therapeutic response in patients with Graves disease can be monitored[11].

Chronic autoimmune lymphocytic (Hashimoto's) thyroiditis

The thyroid gland often enlarged in size and is diffusely hypoechoic with coarse heterogenous echogenicity. Multiple discrete hypoechoic micronodules from 1-6 mm in diameter ('micronodulation') are strongly suggestive of chronic thyroiditis[12]. These nodules are surrounded by multiple linear echogenic fibrous septations. With colour doppler the vascularity is normal or decreased in most patients.

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DNB (Rural Surgery)

National Board of Examinations has launched DNB (Rural Surgery), on pilot basis from June 2006. The concept of rural surgery has evolved in India over the past decade based on the ground reality of surgical practice of surgeons practicing outside high-tech institutions in our country. In India, 400 million people have no access to basic surgical care, termed by the WHO as "essential surgical care". The aim of this course would be to create a cadre of basic multipurpose surgeons, who would acquire the expertise to provide basic and emergency and lifesaving surgical care to rural population of our country. They can form the back bone of health care delivery system and can play a vital role in fulfilling the Rural Health Mission announced by the Government of India.

Goal: After qualifying the final examinations the candidate should be able to function as a consultant (specialist) in Rural Surgery (multiple surgical disciplines) within the constraints of limited resources.

Objectives: At the end of the training period, the candidate should be able to acquire following competencies:

- Basic & general surgery with emphasis on open surgeries.
- Basic orthopaedics including trauma care.
- Obstetrics and Gynaecology.
- Basics of anesthesia, ultrasound and X-Ray.
- Emergency care

Training for DNB in Rural surgery will take place in two kinds of hospitals:

1. Multi specialty hospital which will be called as **Nodal Rural Surgical Training Center**: Two years of training will take place here. This institute will take primary responsibility for the candidate in terms of- Organizing and scheduling the training program for the entire 3 years in consultation with the peripheral institutes. A co-ordinator from both the institutions will be appointed to look after the total training of the candidates; Providing hands on experience to the candidate thus imparting practical surgical skills. Candidate should eventually be able to perform procedures independently and not merely be a first assistant; Placement of the candidate to a peripheral rural surgical centre where the candidate is regularly monitored for skills training and for preparation of the dissertation.

2. **Peripheral Rural Surgical Centre**: One year of training will take place here.This will train the candidate to work in resource limited situations and develop his/her capability to learn to innovate and manage a rural surgical practice; This is also the setting in which the candidate will write up a dissertation based on a topic which is relevant to the rural surgical practice. The candidates will be posted in peripheral Rural Surgical Center for 3-4 months in first, second and third years of training

Eligibility criteria for the Candidates

1. Essential- Any medical graduate with MBBS qualification, who has completed internship and is registered with MCI/State Medical Council can register with the Accredited Institutions for 3 years of training.

2. Desirable- One year experience after completing internship in a peripheral/rural set up. In service candidates from Defence, Central/ State Government, Railways, Public sector institutions may also be given preference.

Management of Common Medical Diseases of Thyroid

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Introduction

Treatment modalities of the common medical thyroid diseases have not changed in the last several decades. However, with the advent of sensitive assays for hormonal levels, there has been a greater emphasis on early treatment, as well as on more accurate dosing to attain as near normal levels as possible. This refers particularly to the new generation TSH tests which can distinguish between normal and subnormal levels.

A goiter whatever it's etiology is a highly visible deformity, and therefore, a distressing cosmetic problem. Thyroid disease is a common problem in the community. It is important to understand the rationale of treatment modalities and to have a proper understanding of effectiveness and adverse effects, so that the best possible advice can be offered to the patient.

This article will deal with therapy of simple goiter, replacement therapy of hypothyroidism, and the management of thyrotoxicosis. Childhood thyroid diseases and surgical diseases will not be discussed.

Simple goiter [1]

Diffuse enlargement of the thyroid occurring in individuals who are clinically and biochemically euthyroid, in the absence of thyroid anti-bodies, is usually due to iodine deficiency, but may also be puberty- related, or due to goitrogens in the food. In these cases the thyroid tissue is being stimulated but is able to produce enough hormone and thus does not result in elevations of TSH, and thyroid hormone levels are in the normal range. Thyroid antibodies are negative. Reassurance is all that is necessary. Alternatively, therapy with thyroxine can be initiated, aimed at suppressing further stimulation of the gland hopefully achieving regression in size. A dose of 100mcg levothroxine is given with the aim of suppressing the TSH level to the low normal range of 0.5 to 1 iU/ml. For the elderly, the starting dose should be 50 mcg/ day. Regression of thyroid tissue can be expected in soft, small glands which have been present for short periods of time. Long-standing large glands usually have significant fibrosis and do not regress. Surgery can be offered for cosmetic reasons.

Hypothyroidism [2]

Overt hypothyroidism is easily recognized if it is suspected and tested for. The most common causes are auto-immune thyroid disease, post-surgical or post radio-iodine ablation. Secondary thyroid failure due to pituitary or hypothalamic disease is less common.

Replacement with thyroxine in the form of levothyroxine is the most widely used therapy. The initial dose should be 50 mcg daily, and needs to be increased to 100 mcgs daily, then 150 mcgs daily at three to four week intervals. Since thyroxine has a long half-life of one week, doses should not be adjusted until a minimum of 3 to 4 half-lives has elapsed to allow a steady –state to be attained. In post-surgical cases where the hypothyroidism has occurred rapidly, the patient can be started initially with 100 mcg, and then titrated upwards rapidly. Once daily administration on an empty stomach is advisable, and other drugs should be taken separately.

Assessment of adequate replacement

After 3 months, the TSH level should achieve a level of 1-2 mU/ ml. If the TSH level continues to be above 5 mU/ ml, the dose of levothyroxine should be increased by 25 mcg, assuming that non-compliance has been ruled out. If the TSH value is suppressed to below 0.1 mU/L. and or the T4 level is above the normal range, it indicates excessive replacement. It is important to not to over-treat the patient. It has been shown that over-treatment can cause increased bone resorption, and arrhythmias. In the elderly who have ischemic heart disease, replacement has to be quite cautious to prevent exacerbation of angina. In these patients a low initial dose of 12.5-50 mcg/day is advised.

Non-compliance

Patients do not feel unwell when they miss thyroxine for a few days, and hence are often erratic with their medications. This can cause problems in evaluating adequacy of therapy. An irregular patient may often become very regular just before a clinic visit. This results in a high TSH, but normal T4 levels. The tests can be repeated after a couple of months of compliance.

Combined therapy with Thyroxine and Tri-iodothyronine

Some researchers have studied the effects of hormone replacement with combinations of T4 and T3. It has been found that supra-physiologic levels of T3 are achieved in a few hours. This causes palpitations, and other thyrotoxic

symptoms which are likely to be detrimental. The level of T3 in tissues and blood is normally a result of conversion of T4 to T3 in extra-thyroidal tissue, as per physiologic requirements. Thus in illness, or fasting, T3 levels decrease, but exogenous administration of T3 upsets this fine physiologically controlled balance. Hence, administration of tri-iodothronine for replacement purposes is not recommended by most experts. Another disadvantage of tri-iodothyronine is that it needs to be given thrice daily because of it's short half-life.

Subclinical hypothyroidism

Subclinical hypothyroidism refers to patients who have normal T4 and T3 but the TSH level is slightly elevated above 5 iU/L. This occurs spontaneously in 3% of adults and 10% of post-menopausal women. It can also occur as a result of surgical or radio-active iodine treatment for hyperthyoidism.

It is still controversial whether sub-clinical hypothyroidism should be treated or not. Those who advocate treatment argue that certain target organs are compromised if left untreated. Among these is cited left ventricular dysfunction, reduced hearing, and hyperlipidemia. There are also claims of increased vulnerability to ischemic heart disease. However, a recent study has shown that there is no increased morbidity or mortality in women with subclinical hypothyroidism who are not given thyroxine replacement. Many clinicians favour treatment with thyroxine because patients feel better, and because there is a 5% rate of progression to overt hypothyroidism every year. The chance of this happening are greater in auto-immune thyroiditis.

If it is decided to treat patients with subclinical hypothyroidism, it is prudent to start with small doses of 50 mcg daily of thyroxine, & check levels after 3 months.

If treatment is started in patients where the TSH is only marginally elevated (e.g less than 10 mU/L), there is no goiter, and thyroid antibodies (microsomal) are absent, it is often the case that 3 or 6 months, the biochemical parameters indicate thyrotoxicosis. It is possible that these patients had transient hypothyroidism(see below), or non-thyroidal illness was the cause for elevated TSH. Therapy should be stopped in these cases.

Transient hypothyroidism

There are certain situations under which hypothyroid state occurs transiently. This happens during recovery phase of sub-acute thyroiditis (de Quervains), post-partum thyroiditis, and even in some cases of chronic auto-immune thyroiditis. Biochemical features of hypothyroidism (elevated TSH and and low T4), may be seen for up to 6 months after surgical or radio-active iodine treatment for Graves' disease. Hence in these mentioned situations, it is prudent to wait for 6 months before diagnosing permanent hypothyroidism.In the event that replacement thyroxine has already been started immediately after the above therapy, careful follow-up at 6 months is warranted to determine continued use.

Sick euthyroid syndrome [1]

Severe non-thyroidal illnesses give rise to low T3 and or low T4 levels, as also abnormal TSH levels. These abnormalities revert once the illness resolves.It is therefore not advisable to test thyroid functions during severe illness unless specifically indicated.

Most experts advise that thyroxine replacement should not be given, but rather to repeat the levels after a few weeks when the patient is better. If however there is a history of thyroid disease in the past, then this can be taken into account when deciding on treatment.

Thyrotoxicosis [3]

The main causes of thyrotoxicosis are Graves disease, toxic multinodular goiter and functioning benign adenoma of the thyroid. Other causes include thyroiditis, drug-induced and pituitary adenomas.

The three modalities of therapy are anti-thyroid drugs, radio-iodine and surgery. The choice of therapy, or combination of therapies depends on the underlying disease, patient preference, and prior response to a treatment regime.

Anti-thyroid drugs

These are favoured for Graves disease as there is an expectation of remission of the auto-immune process after 18 to 24 months. It is specially useful in pregnancy, and in patients who are young and have small glands. Anti-thyroid drugs are not recommended in toxic goiters or adenomas, because there is little scope for spontaneous remission. Drugs are preferred over radio-iodine when patients have Graves ophthalmopathy, as the latter is associated with worsening of eye disease. Drugs are also used prior to surgery or radio-iodine to prevent thyroid storm.

The antithyroid drugs are propylthiouracil, methimazole, and carbimazole. Carbimazole is completely converted to methimazole in the body. The drugs are actively concentrated by the thyroid gland against a concentration gradient.They prevent T4 formation by inhibiting thyroid peroxidase-mediated iodination of tyrosine residues. Propylthiouracil has an additional effect of preventing the peripheral conversion of T4 to T3.The drugs are also considered to have immunosuppressive actions on the gland.

Methimazole and carbimazole can be used once daily, whereas Propylthiouracil needs thrice daily dosing.

Dosing schedule

The drugs can be used in two principal ways; 1) Block and replace schedule, or 2) titration method.

Block and replace regime: A larger dose of anti-thyroid drugs such as Carbimazole 40mgs to 60 mgs, along with thyroxine 100-200mcg daily. This has the advantage of being able to give a relatively higher dose without causing symptomatic hypothyroidism. This regime is preferred in patients who have unstable hyperthyroidism, in whom a small variation in dose causes marked fluctuation in T4 levels.

Titration regime: Lower doses such as 10 to 30 mgs of carbimazole are given and biochemical testing is done periodically every 4 to 6 weeks, and the dose of drugs is lowered (or raised) to make the patient euthyroid. This usually takes about three months, and a maintenance dose of carbimazole 5 to 10 mgs, is needed for 18 to 24 months.

Studies have shown no superiority of one regimen over the other. The adverse effects of anti-thyroid drugs are slightly higher with the block and replace therapy and therefore it is less popular than the titration regime.

Follow-up on treatment

After initiation of treatment, T4 levels are done every 4 to 6 weeks and doses are adjusted accordingly. TSH levels are not used to assess remission of thyrotoxicosis as the level is suppressed even after thyroid function normalizes. TSH level is however useful to correlate if the patient appears clinically hypothyroid. Occasionally the T4 levels appear normal, but the patient is clinically thyrotoxic. This is due to elevated T3 levels and should be tested for. The anti-thyroid drug doses should be increased till T3 levels come down. After euthyroid status has been achieved then for the duration of treatment (18 to 24months), three monthly testing is sufficient.

The relapse rate of thyrotoxicosis after drug therapy is as high as 50 to 68%. Relapse usually occurs within the first 3 months of stopping treatment, but can occur even after several years. Relapses are often treated with a second cause of drugs, or more commonly with radio-iodine or surgery.

Side-effects

Agranulocytosis is the most feared fatal side-effect. It has been reported in .35% with both drugs. Most cases occur within 90 days of treatment. Patients should be advised to report as soon as they have sore throat and fever. Routine WBC counts are not advocated.

Because the onset of agranulocytosis is very rapid. Most cases respond to drug omission, but a few fatalities have occurred. Other side effects are jaundice, vasculitis, and lupus-like syndrome. Pruritis and rash are known.

Adjunctive therapy

Beta-blockers: Non-selective beta blockers, particularly propranolol are very useful in symptomatic therapy of tremor, anxiety and palpitations by direct blockage of the adrenergic system. The doses usually needed are 20 to 40 mgs in divided doses. They also prevent some peripheral conversion of T4 to T3, and are reputed to decrease gland vascularity prior to surgery.

Inorganic iodine: This is given as Lugol's iodine (5% iodine and 10% potassium iodide in water) .1 ml to .3 ml thrice daily. Alternatively Potassium iodide 60 mgs tds. Iodine helps to prevent the release of thyroid hormone from the gland for a few days to a few weeks, but the effect is lost beyond that. This therapy is used as preparatory to surgery.

Radio-active iodine

This is the preferred method of treatment of Graves thyrotoxicosis, in many countries around the world. In India, radio-iodine is available and inexpensive, but may not be accessible outside the tertiary care centers. The advantage of radio-iodine therapy is that relapse rate is very low, and follow-up is simple. It is absolutely contra-indicated in pregnancy (see below). Since radio-iodine works slowly, a patient will usually need to be treated with anti-thyroid drugs for a few weeks or months prior to treatment to make him/her euthyroid. The drugs are usually withdrawn for a few days before radio-iodine is administered and resumed a few days later in order to ensure that entrapment and incorporation of iodine by the gland is not hindered.

In spite of decades of usage of radio-iodine there is still debate about the most appropriate dose. Since delayed hypothyroidism is almost certain, as a late side-effect, efforts have been made to tailor the dose to the gland size and uptake characteristics of the gland. The usual dose delivered for Graves disease is 5 to 10 mCi

Side-effects of radio-iodine

1. The most predictable side-effect is hypothyroidism which occurs anytime from the first year onwards to 25 years after radio-iodine ablation.

2. Radio-iodine has been found to worsen ophthalmopathy, and is therefore avoided in such cases.

3. Although thyroid cancer has been described occasionally in a few patients, several large studies have disproved a cause and effect relationship.

4. Teratogenesis is a concern. However, so far there has been no evidence for increased incidence of congenital anomalies in children born to mothers who have had radio-iodine.

5. If radio-iodine is administered to a pregnant lady by 10th week of gestation at which time the fetal thyroid has developed, it will undergo complete ablation resulting in congenital hypothyroidism.

Surgical treatment

Sub-total thyroidectomy is the surgical procedure for Graves disease. It is rarely a primary treatment. It is reserved for patients who have relapsed on drugs and are not eligible for radio-iodine (pregnancy), or refuse it. Surgery is preferred in patients who have large glands with pressure symptoms.

Surgery should always be preceded by anti-thyroid drugs to produce a euthyroid state, and reduce the risk of thyroid storm. Additional several measures are also taken to reduce the vascularity of the gland. Propranolol has been used alone or in combination with potassium iodide.

Complications of surgery are:

1. Laryngeal nerve damage.
2. Hypoparathyroidism.
3. Bleeding into the neck.

These complications are minimal in expert hands, and mortality is almost zero.

Post-operative Thyroid function

Relapse of thyrotoxicosis occurs in 10% of patients, and usually occurs in the first five years after surgery. However relapses as late as 25 years have also been reported.

Post-operative hypothyroidism is also a feature. As mentioned above it can occur transiently upto six months post-operatively.

Toxic adenomas & toxic multinodular goitres

Radio-iodine is the preferred treatment for these cases, but the doses used are much higher than what is needed for Graves disease, and are in the range of 10 to 50 mCi. Surgical treatment is indicated if goiters are large with pressure symptoms, or if the patient refuses radio-iodine. Antithyroid drugs are not used because the hyperthyroidism is permanent with no chance of remissions, thus indefinite drug therapy would be required with problems of follow-up and side-effects.

Thyroiditis [3]

This should be suspected in patients who have pain in the thyroid region, have almost no enlargement of the gland, and have very low radio-iodine uptake. The thyrotoxicosis is transient and so no treatment is warranted, except perhaps with propranolol for a few weeks for symptomatic relief. NSAID'S and glucocorticoids may be needed to reduce pain; thereafter hypothyroidism may set in and replacement therapy may be needed transiently or permanently. Post-partum thyroiditis should be treated similarly.

Hyperthyroidism in pregnancy [3, 4]

Antithyroid drugs are the treatment of choice. Propylthiouracil is preferred because it not crosses the placenta less than do carbimazole and methimazole. The lowest possible dose of the drug is preferred, so as to prevent as little transplacental passage of the drugs as possible, thereby minimizing fetal hypothyroidism, and goiter formation. If the dose is too low, uncontrolled maternal thyrotoxicosis will not only cause maternal distress but may initiate early labour and thus harm the fetus. To walk this tightrope successfully, frequent thyroid function tests are required, once in every 2 weeks throughout pregnancy. Thyroxine does not cross the placenta, so it is better avoided in the mother in whom an inadvertently excessive does will necessitate an increased dose of anti-thyroid drugs, which in turn will hurt the fetus, as explained above. Breast-feeding is safe on anti-thyroid drugs.

Teratogenecity of anti-thyroid drugs [4]

Very rare instances of "methimazole embryopathy" in which the fetus has choanal atresia, or esophageal atresia, have been reported. However, other studies have shown this to occur irrespective of drug intake.

Drug-induced Thyroid disease [1]

Lithium, and amiadarone are important drug-related causes of thyroid disorders.

Amiadarone toxicity can cause either hypothyroidism or hyperthyroidism. It contains 39% iodine by weight. Hypothyroidism is treated by levothyroxine replacement without discontinuing amiadarone.

Amiadarone –induced hyperthyroidism is more complex to treat. If it occurs in patients with pre-existing goiter or preclinical Graves disease(Type 1), then high doses of anti-thyroid drugs is effective. In type 2 disease (where no pre-existing thyroid disease is present), oral contrast agents such as sodium ipodate 500 mgs/day can be given.Lithium, potassium perchlorate and gluco-corticoids are other forms of therapy. If at all possible, amiadarone should be discontinued.

Thyrotoxic crisis [3]

This is a medical emergency presenting as marked tachycardia, fever, agitation, and has a high mortality if untreated. The drugs of choice are, glucocorticoids, high dose propranolol (2 to 5 mgs IV every 4 hours; 320 to 480 mgs orally daily); potassium iodide orally to block release of thyroid hormones; propylthiouracil100mgs every 6 hours; radiographic contrast ipodate sodium 1 gm per day by mouth. The iodine released from this compound has anti-thyroid effects. The agent also prevents peripheral conversion of T4 to T3.

Conclusion

Hypothyroidism as well as hyperthyroidism can be effectively treated with the available therapeutic agents. Subclinical disease is considered by many experts to be grounds for treatment. Pregnancy, co-morbid illness, age and environmental factors need to be taken into account when treatment is being planned. Accurate dosing is required in order to prevent over- or under-treatment.

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National Board of Examination's CME programmes go high tech on 22nd July 2006

The first Interactive CME session for DNB candidates using Indira Gandhi National Open University satellite infrastructure was held on 22nd July 2006. The Board in collaboration with the School of Health Sciences, Indira Gandhi National Open University has planned five such sessions for August 2006 and gradually the frequency will be increased. These sessions will also be recorded and DVDs will be made available to accredited hospitals and DNB candidates. The transmission will be available at C- BAND (GD1-GD4), 4165 MHz, Horizontal Polarization, Transponder C-12 on INSAT 3C, Symbol Rate: 26,000 SPS, FEC: ½ and also at DTH (KU BAND) GD-1, NSS 6, Down link frequency: 12427.5 MHz, Symbol Rate: 21, 0937, Polarization horizontal, FEC: ¾. All the National Board of Examinations' accredited hospitals may kindly ensure that all the DNB candidates must attend these sessions. The Hospitals, which have not yet installed the reception equipments are requested to contact the Regional Director IGNOU in their respective states (city) and request him/her for making the necessary arrangements for DNB candidates at their centers for reception of satellite transmission on the specified dates and time. The details are on the National Board of Examinations website: www// natboard.nic.in

Review Article

Surgical Management of Common Diseases of Thyroid

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Solitary thyroid nodule, multinodular goiter, thyroid cancer, thyroiditis, Graves' disease and Plummer's disease (multinodular toxic goiter) are the common disorders of thyroid which we come across needing surgical management. Although the surgical procedures described for the above mentioned conditions are fairly standardized, controversy rages about the extent of surgery for benign and malignant thyroid disease. This controversy balances the complete extirpation of the disease with the incidence of two primary potential complications of thyroidectomy in the form of recurrent laryngeal nerve (RLN) injury and hypoparathyroidism. The commonly performed operations on thyroid include lobectomy or hemithyroidectomy, subtotal thyroidectomy, near total thyroidectomy and total thyroidectomy. The extent of surgery in a benign solitary nodule is lobectomy or hemithyroidectomy of the affected lobe. In presence of a malignant solitary nodule the procedure of choice is total or near thyroidectomy. There are some reports that the extent of surgery in well differentiated cancers is determined by the high or low risk factors associated with the malignancy. In high risk patients total or near total thyroidectomy is justified whereas in patients with "low risk" a lobectomy can be done without compromising the results. The surgical procedure for non-toxic and toxic MNG is same in the form of subtotal thyroidectomy or total thyroidectomy. Most clinicians currently recommend near total or total thyroidectomy for all clinical cancers. Conventionally a functional (sparing sternocleidomastoid muscle, internal jugular vein, spinal accessory nerve) or modified radical neck dissection is done when the metastases are confirmed in cervical nodes. Postoperative therapy following surgery for well differentiated thyroid cancer includes radioactive iodine ablation of thyroid remnant and distant metastases. Thyroid stimulating hormone suppression is also done by giving suppressive doses of thyroxine postoperatively. The procedure of choice in familial and sporadic medullary thyroid carcinoma is near total or total thyroidectomy with central compartment lymph node dissection. Anaplastic carcinoma most of the time at presentation is inoperable. Surgery may be needed to palliate airway or esophageal obstruction. In Graves' disease although medical therapy is commonly used, surgical intervention is necessary when there is a possibility of a coincident carcinoma, large bulky glands, patient preference to avoid I^{131} or antithyroid medications and young females in the reproductive age groups where I^{131} therapy may not be advisable. Total or near total thyroidectomy is the surgery of choice. Other options include subtotal thyroidectomy or Hartley-Dunhill procedure where one lobe is completely resected and partial resection of contralateral lobe is done. Subtotal thyroidectomy is the common procedure performed for all types of thyroiditis. In Riedel's thyroiditis this may be difficult due to extensive fibrosis and destruction of normal tissue planes; hence wedge resection of isthmus can provide relief of the pressure symptoms in symptomatic cases. Minimally invasive, video-assisted thyroidectomy (MIVAT) is characterized by a unique central access and external retraction. Pathologies treated are mainly nodular goiter, small differentiated carcinoma without lymph node involvement. Nowadays this minimally invasive surgery, in selected patients, clearly demonstrates excellent results regarding patient cure rate and comfort, with shorter hospital stay, reduced postoperative pain and most attractive cosmetic results.

Introduction

Solitary thyroid nodule, multinodular goiter, thyroid cancer, thyroiditis, Graves' disease and Plummer's disease (multinodular toxic goiter) are common disorders of thyroid needing surgical management. Although the surgical procedures described for the above mentioned conditions are fairly standardized, controversy still exists about the extent of surgery for benign and malignant thyroid disease. This controversy balances the complete extirpation of the disease with the incidence of two primary potential complications of thyroidectomy in the form of recurrent laryngeal nerve (RLN) injury and hypoparathyroidism. The commonly performed operations on thyroid include lobectomy or hemithyroidectomy, subtotal thyroidectomy, near total thyroidectomy and total thyroidectomy. Lobectomy or hemithyroidectomy is removal of one lobe with the isthmus and subtotal thyroidectomy is excision of both lobes leaving behind 2 to 4 grams of thyroid tissue in the tracheoesophageal groove

on either side. Near total thyroidectomy is complete removal of one lobe with the excision of the contralateral lobe leaving behind a small rim of thyroid tissue on the contralateral side to protect the parathyroids and the RLN. Total thyroidectomy is the complete removal of all macroscopic thyroid tissue. This review includes the surgical options, controversies and recent developments in the surgical treatment of common thyroid disorders.

Surgical treatment of thyroid disorders

Solitary thyroid nodule

The common disorders of thyroid which can present with a solitary nodule include a dominant nodule of a multinodular goiter, thyroid adenoma; thyroid cancer especially well differentiated type, thyroiditis and rarely a thyroid cyst. A colloid nodule can be euthyroid or a toxic nodule. Conventionally the indications for surgery in a fine needle aspiration cytology (FNAC) reported benign solitary nodule comprises of extreme age (younger than 20 or older than 45), male sex, pain, pressure symptoms, large nodule (> 4 cm), rapid growth, history of radiation to neck, family history and a toxic nodule when medical or radioiodine therapy has failed.

The extent of surgery in a benign solitary nodule is lobectomy or hemithyroidectomy of the affected lobe[1]. This comprises of removal of the lobe with the isthmus. If the nodule is limited to the isthmus only then an isthmusectomy is the surgical procedure of choice when benign. When there is a suspicion regarding malignancy, a frozen section is performed on the excised lobe and further procedure is done based on the report. In cases of follicular neoplasm reported on FNAC even a frozen section may not be able to rule out malignancy. In these cases it is necessary to await the paraffin section report and perform completion thyroidectomy the excised specimen is reported as malignant.

In the presence of a malignant solitary nodule the procedure of choice is total or near thyroidectomy. In low volume centers near total thyroidectomy is preferable to reduce the risks of injury to recurrent laryngeal nerve and hypoparathyroidism. There are some reports that the extent of surgery in well differentiated cancers is determined by the high or low risk factors associated with the malignancy [2,3]. The patients with "high risk" factors are extremes of age, lesions greater than 4 cm, extrathyroidal spread, regional or distant metastases or high grade tumors. In these patients total or near total thyroidectomy is justified whereas in patients with "low risk" hemithyroidectomy and a small adjoining part of the opposite lobe at its junction with the isthmus can be done without compromising the results. We are performing a total thyroidectomy at our centre for a malignant solitary nodule.

Multinodular goiter

Multinodular goiter (MNG) is the commonest thyroid disorder encountered in most of the hospitals in our country. MNG can be toxic or non-toxic, the latter being more common. The common cause is due to iodine deficiency [4]. Therapy for MNG can be medical or surgical. Surgical therapy in a euthyroid MNG is indicated in a large MNG, when patient has pressure symptoms due to long standing goiter, there is suspicion of malignancy, substernal extension or for cosmetic reasons. In toxic MNG, surgery is indicated when medical treatment has failed, it is very large or there is failure of radioiodine therapy. Surgery in toxic MNG is also performed for the indications mentioned for non-toxic MNG.

The surgical procedure for non-toxic and toxic MNG is same in the form of subtotal thyroidectomy or total thyroidectomy. The patient has to be well prepared before attempting surgery in a patient with toxic MNG. This includes preoperative cardiac evaluation, antithyroid drugs, beta blockers and potassium iodide to make the patient euthyroid before surgery. Control of toxicity prior to surgery reduces the chances of precipitating postoperative thyroid crisis which can sometimes be fatal. Although many centers may prefer subtotal thyroidectomy for a non-toxic goiter that leaves behind less than 2 gm of thyroid tissue on either side, for a toxic MNG total thyroidectomy is recommended. As the treatment of recurrent thyrotoxicosis following subtotal thyroidectomy is difficult, total thyroidectomy is commonly performed for this condition. The surgical techniques in patients with toxic or non-toxic MNG should allow for the best chance for removal of the abnormal thyroid tissue with the least morbidity. This depends on the volume of thyroid surgery being performed at the center and the surgeon's experience [5-7]. Muller et al have reported in a large retrospective review that the complication rates between subtotal and total thyroidectomy are similar [8]. In this review, the complications following total thyroidectomy were a wound infection rate of 0.9%, a secondary hemorrhage rate of 0.6%, 8% transient recurrent nerve palsy rate, 0.9% permanent nerve palsy rate, 28% rate of immediate hypocalcemia and 0.9% patients of permanent hypocalcemia. The corresponding complications in patients with subtotal thyroidectomy were, 1.6% wound infection rate, 1.8% secondary hemorrhage rate, 0.7 % permanent recurrent nerve palsy rate and 0.7% rate of permanent hypocalcemia [8].

Postoperatively, following subtotal thyroidectomy for non-toxic MNG, the patient can be put on thyroxine to provide thyroid replacement and reduce the chances of recurrent nodular formation[9]. Although we follow this practice routinely, a benefit in outcome following postoperative thyroxine therapy is not proved yet [10]. Percutaneous ultrasound guided ethanol injection is also reported as an alternative therapy in patients with toxic MNG when other non-surgical methods have failed and surgery is contraindicated due to co-morbid reasons[11]. Hyperthyroidism resolves in 42% of the lesions at 3 months and 66% at 1 year. The chances of control of toxicity are more in nodules less than 3 cm. Weekly 2 to 4 cc of 95% ethanol is injected in the nodules till euthyroid status is achieved[11]. We have no personal experience of this procedure.

Thyroid cancer

Thyroid cancer can be broadly divided into well differentiated thyroid cancer (WDTC), medullary thyroid carcinoma (MTC) and other rare tumours of the thyroid. WDTC constitutes about 85 to 90% of all thyroid cancers, MTC about 8 to 10% and the remaining form the rare tumors of the thyroid [12].

Well differentiated Thyroid cancer

Well differentiated thyroid cancer includes papillary thyroid carcinoma (PTC), follicular thyroid carcinoma (FTC) and Hurthle cell carcinoma. Papillary carcinoma predominantly represents this group. Surgery is the first line therapy for the treatment of well differentiated thyroid cancer. However, the extent of resection for WDTC remains controversial. Conventionally the operation of choice is near total or total thyroidectomy. As mentioned earlier for solitary nodule morbidity following total thyroidectomy will be less at high volume centers for thyroid surgery. Hence near total thyroidectomy should be done at low volume centers. The protagonists of total or near total thyroidectomy argue that as there is high risk for contralateral lobe malignancy (more common with PTC), enhanced postoperative I^{131} ablation, better postoperative surveillance by clinical exam and thyroid scan and as this facilitates use of thyroglobulin (Tg) as a tumor marker; near total or total thyroidectomy is the procedure of choice for WDTC. Studies have also shown reduced recurrence and improved survival following total thyroidectomy when compared to lobectomy for an ipsilateral disease [13,14]. The opponents of total thyroidectomy in early stage tumors believe that the increased risk of RLN injury and hypocalcemia are not justified by an improvement in disease control or survival rates over those attained by unilateral thyroid lobectomy [15]. Although the extent of surgery is still controversial, most clinicians currently recommend near total or total thyroidectomy for all clinical cancers [16].

Most WDTC are cured by initial operation. Sometimes these cancers might be advanced with extrathyroidal spread and distant metastases when radioiodine therapy and external beam radiotherapy (EBRT) with adjuvant chemotherapy (doxorubicin) can be given. Lymph node metastases are more often seen in patients with PTC. Elective neck dissection is not indicated in WDTC although papillary carcinomas can have occult metastases in as many as 90% of elective neck specimens as the impact of such finding on survival is debatable [17,18]. Hence, conventionally a functional (sparing sternocleidomastoid muscle, internal jugular vein, spinal accessory nerve) or modified radical neck dissection is done when the metastases are confirmed in cervical nodes. Usually Level I (submental and submandibular) nodes rarely get involved with thyroid metastases and hence are not included in the dissection. The block dissection includes Level II to VI lymph nodes. The risk of bilateral disease is greatest with male sex, advanced tumor stage, bulky ipsilateral nodal disease, involvement of the thyroid isthmus, and extrathyroidal extension [19]. Contralateral neck dissection is indicated in these conditions.

Postoperative therapy following surgery for WDTC includes radioactive iodine (RAI) ablation of the thyroid remnant and distant metastases. Thyroid stimulating hormone (TSH) suppression is also achieved by giving suppressive doses of thyroxine postoperatively as WDTC is a TSH dependent tumor. The TSH levels should be near zero for an adequate suppressive therapy. The advantages of postoperative RAI include the ablation of micrometastases and residual thyroid tissue. The latter facilitates optimal follow up as in presence of normal thyroid tissue RIA trapping by metastases may not occur and their identification becomes difficult by I^{131} total body scan (TBS). The absence of thyroglobulin production by the thyroid tissue helps in increasing the accuracy of thyroglobulin tumor marker for detecting recurrence. The need for RAI ablation as a routine in younger patients with smaller lesions confined to the thyroid gland remains controversial [20].

RAI administration can produce complications that include radiation thyroiditis (when a large thyroid remnant is present), dysphagia, sialoadenitis, glossodynia, tumor edema and hemorrhage and pulmonary fibrosis in patients with extensive lung metastases. A high level of TSH is necessary for an optimum I^{131} TBS. To achieve this thyroxine hormone replacement therapy is withdrawn before TBS. Patients receive a dose of 2 to 5 mCi for a TBS. The

scanning is performed 2 to 3 days after I^{131} administration. The serum concentration of TSH should be between 25 to 30 mIU/L for an optimum scan[21]. As the production of Tg is also dependent on TSH ideally this should also be done when the TSH level is high. This standard method of increasing the level of TSH by producing hypothyroidism can lead to physical disturbances, psychological alterations, and disruption of patient's family, social and working life [22].

Recent development is the use of an alternative method in the form of recombinant human TSH (rhTSH) [23,24]. The rhTSH allows the quicker clearance of RAI with the potential for fewer side effects and patients no longer need to experience symptoms of prolonged hypothyroidism before TBS as patients continue on their replacement therapy before the scan. RhTSH is administered as a single intramuscular dose of 0.9 mg on two consecutive days. It has been reported that when a combination of RAI TBS and serum Tg was performed after rhTSH stimulation, the assays together detected the remnant thyroid tissue or cancer within thyroid bed in 93% of patients and in 100% of patients with metastatic disease [25]. The generally used cut-off for the Tg level is 2 ng/ml. Mazzaferri et al reported in a recent review that Tg levels and RAI scan are used in combination for detection of recurrence[26]. If Tg is detectable, neck ultrasound and chest radiographs are advised, and RAI therapy or surgery is considered. If Tg is undetectable then rhTSH stimulation is used to assess the Tg levels. In patients with greater than 2ng/ml assessment is done for location of recurrence. In patients with elevated Tg levels and negative RAI TBS, a positron emission tomography (PET) scan is done to detect the recurrence [26].

The prognosis is excellent in patients with WDTC with the 10 year survival rate for papillary cancer being 95% and 90% for follicular cancer [20]. Although the overall prognosis is excellent there is a small subgroup of patients with high risk factors who have lower survival.

Medullary Thyroid cancer

Medullary thyroid cancer is relatively rare when compared to WDTC, however, the mortality due to this disease is higher compared to WDTC [27]. MTC arises from the parafollicular C cells which are neuroendocrine in origin. Surgery is the mainstay of therapy in MTC like other thyroid malignancies. The high incidence of multifocal disease, the lack of efficient adjuvant therapies, and a good response to complete surgical extirpation are justifications for a more radical approach. Familial MTC is almost always multifocal and bilateral [28]. 67% of sporadic cases have bilateral disease [29]. The procedure of choice in familial and sporadic MTC is total thyroidectomy with central compartment lymph node dissection. Central compartment dissection includes removal of pretracheal and paratracheal lymph nodes from the level of the hyoid bone above down to the level of the suprasternal notch and laterally to the carotid sheaths. These nodes are sent for frozen section and if found positive for malignant cells, a complete functional neck dissection is done form Level II to Level VI. The involvement of superior mediastinal nodes (Level VII) is higher with MTC when compared to other thyroid cancers and these nodes should be included in dissection if involved. Radiation therapy is used as an adjuvant therapy when patient has significant extrathyroidal spread after removal of gross disease [30]. Serum calcitonin and carcinoembryonic antigen (CEA) are used as tumor markers for MTC.

The overall survival for patients with MTC is 72% at 5 years and 56% at 10 years [31]. Familial MTC has better prognosis than sporadic MTC. Higher levels of Calcitonin content, DNA euploidy and the absence of capsular involvement are associated with better prognosis [32].

Anaplastic carcinoma and lymphoma of Thyroid

Anaplastic carcinoma is a rare tumor of the thyroid and accounts for less than 2% of all thyroid cancers [33]. Although very rare this tumor is very aggressive and rapidly invades the surrounding tissues leading to an overall survival of less than 6 months in the majority of the cases [33]. Most of the time at presentation this tumor is inoperable. Surgery may be needed to palliate airway or esophageal obstruction. Rarely when surgical resection of the tumor is possible a multimodality approach may be tried with radiation and chemotherapy. Inspite of these efforts the prognosis is bad with a patient survival of only a few months.

Primary thyroid lymphoma is very rare occurring in less than 5% of thyroid cancers [34]. Primary thyroid lymphoma is associated with Hashimoto's thyroiditis in 85% of patients [34]. Surgical therapy is limited to patients with localized MALT lymphomas where complete excision is possible. Otherwise radiation or chemotherapy is the treatment of choice for therapy [35].

Graves' disease

Graves' disease is an autoimmune disease characterized by hyperthyroidism, goiter and ophthalmopathy [36]. Sometimes patients might present with dermatopathy or acropachy [37]. Although medical therapy is commonly used for treating this condition, sometimes surgical intervention is necessary when there is a possibility of a coincidental

carcinoma, patients with large bulky glands, patient preference to avoid I^{131} or antithyroid medications and young females in the reproductive age groups where I^{131} therapy may not be advisable [38]. In patients with severe ophthalmopathy I^{131} administration may lead to complications, hence surgery might be preferable [39]. Total or near total thyroidectomy is the surgery of choice. Other options include subtotal thyroidectomy or Hartley-Dunhill procedure where one lobe is completely resected and partial resection of contralateral lobe is done [40]. Surgery should always be done after a good preoperative preparation of the patient.

Thyroiditis

Thyroiditis is a group of inflammatory thyroid disorders which includes Hashimoto's thyroiditis, de Quervians's disease, Riedel's thyroiditis and rarely infectious and amiodarone induced thyroiditis. Therapy is usually medical and surgery is indicated only for cosmetic reasons, suspicion of malignancy or pressure symptoms. Pressure symptoms are common with Riedel's thyroiditis where fibrosis is predominant. Subtotal thyroidectomy is the common procedure performed for all types of thyroiditis. In Riedel's thyroiditis this may be difficult due to extensive fibrosis and destruction of normal tissue planes; hence wedge resection of isthmus can provide relief of the pressure symptoms in symptomatic cases [41]. Glucocorticoids and tamoxifen have also been used with good results for therapy of Riedel's thyroiditis [41].

Minimally invasive video-assisted thyroidectomy (MIVAT) was first used in Pisa in 1998[42]. The technique is characterized by a unique central access and external retraction. Although there is some controversy about the validity and indications of this procedure and other minimally invasive thyroidectomy techniques, MIVAT looks promising. The advantages of MIVAT are similar to other minimimally invasive procedures. Less trauma, better post-operative course, early discharge from hospital and improved cosmetic results are seen with MIVAT. Minimally assisted video-assisted thyroidectomy is a gasless procedure performed under endoscopic vision through a single 1.5-2.0-cm skin incision, using a technique very similar to conventional surgery. This is conventionally performed for small thyroid nodules usually less than 35 mm or thyroid volume less than30 ml and when no previous conventional neck surgery has been done [43].The minimally invasive approach wound is much shorter (1.5 cm for small nodules, up to 2-3 cm for the largest ones). Patients also experience much less pain after MIVAT surgery than after conventional thyroidectomy. This is due to less dissection and destruction of tissues. The usual indication is a nodular goiter. The only kind of thyroid cancer which may be approached with MIVAT is a small differentiated carcinoma without lymph node involvement [44]. Nowadays this minimally invasive surgery, in selected patients, clearly demonstrates excellent results regarding patient cure rate and comfort, with a shorter hospital stay, reduced postoperative pain and more attractive cosmetic results.

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Six monthly appraisal of DNB candidates and accredited hospitals- for further improving the DNB training programmes

The purpose of introducing six monthly appraisals of NBE accredited hospitals/institutions is to further improve the quality of training, assess the training infrastructure for the DNB candidates and also assist the local institutions to develop in to a center of academic excellence. This would further add value to the services being rendered in these accredited hospitals/ institutions. Please do not think that this assessment has negative connotation. Please plan the appraisal in such a way as to minimally affect the routine working of the department. The Board expects the local appraiser to be a post graduate in the speciality with teaching and research experience. He/She should have enough time and expertise to carry out the following activities in the allotted hospitals/ Institutions:

i. He/she should participate in thesis protocol/progress presentation & discussion; assist the DNB candidates in their thesis work by giving them suggestions and monitoring their progress. He/she should give specific remarks to improve the Thesis work after reviewing the objectives, methodology (sample size, sampling technique, data collection tools etc.), data analysis plan and statistical tests, results and discussion plan etc. of thesis of each candidate. These remarks should also be communicated in writing to the supervisor and the concerned candidate by the appraiser and a copy be sent to National Board of Examinations.

ii. He /she is expected to examine the log book maintained by the candidates and give specific remarks to improve the log book maintenance after reviewing the contents of the log book (name of procedure, details of the case, salient findings, remarks of the supervisor for the improvement of the candidate etc). These remarks should also be communicated in writing to the supervisor and the concerned candidate by the appraiser and a copy be sent to National Board of Examinations.

iii. He/ should prepare question paper containing ten short structured questions in the speciality on the topics covered during the preceding six months and evaluate the answer sheets. He/she will maintain total confidentiality in these activities. The arrangements for six monthly theory and practical examination will be made by local accredited hospitals/institutions.

iv. He/she will formally conduct practical examination (On the topics/ areas covered in preceding six months). The practical will have long case, short cases; ward round, spots and viva voce as per the DNB format.

v. He/she will communicate the result of assessment to the concerned candidates along with detailed feed back on their performance. He/she will give detailed suggestions to each candidate in writing for improving his/ her performance. He/she will act as counselor and give specific remarks for improving the overall performance level of the candidate. These remarks should also be communicated in writing to the supervisor and the concerned candidate by the appraiser and a copy be sent to National Board of Examinations.

vi. He/she will prepare the Examination worksheet for each candidate and submit the same to the concerned hospital for records with a copy of the same to the National Board of Examinations. He/ she will submit the report to the Executive Director, NBE, on the given format.

vii. He/she will also send six monthly report on the infrastructure, patient load and manpower in the concerned speciality of the accredited hospital, to the Executive Director, National Board of Examinations, Ring Road, Ansari Nagar, New Delhi-110029.

Thyroid Gland: Anaesthetic Implications

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Thyroid gland is one of the important endocrine glands in the body which secretes thyroxine (T_4) and 3,5, 3' tri-iodothyronine (T_3), and these are the major regulators of the cellular metabolic activity. Thyroid hormones carry out variety of actions by regulating the synthesis and activity of various proteins for proper cardiac, pulmonary, and neurological function during both health and illness. Thyroid hormones increase carbohydrate and fat metabolism and are important factor in determining growth and metabolic rate.

Physiology

Dietary iodine is absorbed by the gastro-intestinal tract, converted to iodine ion, and actively transported into the thyroid gland. Iodide is oxidized back into T_3 and T_4 (organification, mono-iodotyrisine or di-iodotyrosine and is coupled enzymatically by thyroid peroxidases) – which are bound to proteins and stored within the thyroid gland. Production of thyroid secretions is maintained by secretion of thyroid stimulating Hormone (TSH) in the pituitary, which in turn is regulated by secretion of thyrotropin- releasing hormones (TRH) in the hypothalamus. Secretion of TSH and TRH appears to be negatively regulated by T_4 and T_3. Many believe T_3 mediates all effects of thyroid hormone and T_4 functions as prohormone. The thyroid gland releases more T_4 than T_3, the later is more potent and less protein bound. Under normal circumstances 80-85% of T_3 is produced outside the thyroid gland. The half-life of T_3 is 24 to 30 hours.

Thyroid hormones create their effects through several mechanisms. Binding of T_3 to high-affinity nuclear receptors (TRa and TRß) and subsequent activation of DNA-directed mRNA synthesis may account for the anabolic growth and development effects, plus some calorigenic effect.

Although thyroid hormone is important to many aspects of growth and function, the anaesthesiologist most often concerned with cardiovascular manifestations of the disease. Thyroid hormones affect tissue responses to sympathetic stimuli and increase the intrinsic contractile state of cardiac muscle. ß-adrenergic receptors are increased in numbers and cardiac a-adrenergic receptors are decreased by thyroid hormones.

Thyroid diseases that have anaesthetic implications include hypothyroidism, hyperthyroidism and conditions requiring thyroidectomy. The patients with well-controlled hypo- or hyperthyroidism do not present much difficulty for the anaesthetists. However, patients with uncontrolled myxoedema, or those with uncontrolled hyperthyroidism presenting as an emergency, are at considerable risk.

Hypothyroidism

The incidence of hypothyroidism in iodine-sufficient areas is five per thousand and that for subclinical form is 15 per 1000 and it depends on the level of iodine in the diet[1]. It is caused by autoimmune disease (Hashimoto's thyroiditis), thyroidectomy, radioactive iodine, antithyroid medications, iodine deficiency, or failure of the hypothalamic-pituitary axis(secondary hypothyroidism).

Clinical Features: The sign and symptoms of hypothyroidism result from depression of myocardial function, decreased spontaneous ventilation, abnormal baroreceptor function, and reduced plasma volume. These are weight gain, cold intolerance, constipation, hypoactive reflexes, dull facial expression, depression, muscle fatigue, lethargy, slow mental functions, slow movements, slow heart rate, decreased cardiac output and myocardial contractility, increased peripheral resistance, low voltage ECG (accumulation of cholesterol- rich pericardial fluid, CHF, angina, ventilatory response to decrease O_2 and increase CO_2 is blunted, anaemia, coagulopathy, hypothermia, sleep apnoea, impaired renal free water clearance, and hyponatremia, decreased GIT motility[2]. Pleural, abdominal and pericardial effusions are also common. Stress response blunted and adrenal depression may occur.

Hypoglycemia, and difficulty in intubation because of large tongue (Amyloidosis) are other potential problems in hypothyroid patients.

Diagnosis is confirmed by thyroid function tests.

Myxoedema coma results from extreme hypothyroidism and is characterized by impaired mental function, hypoventilation, hypothermia, hyponatremia, . It is more common in elderly patients and is precipitated by infection, surgery or trauma.

The hypothyroid patients should be rendered euthyroid before surgery by replacement therapy. However mild to moderate hypothyroid does not appear to be an absolute contraindication to surgery. Hypothyroid patients with symptomatic coronary artery disease may benefit from delay in thyroid surgery until after coronary artery surgery.

Thyroxine has a half life of 7 days and it will not have any effect for sometime after administration. The half life of T_3 is 1.5 days. The combinations of T_3 and T_4 is recommended in the management of preoperative myxoedamatous coma. A loading dose of T_3 or T_4 (300-500µg IV over 5-10 min initially and 100 µg IV daily of levothyroxine in patients without heart disease)[3]. The ECG must be monitored during therapy to detect myocardial ischaemia or arrhythmias. Hydrocortisone 100mg intravenously 6-8 hourly is routinely given in cases of adrenal suppression. Fluids and electrolyte therapy, ventilatory support and external warming may be required in some patients.

Regional anaesthesia is the technique of choice wherever possible. The presence of hypo metabolic state warrants the careful peri-operative cardiovascular monitoring and judicious use of anaesthetic drugs. Hypothermia should be prevented and hydrocortisone cover should be given during peri-operative period.

Hyperthyroidism

The prevalence of overt hyperthyroidism in iodine-sufficient areas is 2 per 1000 and that of sub-clinical hyperthyroidism is 6 per 1000[1]. The causes of excess hypothyroidism are Graves disease, toxic multinodular goitre, thyroiditis, TSH secreting pituitary tumours, functioning thyroid adenomas, or overdosage of thyroid replacement therapy or may occur after iodide exposure (angiographic contrast media) in patients with chronically low iodide intake (Jod-Baselow phenomenon). The classical features of hyperthyroidism are hyper active reflexes, tachycardia, increased systolic and decreased diastolic blood pressure, weight loss, heat intolerance, warm moist skin, muscle weakness, diaorrhea, nervousness, hypercalcemia, menstrual abnormalities, osteopenia, thrombocytopenia, mild anaemia, ophthalmopathy (exopthalmos) and tremors. Atrial fibrillation, mitral valve prolapse, congestive heart failure and ischaemic heart disease are the cardiovascular effects, which are important to the anaesthetist.

Thyroid function tests

There will be elevated levels of T3, T4 and decreased level of TSH.

In an attempt to prevent thyroid storm, patients should be euthyroid before surgery. This is achieved by the use of carbimazole, methimazole or propylthiouracil[4]. These drugs block the synthesis of thyroxine but take 6-8 weeks to act. ß- blockers (propanolol) are used to ameliorate the effects of thyrotoxicosis. These impair peripheral conversion of T_4 to T_3 over 1-2 weeks and decrease heart rate, heat intolerance, anxiety and tremors. Propanolol and iodides (2 – 5 drops every 8 hours) alone is more quicker than traditional approach (7-14 days versus 2-6 weeks). It shrinks the thyroid gland and treats symptoms but may not correct abnormalities in left ventricular function. Inorganic iodides inhibits iodide organification and thyroid hormone release – the Wolf-Chaikoff effect. Antithyroid drugs should be started before iodide treatment because of the possibility of worsening the thyrotoxicosis. Iopanoic acid (radio contrast agent) decreases peripheral conversion of T_4 to T_3 and releases iodine that inhibits synthesis and is useful in emergency preparation. Dexamethasone (8-12mg) is used in the management of severe thyrotoxicosis because it decreases secretion of thyroid hormone and peripheral conversion of T_4 to T_3.

Anaesthetic drugs may be affected by the hypermetabolic state of hyperthyroidism. The clearance and distribution volume of propofol have been seen to be increased.

Thyroid crises (Thyroid Storm)

Thyroid crises are seen in uncontrolled hyperthyroidism patients as a result of a trigger such as surgery, infection or trauma but are rare now due to widespread use of antithyroid drugs and beta blockers. It is characterized by hyperpyrexia, tachycardia, altered consciousness (agitation, delirium and coma) and hypotension. The differential diagnosis of thyroid crises is malignant hyperthermia and pheochromocytoma. Dantrolene sodium has successfully been used in the management of thyroid crises. Magnesium sulfate would also seem to be, theoretically, a useful drug as it reduces the incidence and severity of dysrhythmias caused by cathecholamines. The treatment consists of hydration, cooling, an esmolol infusion (50-500µg/kg titrated) or intravenous propanolol (0.5mg increments until heart rate is < 100/min), propylthiouracil (250-500mg every 6h orally or by Nasogastric tube) followed by sodium iodide (1g intravenously over 12h), and correction of any precipitating cause. Hydrocortisone 100-200mg is recommended to prevent complications from co-existing adrenal gland suppression.

Amiodarone and thyroid

Thyroid dysfunction occurs in more than 10% of patients treated with antiarrhythmic agent amiodarone. Approximately 35% of the drug in weight is iodine, and a 200mg tablet releases about 20 times the optimal daily dose of iodine. This iodine can lead to reduced synthesis of T_4 or increased synthesis. In addition, amiodarone inhibits the conversion of T_4 to T_3[5].

Patients receiving amiodarone might be considered to be in need of special attention preoperatively and may even require special attention to anaesthesia, not just because of arrhythmias that led to such therapy but also to ensure that no perioperative dysfunction or surprises occur because of unsuspected thyroid hyperfunction or hypofunction[6].

Thyroidectomy

Thyroid malignancy, obstructive

symptoms, retrosternal goiter, hyperthyroidism unresponsive to medical treatment, recurrent hyperthyroidism, and cosmetic reasons are the indications for thyroidectomy. It is also indicated if there is any evidence of superimposed lymphoma in patients with a small goiter and Hashimoto's disease.

Preoperative assessment

A thorough preoperative check up should be done in these patients to rule out any evidence of hypo- or hyperthyroidism. Evidence of other medical conditions such as cardiovascular, respiratory and associated endocrine disorder should be looked into. There can be association of pheochromocytoma in patients with medullary cancer. History of respiratory difficulties like dyspnoea, may be associated with dysphagia, specially in patients with goitre. Signs of vena cava obstruction may be present in patients with retrosternal extension. So the airway assessment should be done carefully to plan the anaesthetic management.

Investigations

The investigations include thyroid function tests, haemoglobin, white cell and platelet count, urea and electrolytes, serum calcium, chest x-ray, x-ray neck antero-posterior and lateral view (for compression and deviation of trachea) and indirect laryngoscopy for preoperative vocal cord dysfunction. It is also useful, since the need of fibreoptic laryngoscope may be required for difficult intubation cases. Although not done routinely Computerized tomography (CT) and magnetic resonance imaging (MRI) may provide excellent views of retrosternal goitre ,trachea and larynx respectively. Respiratory functions tests are of debatable value and are not routinely recommended.

Preoperative preparation and medication: All the medication which the patient is taking should be continued on the day of surgery (both antithyroid, beta blockers or replacement therapy as the case may be). Benzodiazepines are a good choice for preoperative sedation in hyperthyroid patients, but care should be taken in patients with compromised airways, where as in hypothyroid patients sedation should be avoided as they are more prone to drug induced respiratory depression. Consideration should be given to premedicating hypothyroid patients with histamine H_2 antagonists and metoclopramide because of their delayed gastric-emptying times.

Intra-operative monitoring: Cardiovascular functions (Pulse, BP), temperature, oxygen saturation, end-tidal carbon dioxide, and urine output are important parameters to be monitored intraoperatively.

Anaesthesia technique

After a careful preoperative assessment, the anaesthetist can plan the anaesthesia technique for a particular patient and discuss with the him the same. Awake fibreoptic intubation should be the method of choice if there is any concern of loss of airway during intubation in patients with inability to visualize vocal cord by indirect laryngoscopy. Difficult intubation cart (different sizes of endotracheal tube, gum elastic bougie, McCoy blade, straight blade, laryngeal mask airway (LMA), intubating fiberscope, transtracheal jet ventilation) should always be kept ready for these patients. The anaesthetist should be well versed with technique of awake fibreoptic intubation. It has been reported that 6% of tracheal intubations for thyroid surgery would be difficult. Induction of anaesthesia with sevoflurane has gained popularity in these patients, especially in anxious and patients with small goitre, where the anaesthetist believes that airway will not be lost after induction of anaesthesia.

General anaesthesia with tracheal intubation and muscle relaxant is the most popular technique. However, the cases can be done without the use of muscle relaxants under adequate depth of anaesthesia using inhalational agents. LMA has been used with spontaneous ventilation and intermittent positive pressure ventilation in thyroid surgery but this technique is contraindicated in patients with tracheal narrowing and/or deviation.

There are risks that the LMA will be displaced during surgery and laryngospasm occurs in relation to surgical manipulation.

Anaesthesia can be induced with thiopentone in both hypo or hyperthyroid patients, when no difficulty with intubation is suspected. Thiopentone is an induction agent of choice in thyrotoxic patients since it possesses some antithyroid property at high doses. Thyrotoxic patients can be chronically hypovolemic and vasodilated and care should be taken during induction of anaesthesia. Ketamine, pancuronium, indirect-acting agonists and other drugs that stimulate the sympathetic nervous system are best avoided in thyrotoxic patients where as ketamine is often recommended in patients with hypothyroidism. Hypothyroid patients are more susceptible to the hypotensive effect of anaesthetic agents because of their diminished cardiac output, blunted baroreceptor reflexes, and decreased intravascular volume. Neuromuscular blocking agents (NMBAs) should be administered with care, because thyrotoxicosis is associated with increased incidence of myopathies and myasthenia gravis.

The different tubes used are PVC, reinforced, and north-pole RAE tubes. Care should be taken that the tracheal tube should not kink during surgery, especially when it attains body temperature. After intubation, the position of tracheal tube should be checked, the tube secured and eyes are protected. Both arms are placed on sides and a 15 -25^0 head up tilt is given to

prevent venous congestion. Although it can increase the risks of venous air embolism. Slight head extension will allow the surgeon excellent access to the thyroid gland. Postoperatively the vocal cords are checked. A fibreoptic endoscope may be used to view vocal cords atraumatically. However routine postoperative visualization of the vocal cord is not warranted. Patient is extubated after return of laryngeal reflexes. The patient is carefully observed for any respiratory obstruction and cervical haematoma.

Endoscopic removal of thyroid is being practiced with good results. The advantages for this approach is minimal incision, less pain, less bleeding and early discharge.

Regional anaesthesia: Thyroidectomy can be performed under bilateral deep and superficial cervical plexus blocks in high risks patients. I have successfully done the thyroidectomy under regional anaesthesia in a case of thyroid malignancy with multiple metastasis in spine and lungs.

Postoperative complications

1. **Thyroid storm**: It manifest between 6-24 hours after surgery but can occur intra-operatively also mimicking malignant hyperthermia (MH), pheochromocytoma, or neurologic malignant syndrome. Unlike MH, however it is not associated with muscle rigidity, elevated creatine kinase or a marked degree of metabolic and respiratory acidosis.

2. Bleeding is potentially catastrophic when one is operating on the neck. I have experienced a patient developing severe bleeding leading into respiratory obstruction and hypotension minutes after the extubation. Sutures should be opened immediately to relieve pressure on the airway and hemostasis should be done at the earliest. Intubation is required immediately and it may be difficult. Although due to meticulous hemostasis, this complication is rare but should always be kept in mind.

3. **Extubation problems**: coughing, oxygen desaturation, laryngospasm, and respiratory obstruction. These can be prevented by extubation under deep anaesthesia or administration of short acting narcotics or intravenous or topical lignocaine. Respiratory obstruction may be caused by laryngeal and pharyngeal oedema as a result of venous and lymphatic obstruction by the haematoma.

4. **Recurrent Nerve damage**: It can occur due to ischaemia, contusion, traction, entrapment and actual transaction. There is greater incidence of nerve damage during surgery for thyroid cancer. Intraoperatively the damage can be prevented by careful dissection and stimulation and identification of the nerve. Unilateral vocal cord paralysis leads to glottic incompetence, hoarseness, breathlessness, ineffective cough and aspiration. Bilateral vocal cord paralysis will lead to stridor (aphonia) requiring intubation.

5. Laryngeal oedema has been seen after thyroidectomy in hypothyroidism, thyroid lymphoma, tracheal manipulation during surgery and after large haematoma.

6. **Tracheomalacia**: It results from prolonged compression of trachea (neglected goitre) and malignancy involving infiltration of trachea. It is life threatening complication and requiring re-intubation or tracheostomy. Tracheomalacia can be anticipated by absence of leak around the deflated cuff of tube.

7. **Hypocalcaemia**: It can result after excision of large multinodular goitre and unintentional parathyroidectomy after total thyroidectomy. It manifests between 24 to 96 hours post-operatively and require calcium supplementation.

8. **Delayed recovery**: Recovery from anaesthesia may be delayed in hypothyroid patients due to hypothermia, respiratory depression,, or slowed biotransformation. These patients may require prolonged mechanical ventilation.

9. **Others**: Wound complication, post operative nausea and vomiting, post-operative pain. These should be identified and tackled accordingly.

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education and research. A family doctor provides primary and continuing care to the entire family within the communities; addresses physical, psychological and social problems; and coordinates comprehensive health care services with other specialists, as needed. The practitioners in family medicine can play an important role in providing healthcare services to the suffering humanity. The General practitioner's responsibility in Medicare includes management of emergencies, treatment of problems relating to various medical and surgical specialties, care of entire family in its environment, appropriate referrals and follow up. He is the first level contact for the patients and his family. In a country with large population spread over to rural sector, the need for adequately trained, properly qualified, competent general practitioners is acutely felt. NBE is keen to encourage Family Medicine as a specialty programme since it serves the need of the society by providing comprehensive and continuing care of the patients in their own family settings.

Objectives of DNB (Family Medicine) Programme

1) The present undergraduate medical curriculum and the internship period are inadequate to turn out well trained, safe and competent medical professionals to serve the Community Needs.

2) Preventive, Promotive and Rehabilitative aspects which form an integral part of healthy living has lost its focus with most of the medical practitioners.

3) More than 80 percent of our population are either urban poor or Rural based. They are unable to get access to medical care facilities from existing hospitals.

4) To practice holistic medicine the treating physician should understand the social, cultural and economic conditions of the family.

5) Family physician needs to make optimal use of funds and Judicious selection of Investigations.

6) Family Physicians form the backbone of any health delivery system. Management of emergencies and appropriate two way referral to the specialist and back for follow up will facilitate patient care.

Which are the Institutions eligible to apply?

1) All hospitals attached to Government and Private Medical Colleges

2) All Government hospitals including General Hospitals, District hospitals, ESI, Defence, Railways, etc

3) Multispeciality hospitals already accredited by the NBE (Single speciality Hospitals not eligible)

4) Public Sector Hospitals, Corporation, Port Trust & Mission hospitals and multi speciality private Hospitals

Inspection Fee

No Inspection fee for above categories 1, 2 & 3.

For category 4, Inspection fee is Rs.10,000/- only.

What are the minimum requirements for eligibility

1. The hospital should have full time consultants with Postgraduate qualifications MD/MS or DNB or equivalent in the speciality of Internal Medicine, General Surgery, Obst & Gyn. and Pediatrics.

Full time or part time or visiting consultants can provide training in other specialities.

2. The hospital should have a minimum number of 50 beds (for 2 candidates) and 100 beds (for 4 candidates)

3. The hospital should have causality/ emergency medicine department with 24 hours service including availability of Anesthetists and Blood transfusion services.

4. The hospital should have Radiological, Imaging and Laboratory Investigation facilities viz Biochemistry, Microbiology, Pathology, etc.

5. Facilities for teaching in small groups, seminars and bed side clinics.

6. Library with standard text books and journals and access to internet.

Eligibility criteria for the Candidates

1. Any Medical Graduate with MBBS qualification, who has completed Internship and registered with MCI/State Medical Council (age limit upto 50 years).

2. Any medical graduate holding P.G. diploma qualification from Indian universities and Foreign Medical graduates who have passed screening test conducted by the NBE and Registered with MCI/State Medical Council.

3. In service candidates from Defence/ Central/State Govt. or Railways and Public sector institutions.

How to apply

1. The Institutions which are keen on starting the programme shall fill in the forms available at NBE Office or downloaded from NBE Website – Complete details should be provided about the Faculty members and availability of ancillary services.

2. The accredited institutions shall send the information about the candidates selected for Registration with NBE.

Evaluation

1. There will be no entrance test to join for the course. The Institution shall select suitable candidates with aptitude for general practice, their concern and compassion to live within the community to ensure healthy living.

2. The candidate will be evaluated for various technical skills, medical ethics and communication skill at the end of 12-18 months.

3. The candidate shall maintain a Log Book recording learning schedule management of emergencies, complications and also submit a thesis on common subject relevant to general medical practice.

4. The candidate will be awarded credit hours for attending various academic programmes/seminars/ professional conferences conducted by IMA/Professional bodies and others.

14

Review Article

Key Issues Related to the Management of Pregnant Mother with Common Disease of Thyroid & Related Recent Advances

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Introduction

Thyroid disease is relatively common in women of reproductive age group and therefore commonly in pregnancy. Disorders of thyroid hormone production and their treatment can affect fertility, maternal well being, fetal growth and development.

Fetal and neonatal thyroid disease may occur as a consequence of maternal thyroid dysfunction or independently, but in both cases the diagnosis and management can be challenging. As regards with thyroid hormone levels in pregnancy – the pregnancy is a state of thyroid hyperstimulation, therefore of changes of thyroid hormone values. Pregnancy has an effect on thyroid economy with significant changes in iodine metabolism, serum thyroid binding proteins and the development of maternal goiter especially in iodine deficient areas. Pregnancy is also accompanied by immunologic changes, mainly characterized by a shift from a T helper-1 lymphocyte to a Th2 lymphocyte state [1] Fetal brain development depends on T transport into the fetus which in turn depends on sufficient maternal iodine supply.

Common Thyroid disease during pregnancy are Hypothyroidism and Hyperthyroidism and Postpartum Thyroiditis.

Hypothyroidism in pregnancy

Hypothyroidism was reported to occur in 0.05% of pregnancies[2], however, population-screening studies have suggested a higher incidence. In a U.S. study, 49 of 2000 women who had their serum TSH levels checked between 15 and 18 weeks of gestation had levels that were elevated to 6 mU/L or greater. Of these 49 women, 58% had positive thyroid antibodies compared with an 11% rate in the group that was euthyroid [3]. In a more recent study that examined mid trimester TSH levels in pregnant women, only 75 of the 25, 215 women (0.30%) had elevated TSH levels [4]. When combined with sub clinical hypothyroidism much higher incidence (2.5%) has been reported by recent study.[1] The urge to determine the true incidence of hypothyroidism in pregnancy is driven by the knowledge that these women have increased rates of miscarriage, preeclampsia, placental abortion, growth restriction, prematurity and stillbirths and their fetuses are at risk for impaired neurologic development.

Causes of Hypothyroidism

The most common cause of hypothyroidism is iodine deficiency. One to 1.5 billion people are at risk; 500 million live in areas of overt iodine deficiency. Because the transplacental passage of maternal T 4 is necessary for fetal brain development early in the first trimester before the development of the fetal thyroid gland, lack of iodine during this time may lead to impaired neurologic development. Moreover, even when the fetal thyroid gland has developed, if there is no iodine substrate for the gland to use, then the fetus is unable to synthesize 11s own thyroid hormones. The result of severe iodine deficiency (intake of20-25 μg/dg) is endemic cretinism. These infants are characterized by severe mental retardation, deafness, muteness, and pyramidal or extrapyramidal syndromes; the most common cause of mental retardation worldwide is iodine deficiency.

Other common causes of hypothyroidism are primary thyroid failure (autoimmune), iatrogenic and congenital hypothyroidism. Diagnosis of primary thyroid failure is made by elevated TSH and low FT4 and FT3 concentrations. In two studies [3, 4] sub clinical hypothyroidism was found in over 2% of pregnancies, with apparently two-thirds of these resolving spontaneously within 10 weeks of diagnosis. [6] There is a suggestion that screening for thyroid function in early pregnancy and levothyroxin intervention therapy for maternal subclinical hypothyroidism should be considered but evidence is still awaited. [1]

Treatment of Hypothyroidism

Treatment is with thyroxine replacement and should be initiated as soon as diagnosis is made. The starting dose of thyroxinsis 0.1 mg/d to 1.15 mg/d. the dosage is adjusted every 4 weeks to keep TSH at the lower end of the normal women who are enthyroid or on thyroxine at the beginning of pregnancy should have their TSH and free T 4 levels checked every 8 weeks. T 4 requirements most likely will increase as the pregnancy progresses[7]. This increase in requirement can be secondary to the increased demand for T4 during pregnancy as well as its inadequate intestinal absorption that is caused by ferrous sulfate. Therefore ferrous sulfate and thyroxine dosages should be spaced at 4 hours apart. Some have found that thyroxine requirements in the first trimester of pregnancy increase by 50-1 00%.[8, 9]. This increased thyroxine requirement is usually sustained

throughout pregnancy. Some hypothesise that this increased requirement, even in the third trimester, may be due to increased transfer ofT4 to the fetus, increased maternal clearance, placental catabolism and maternal weight gain [10]. Others claim that many women could go through pregnancy on the same prepregnancy thyroxine dose and any increase in pregnancy is a reflection of inadequate treatment prepregnancy. [11] Roti et al.[12] and Mandel et al.[9] have recommended that thyroid function tests are performed in each trimester as mild hypothyroidism may be asymptomatic and could have potentially deleterious consequences. Using these results with appropriate reference ranges, together with maternal signs and symptoms as a guide, the dose of thyroxine can be adjusted accordingly. Following a dose adjustment, the thyroid function should be checked again in a month's time.

With maternal throxine therapy, the fetus is not at risk of thyrotoxicosis (as the placenta metabolises most of the thyroxine presented to it) and breast-feeding is safe. Pregnant women on adequate replacement ITom the start of pregnancy should expect a good obstetric outcome.

However, they are still at increased risk of postpartum thyroiditis regardless of control during pregnancy. [2]

Obstetric outcome in Hypothyroidism

Inadequate thyroxine replacement, on the other hand, can lead to maternal and fetal complications. Interestingly, women who are hypothyroid at the start of pregnancy are more at risk of preeclampsia and possibly fetal distress in labour, despite subsequent euthyroidism with treatment during pregnancy. [13,14] Hypothyroidism at term is also associated with an increased risk of pregnancy induced hypertension with the subsequent need for premature delivery, placental abruption, postpartum haemorrhage and cardiac dysfunction. [15] Increased risks of fetal distress in labour, low birth weight, stillbirths and reduced intellect in the offspring have all been reported in maternal hypothyroidism.[16] There does not appear to be an increased risk of major congenital anomalies associated with hypothyroidism. [15, 14, 17, 18] The majority of infants are healthy and are without any evidence of thyroid dysfunction. In general, the poorer the control of hypothyroidism the more at risk the pregnancy.

Maternal Hyperthyroidism

The incidence of thyrotoxicosis in pregnancy is 0.05-0.2%, with over 90% due to Graves' disease.[12,18,19] This autoimmune condition is caused by antibodies that can stimulated the TSH receptor (TSAbs) resulting in thyroid hyperactivity and glandular enlargement.

Pregnant women can tolerate mild thyrotoxicosis quite well. Weight loss despite increased food intake, tremor, anxiety, and lid lag are all characteristic of thyrotoxicosis whilst pretibial myxoedema and exophthalmos are extrathyroidal manifestations of Graves' disease. A goiter associated with hyperthyroidism can further expand in pregnancy and may cause retrodsternal obstruction resulting in enhanced anaesthetic risks.[20]

Causes of Hyperthyroidism

Graves' disease is the most common cause of hyperthyroidism during pregnancy and accounts for 95% of the case [21] other causes include gestational trophoblastic disease, noduler goiter or solitry toxic adenoma, viral thyroiditis and tumours of pituitary gland or ovary (stuma ovarii) women can also present with transient hyperthyroidism as seen in cases of hyperemesis gravidarum and gestational transient thyrotoxicity.

Treatment of Hyperthyroidism and Thyrotoxicosis

Hyperthyroidism requires a multidisciplinary management. Treatment with antithyroid drugs is a compromise between the risk of uncontrolled maternal hypothyroidism and the risk of fetal hypothyroidism [22].

Propylthiouracil (PTU) and carbimazole are very effective drugs which are commonly used. PTU is started at dosages of 100-150 mg every 8 hours (total daily dose should be 300-450 mg, depending on severity of disease) free T4 levels should be monitored monthly. The dosage should be tapered once the mother is enthyroid.

Carbimazole and propylthiouracil (PTU) inhibit thyroid hormone synthesis and are equally effective in pregnancy. The aim of treatment is to maintain the maternal serum FT4 at the upper end ofthe normal range using as Iowa dose of the drug as possible in order to minimize the sideeffects on the fetus.[23]

Both carbimazole and PTU can cross the placenta. As clearance of these drugs is very slow in the fetus, they tend to accumulate with the risk of fetal hypothyroidism and goitrogenesis. The reported incidence of goiter in neonates is 10% following in utero exposure to either drug.[24, 25] Therefore, block and replace regimens (combined carbimazole or PTU and thyroxine) have no place in pregnancy because inadequate amounts of thyroxine are transferred to the fetus to comensate for the effect of the antithyroid drug. Neither carbimazole nor PTU is teratogenic.

Overall 2% of patients taking carbimazole or PTU suffer side-effects, the most serious of which is agranulocytosis, a rapidly developing idiosyncratic phenomenon which occurs in 0.3% of patients on PTU It can also occur with high doses of carbimazole. [23] Hepatitis and vasculitis are also recognized side-effects of PTU A drug

rash or urticaria occurs in 1-5% of patients on either drug. Carbimazole, which is more widely used in the UK during pregnancy, has a'ionger half-life so patient compliance is improved with less fTequent dosing. There are fewer major toxic side effects with carbimazole and it is cheaper. [24] Women who are already stable on one drug need not switch over to the other during pregnancy.

Obstetric outcome in Thyrotoxicosis

If thyrotoxicosis is well controlled, a good obstetric outcome can be expected. There are reports of increased obstetric complications in uncontrolled thyrotoxicosis, especially in the second half of pregnancy, like preterm labour, intra-uterine death, intra-uterine growth restriction, low birth weight, pre-eclampsia, placental abruption, and maternal infection. [28, 29] Overall, there is increased perinatal and neonatal mortality associated with maternal thyrotoxicosis.

Postpartum Thyroiditis

Biochemical evidence of postpartum thyroid dysfunction has a world-wide prevalence of about 5%, usually developing 1-8 months postpartum. There is wide geographical variation in prevalence rates. Amongst the highest reported is 16.7% in Mid-Glamorgan (UK), but most of these women were asymptomatic with only biochemical evidence of the condition. About 70% of women who are positive for thyroid anti-microsomal antibodies in early pregnancy [31] and about 25% of women with type I diabetes mellitus develop postpartum thyroiditis. Women with a family history of autoimmune hypothyroidism are also at increased risk of this condition.

The recent findings have been summarized by Lao TT [32]

1. Thyroid disorders constitute the commonest group of pregestational endocrine disorders found in pregnant women.

2. In mother's taking antithyroid drugs, breast feeding is considered safe.

3. The relatively high prevalence of hypothyroidism, especially subclinical hypothyroidism, the significance of screening and treatment, and the roles of iodine insufficiency and thyroid antibodies on the outcome of pregnancy and long term neurological development of the offspring have been documented

4. In hypothyroid women, the dose of thyroxine replacement often needs to be adjusted from as early as the first trimester to maintain an adequate circulating thyroxine concentration.

5. Apart from overt hyperthyroid and hypothyroidism diagnosed before and during pregnancy, biochemical abnormalities in clinically euthyroid women can affect both obstetric outcome and long term neurological development of the child.

6. Screening for thyroid function and autoimmunity and timely and appropriate treatment, will improve pregnancy outcome.

7. The thyroid function of infants born to mothers with thyroid disorders should also be assessed as serial monitoring and treatment may be necessary.

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Post Doctoral Fellowship Courses In Sub-specialties

National Board of Examinations offers courses in post doctoral fellowships(duration is two years) in highly specialized areas to provide opportunities with in the country for development of Technical expert manpower at the selected centers of excellence.

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- Peripheral Vascular Surgery
- Spinal Surgery
- Paediatric Orthopedics

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- Paediatric Urology
- Advanced Endoscopic & Laparoscopic Urology
- Organ Transplantation
- Human Genetics
- Laboratory medicine
- Diabetology
- Rheumatology
- Haematology

Review Article

Role of Radiotherapy in Cancers of Thyroid

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Introduction

For many years the line of management of thyroid carcinomas has been controversial. However, inspite of these controversies a consensus has emerged in the line of management and treatment of this entity in recent years. For treatment purposes the thyroid cancers are divided into Differentiated cancers of thyroid and other group comprised by rest of malignancies seen in this organ mainly depending upon the histopathological characteristics and their natural history & clinical behavior.

The treatment modalities for cancer Thyroid include surgery, thyroid hormone therapy, Radioactive Iodine therapy (RAI-I^{131}, External Beam Radiation Therapy (EBRT) and Chemotherapy. The management of Paediatric thyroid cancers has been described by Herzog B [1]. In majority of thyroid cancers specially in differentiated thyroid cancers surgery followed by radioactive Iodine 131(RAI) and suppressive therapy of thyroid hormones has been accepted as the ideal mode of treatment [2, 3]. Except for the conditions that prohibit surgery, the surgical treatment is the starting point of treatment and management.

The 10 year survival of differentiated thyroid cancers which have been optimally managed remains higher than 80-90% [4, 5, 6, 7, 8]. The poor outcome to the treatment in thyroid cancer is predicted depending upon various factors viz., presence of distant metastasis at presentation, age greater than 50 years, tumour size, nodal involvement, histopathological type, marked vascular invasion, high histologic grade etc.

External beam radiotherapy in cancer Thyroid

The vast majority of thyroid cancers receive Radioactive iodine therapy I^{131} as the main form of radiation treatment. External Beam Radio therapy (EBRT) has a modest role in this entity. Thyroid cancers are moderately radiosensitive except for the rare varieties like Medullary carcinoma, Anaplastic carcinoma thyroid and Lymphomas. The response to radiotherapy is usually slow and regression is seen to continue upto a year after radiotherapy. For residual, recurrent and nodal involvement, EBRT has been suggested to play an important role in preventing distant metastasis[9,10]. However, radio-resistance of thyroid cells and lack of benefit of EBRT have also been reported by Samaan et al [11].

Conventional radiation-therapy may prove to be detrimental to the success of radioactive iodine therapy in thyroid cancer and should not precede the therapeutic efforts with RAI. The role of EBRT in thyroid cancers is now well defined.

It is mainly indicated in Anaplastic carcinoma, Medullary cancer thyroid, Lymphomas and the differentiated thyroid cancer which are non functional or which do not take up radioactive iodine or lack the ability to concentrate radioactive iodine. The main indications of EBRT can be summarised as in the following table:

Indication of EBRT in Thyroid cancer

1. Preoperative in borderline inoperable case
2. Large bulky, nonfunctional thyroid cancers
3. Inoperable thyroid cancers
4. P.O. Residual or Relapsed thyroid cancer after max. RAI therapy
5. Macroscopic or Microscopic residual non functional differentiated cancer thyroid
6. P.O or as Primary radical treatment of Anaplastic cancer, Medullary cancer, or lymphoma
7. Palliative in Stage IV disease with or without CCT or RAI
8. Palliative in Bone mets, SVCS, Brain, Hepatic Metastasis with or without RAI.

In differentiated cancer Thyroid, EBRT is indicated only when there is no concentration of RAI or the tumour is unresponsive to RAI I^{131} therapy. Medullary and Anaplastic cancers do not generally concentrate I^{131}. Post-operative EBRT is indicated in these type of thyroid cancers as the incidence of lymph node involvement and spread to adjacent organs and distant organs is quiet common. Even if optimal surgery has been done, there are high chances of loco-regional failure or distant metastasis. A dose of 50 Gy to 60Gy is usually required for achieving good local regional control. Thus EBRT is mainly indicated in Anaplastic cancer thyroid, Medullary cancer thyroid, Lymphoma of thyroid and

in non functional differentiated cancers of thyroid.

EBRT in differentiated cancer Thyroid

Post-operative adjuvant EBRT is effective in differentiated non functional thyroid cancers However, it is indicated for poor prognostic group of these patients. Indications for post operative EBRT could be residual disease microscopic/macroscopic positive, advance age at diagnosis, extrathyroidal invasion, high grade cancer, retrosternal thyroid extension, high number of lymph node involvement.

Sheline etal in 1966, reported the use of adjuvant P.O EBRT in thyroid cancers and their study suggested a positive role of EBRT in controlling the residual or gross disease in differentiated thyroid cancers although the dose of EBRT was suboptimal 50 Gy, by present standards.[12]

Tubiana & colleagues also advocated post operative EBRT for patients with microscopic or macroscopic residual disease. Since 1956,their practice has been to deliver 50Gy/25Fr/5weeks to the neck with boost of 5 to 10 Gy to residual disease with cobalt-60 teletherapy. The spinal cord dose limited to 42 Gy. They observed a 5 yr. survival rate of 94% (62 of 66) for patients with complete surgery and 78% (76 of 97) patients with incomplete surgery. [13]

Farahate and coworkers evaluated the role of adjuvant EBRT in 238 patients with differentiated thyroid cancers after primary optimal treatment of surgery , RAI therapy and TSH suppressive therapy with thyroid hormones. Analysis of 99 patients showed that adjuvant EBRT improves the recurrence free survival in patients older than 40 years with invasive papillary thyroid cancer and lymph node involvement.[14]

At Princess Margaret Hospital the prescription of irradiation is 40 Gy given in 15 fractions in 3 weeks for microscopic disease. A boost of 10 Gy in 5 fractions in 1 week delivered to areas of gross tumour [15].

Pre operative EBRT can be used for borderline inoperable differentiated thyroid cancers to make them operable or should be approached with curative intent specially in the patients where surgery is contraindicated because of co-morbid conditions.

Inoperable, bulky disease should be approached with curative intent. Inoperable, papillary thyroid cancer treated with local EBRT has regressed markedly or disappeared with patient surviving as long as 25 years. The treatment field shall encompass the entire thyroid tumour, neck and superior mediastinum. A tumour dose of 65-70 Gy in 7-8 weeks is recommended.[16]

The tumour volume for post operative EBRT should include the thyroid bed with 2-3 cm. margin around the primary and draining lymph nodes. Aim of EBRT should be homogenous dose distribution and with due care of the spinal cord tolerance as it is very close to the skin surface in the region of thyroid. A direct field with electron beam with 12-16 MeV energy is preferable, though a multifield wedge pair set up with cobalt-60 can be other option**.** The recent techniques of 3-D Conformal Radiotherapy (CRT) and Intensity modulated Radiation therapy (IMRT) may help in achieving better results with minimum possible toxicity and late complications otherwise reported by conventional EBRT in these malignancies.

EBRT in medullary cancer Thyroid

The role and effectiveness of EBRT in medullary ca. thyroid is still controversial, but it can be used in its treatment as post operative adjuvant for any microscopic residual or gross residual disease.[17,18,19,20,21,22] The radiosenstivity of this type of thyroid cancer falls between that of differentiated and anaplastic cancers. The recommended dose is 60 Gy in 6-7 weeks. In in-operable disease, the dose required might be higher 65-70 Gy and shrinking field may be appropriate to decrease the acute and late complications or recent techniques of 3-D CRT or IMRT may be the answer for delivering high precise dose required .

The results of treatment of Medullary thyroid carcinomas with EBRT or CCT are disappointing.[23,24] EBRT leads to increased toxicity and moreover the local recurrence rate has also not shown any improvement. A study reported from France of 59 patients reported local recurrence within the radiotherapy field in 30% of patients[25]. In medullary carcinoma thyroid , a modified mantle from the level of chin to the 4th Dorsal vertebra and laterally covering the whole extent of the neck should be used with special attention to the radiation dose to spinal cord.

EBRT in anaplastic Thyroid cancer

It is one of the most aggressive cancers of thyroid and lacks the ability to concentrate radioactive I^{131}. A distinct pathological type of this variety small cell anaplastic carcinoma of thyroid (Insular carcinoma) has shown the ability to concentrate radioactive I^{131}. Aggressive local therapy is indicated in all patients who can tolerate it and in whom it is technically feasible.

EBRT has been used in its treatment as primary modality with or without surgery and with or without CCT. EBRT has also been used with limited success to treat Anaplastic thyroid carcinoma. It is considered to be not much sensitive to radiotherapy.

One study from London reported 10 of

17 patients with an objective response to accelerated radiotherapy (3 CR and 7 PR) but the toxicity was considerable[26].

In mid 1980's Kim & Leeper reported improved response to a combination of EBRT and relative low dose doxorubicin as an apparent synergistic agent achieving response in 84% of 19 patients but with a median survival of 12 months only.[27]

Early diagnosis with aggressive surgical therapy supplemented by EBRT and doxorubicin based CCT is the most appropriate treatment for patients with Anaplastic thyroid cancer.

Tallroth and associates have reported the Swedish experience of anaplastic giant cell cancer at the Radiumhemmet using three-drug combination of bleomycin, 5-flourouracil & cyclophosphamide with conventional radiation therapy and accelerated radiotherapy with equivocal results.[28]

EBRT in Thyroid Lymphoma

The optimal treatment of thyroid lymphoma has evolved with the success of combination chemotherapy used in non-Hodgkin's Lymphoma. Role of surgery in the thyroid lymphoma is just to obtain adequate tissue for diagnosis by large needle or core needles biopsy. The primary treatment should be EBRT plus combination chemotherapy.[29]

Some people still advocate surgery for the primary disease plus EBRT especially in patients where there is no evidence of extra-thyroidal disease.[30] Any extension of the disease by direct extension or lymph node involvement should be considered as systemic disease.

The dose of EBRT in lymphomas is from 30 – 45 Gy over 3 to 4 weeks with CCT.For very bulky disease higher dose or boost radiotherapy can be considered.

EBRT in metastatic cancer Thyroid

In advanced disease with metastasis, EBRT has an important and established role for symptom control and achieving good palliation. EBRT with or without RAI and combination chemotherapy has been utilized for the purpose in different judicious combinations. A fractionated dose of 30-45 Gy over 2-4 weeks is justified in view of expected long term survival in advanced cancer thyroid. An accelerated high dose palliative EBRT can also be prescribed in individual situations. Palliative EBRT is used for bone, brain, hepatic and soft tissue metastases impending pathological fractures, neurological complications and in cases of SVCS .

EBRT in secondary Thyroid malignancies

The incidence of involvement of thyroid gland by secondary metastasis from other sites is fewer than 1% in clinical situation and its incidence in various autopsy based series ranges from 2-25% . The most common malignancies, which metastasize to thyroid gland, are cancer of lung and breast. Each accounts for about 25% of them[31].

Melanoma, renal cell carcinoma and gastrointestinal malignancies account for approximately 10%. EBRT can be utilized in some of these patients to palliate the local symptoms in individual situation.

Future directions in the management of cancer Thyroid

The recent explosion of knowledge regarding the molecular and cellular pathogenesis of cancer has led to the development of range of targeted therapies and these are being evaluated in clinical practice of various cancers including thyroid cancers. These hold promise and can be advocated on experimental basis in the patients with life threatening disease unresponsive to the available treatment modalities.Targeted therapies can be Oncogene inhibitor(tyrosine kinase inhibitors ,RAS,RAF and MEK kinase), Modulators of growth or apoptosis (Cox inhibitors, retinoids), Angiogenesis(VEGF) inhibitors, Immunomodulators & gene therapy[32]. Long term high dose octreotide treatment in patients of medullary carcinoma thyroid has shown beneficial effects in tumour bearing somatotastin receptors.[33]

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Special placement in hospitals for the DNB candidates who fail repeatedly

As a part of the student support services for DNB candidates, the Board has identified certain hospitals in major cities, where candidates can be placed as observer for participation in academic activities. The candidates who wish to utilize these facilities should sent their request addressed to the Executive Director, National Board of Examinations.

Wireless Capsule Endoscopy

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History

Iddan G, Meron G, Glukhovsky A and Swain P published a short paper describing miniaturised camera capsule form of gastrointestinal endoscopy in May 2000.[1] This was approved by FDA on 1st August 2001. In October 2003, FDA approved its use in children aged 10-18 years. This novel marvel is available in nearly thirty three countries worldwide including India.

Why need for this device?

Small bowel endoscopy is limited by its length and also by distances from accessible orifices. Prior to the development of capsule endoscopy, the non surgical evaluation of patients with obscure gastrointestinal bleeding was limited to push enteroscopy, Sonde enteroscopy, small bowel follow through X-ray series, small bowel MR enteroclysis, technetium 99m labelled red blood cell scan and angiography. Twenty seven percent of patients with obscure GI bleeding have been shown to have small bowel lesions.[2] Wireless capsule endoscopy is a boon for detecting pathology of small bowel that is difficult by radiology. The data about usefulness of this device in successfully locating pathologies are encouraging.[2] however, at present the exact role is yet to be established.

The capsule endoscopy system [3,4]

It has three components:

(1) The wireless capsule endoscope – disposable biocompatible plastic capsule weighing 3.7gm and measuring 26mm in length with 11mm diameter. The capsule is disposable, resistant to gut digestion and is propelled by peristalsis. The contents include complimentary metal oxide silicon (CMOS) chip camera, a lens, 4 white light emitting diode (LED) illumination sources, 2 silver oxide batteries and a UHF band radio telemetry transmitter. Image features include a 140 degrees field of view, 1:8 magnification, 1 to 30mm depth of view and a minimum size of detection of about 0.1mm. The capsule is in ready to use pack and is activated on removal from a magnetic holder. The time elapsed between capsule activation and ingestion should not exceed 1 minute. The activated capsule has image accrual and transmission at frequency of 2 frames per second until the battery expires after 6-8

2) Receiver/recorder unit – patients wear an antenna array consisting of 8 leads (just similar to 12 leads of ECG) that are connected by wires to the recording unit. Patient also wears shoulder supported belt pack holding a power supply of 5 nickel 1.2V batteries and a 305GB hard drive recording device. The antenna array and battery pack can be worn under normal clothing. The patient should be instructed to never remove the belt during the examination.

(3) Computer workstation – Data are downloaded from belt pack recorder to computer workstation over 2-3 hours where it becomes available to physician as a digital video. The software allows the viewer to watch video and to capture individual frames as video clips. Enhanced software's are developed that allow capsule localisation in correlation to video images and highlighting the images from suspected bleeding sites.

The newly developed capsule that acquires images from both ends shows high correlation with the endoscopic views for oesophageal disorders.[5]

The procedure

Patients are instructed overnight fasting and no formal bowel preparation is mandatory. The physician may consider prescribing simethicone to enhance viewing. Water intake can begin 2 hours

after capsule swallow and food ingestion after 4 hours. 7-8 hours after swallow, the examination can be considered complete however transit time may vary for hypo-hyper motility states and patient should be instructed of the repeat procedure if necessary. Patient can be ambulatory but should avoid exercise during these 7-8 hours and also should check a blinking light on the belt pack for confirming signal reception. Electromagnetic fields can interfere with signal perception and MRI should not be performed while capsule is still in-situ however, patient can use cellular phones, faxes and computers.

Indications

(1) Obscure gastrointestinal bleeding (after negative upper/lower endoscopy push enteroscopy and small bowel radiography) is the most important indication to wireless capsule endoscopy.

(2) Surveillance in patients with poylposis syndromes.

(3) Chronic gastrointestinal blood loss.

(4) Recurrent bleeding in patients with negative results of endoscopic examinations

(5) Evaluation of malabsorptive, inflammatory or infiltrative conditions that are incompletely characterised by standard studies.

(6) Small bowel transplantation

(7) Chronic diarrhoea of unknown cause.

Studies thus far indicate that it is more sensitive than other non-surgical procedures for diagnosing the etiology of obscure GI bleeding. Lewis B and Swain P [6] in a blinded analysis for evaluation of patients with suspected small intestinal bleeding found capsule endoscopy to be superior to enteroscopy in locating the bleeding source and also patients preferred capsule endoscopy.

Contraindications

Intestinal obstruction is the absolute contraindication.

(1) Known or suspected gastrointestinal obstruction/ pseudoobstruction and strictures or fistulas.

(2) Cardiac pacemakers or implanted electromechanical devices.

(3) Swallowing disorders

(4) Zenkers diverticulum

A recent case report documents 3hour loss of capsule recording in a patient with an abdominal pacemaker while the capsule was in proximity to the pulse generator, but no adverse pacing events were noted.[7, 8] Safety of the device is not established in pregnancy, children < 10 years age and patients with significant gastrointestinal diverticular disease.

Drawbacks

(1) No therapeutic potential.

(2) Difficulty in identifying precise location of pathology.

(3) Expensive and insurance company reimbursement is poor.

The wireless capsule views the bowel in a functioning semi collapsed state and so part of the bowel mucosa may not be visualised even if the capsule passed through it. There is a learning curve to analyse the villus based capsule images, which are very different from the standard endoscopic images. Manufacturers are developing technology for identifying the anatomy, sampling the luminal contents, biopsy of the mucosa, controlling the movement of the device and even disintegrable capsule (for use in patients with obstruction).

Complications

Can obstruct the bowel at site of stricture or stenosis or get lodged in the diverticula. Endoscopic retrieval of entrapped capsules has been required from the cricopharyngeus [9] and an appendicular stump[10]. Surgical retrieval has been required for impaction at the stricture site in small bowel.[11]

A capsule endoscope which auto disintegrates after 100 hours (if not already expelled) has been designed for patients with stenoses or strictures.

The current status

Hartmann D, Schmidt H et al [12] in a prospective study of 47 patients concluded that capsule endoscopy showed source of bleeding in 74.4% of all patients and that the method is more effective in patients with ongoing bleeding. The also report overall sensitivity, specificity, and positive and negative predictive values of 95%, 75%, 95% and 86% respectively. Golder S K, Schreyer A G et al [13] in a study of 36 patients concluded that wireless capsule endoscopy revealed significant more inflammatory lesions in the proximal and middle part of the small bowel in comparison to MR enteroclysis where as in patients with obscure GI bleeding wireless capsule endoscopy was superior. Maieron A, Hubner D et al [14] in a multicenter retrospective evaluation of capsule endoscopy in 191 patients concluded that visualisation of entire small bowel was adequate in 78.4% examinations, relevant pathological findings were identified in 56.2% of patients with obscure GI bleeding and the most common finding was angiodysplasia [39.7%]. Sriram P V, Rao G V and Reddy D N [15] in a study of 24 patients from India also explain that capsule endoscopy has a high diagnostic yield for small bowel mucosal disease (like tuberculosis, Crohn's disease) and

is very limited in use for undiagnosed abdominal pain. Many studies done show that although the diagnostic yield is high, the proportion of patients in whom the management changes is less.

The future

Prolonging the battery life can help for visualising the colon taking in mind the need for colonic preparation and delay in cecal transit. Insertion devices are designed to allow for capsule placement in the duodenum or stomach for cases of pyloric stenosis or esophageal structuring.[8, 16] Capsules have been sewn into the wall of gastrointestinal tract for prolonged viewing. Magnetic devices are designed to allow retrieval of capsules lodged in intestine.[8, 16] Smaller devices intended for paediatric age groups are also under development.

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Objective Structured Clinical Examination (OSCE)

The assessment of Post-graduate medical students has always been a cause of concern for medical teachers. As a consequence of this concern, the Board had tried and tested different modalities of assessments. In order to overcome the limitations in the traditional methods of clinical evaluation, the Board has introduced Objective Structure Clinical Examination (OSCE) in the disciplines of ENT, Ophthalmology & Pediatrics. OSCE in the specialties of Orthopedics, Anesthesia, Psychiatry, Dermatology would be soon introduced in DNB examinations.

Multifocal IOLs

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The gold standard for visual rehabilitation in the psuedophakic patient is to precisely reproduce the optical performance of the prepresbyopic crystalline lens while establishing emmetropia. Till date, cataract surgeons have made tremendous strides in establishing emmetopia post-operatively, however they have fallen short in duplicating the optical performance of the pre-presbyopic crystalline lens. Efforts have been made to achieve pseudo-accommodation by targeting small amounts of postoperative myopia or by the monocular vision, also by implanting various bifocal and multifocal intraocular lenses 1-4. Multifocal lenses have provided this pseudo-accommodation with varying degree of success.

Multifocal lens is a zonal progressive lens because it uses concentric zones of progressive aspheric surfaces to provide a progressive power distribution not unlike a progressive reading spectacle design.

Functioning of a multifocal lens

The Multifocal IOLs work on the refractive multifocal technology, which offers patients a continuous range of focus through distance, intermediate and near vision, thereby increasing the amplitude of functional vision. There are few manufacturers of multifocal IOLs. AMO ARRAY is most widely used. India has also started manufacturing acrylic foldable multifocal lenses. We have tried them with excellent results.

ARRAY Multifocal	PREZIOL (conta care)
1. Multipiece	Single piece
2. Silicone optic with PMMA haptics	Acrylic
3. Zones – 5	Zones – 3
4. Distant dominant – 1, 3 & 5	Distance – 1
5. Near dominant – 2 & 4	Near – 2 & Intermediate – 3

Pre-operative evaluation

1. Detail anterior and posterior segment examination under full mydriasis.

2. Accurate Keratometry and Biometry by operating surgeon himself.

3. SRK-II / SRK – T Formula for IOL calculation.

4. Pupil size should be more than 2.5 mm.

5. Astigmatism should be less than 1.0 D

6. Proper counseling is a must.

1. Selecting the right patients

A. Physical factors

- **Pathology**

Patients should be free from any pathology that could potentially affect visual outcome. Poor macular function may inhibit the benefits of multifocal. A patient's potential best-corrected visual acuity should be 20/40 or better at distance and at near. Patients with best-corrected visual acuity worse than 20/80 certainly won't be able to appreciate the increased visual function afforded by the lens.

- **High astigmatism**

Patients should have 1.5 D or less of astigmatism. More cylinder than that reduces near visual function. It is permissible to make the limit by surgically reducing the astigmatism; patients do best if you get cylinder to 1 D or less.

- **High ametropia**

Patients with abnormally long or short eyes are not ideal candidates due to more inaccuracy in IOL power calculations. Patients with a great deal of anisometropia are also sub-optimal candidates.

- **Small pupils**

Patients with pupils smaller that 2.5 mm are not good candidates because the central 1.5 mm of the lens is distant dominant; however, a surgical or post-op laser sphincterotomy can correct this.

B. Psychological factors

- It helps if the patient is practically eager to minimize the use of glasses. These patients are more willing to put up with unwanted visual tradeoffs that sometimes occur with this lens, including glare, halos and reduced contrast sensitivity in low contrast levels.

- Patients with flexible, easygoing personality have the best success with multifocal IOLs. Patients who work in demanding occupations or have demanding life styles are usually not the best candidates. It is also not advisable to recommend the lens for professional

drivers or for patients who frequently drive at night.

2. Thorough counseling of patients

The next step is that the doctors must personally counsel the patients to whom they offer the lens rather than leaving this task to their staff.

- The foremost goal of counseling is to ensure that the patient has reasonable expectations for the outcome. For this make the patient aware that he will not be able to "throw away his glasses" after the procedure. This happens only about 40 percent of the time. More commonly, the typical patient achieves excellent vision at distance and good vision over a range of intermediate and near distances. It is often possible for the patient to go grocery shopping or read a menu without ever needing glasses. However, for long periods of reading or craftwork, glasses will still be more comfortable.

- Also it is advisable to tell the patients that there is some risk involved with these lenses. As with refractive surgery, not all patients respond favorably to the vision they receive with the lens.

3. Careful calculation of IOL power

A very careful IOL power calculation is the final key to success with this lens. With monofocal lenses, some surgeons leave the calculations and selection up to their surgical and clinical staff. But we recommend not doing this with multifocal lenses; instead the doctor should be involved in the calculation of IOL power.

- Firstly, Biometry and Keratometry on each patient has to be carefully reviewed and while doing so pay close attention to technician training and proper calibration of the instruments. If your practice is large and has multiple sets of instruments, make sure your patients are measured on just one of the instruments.

- Use a third generation IOL power formula that's based on theoretical optics to do the IOL calculation. Programs such as the SRT, Holladay and Hoffer Q, provide more accurate results than the old formulas.

- Before you begin implanting the multifocal, establish a personalized surgeon constant. This consists of the A-constant, anterior chamber depth and/ or surgeon factor.

From our clinical studies it has been known that for most patients, its best to err on the side of very low hyperopia, preferably +0.1 and +0.5 D. We have found that slightly hyperopic patients tend to be more satisfied than those who are slightly myopic. This is probably related to their visual capabilities and unwanted visual problems such as halos and night glare that slightly myopic patients might experience under scotopic conditions with point sources of light. This may very however depending on the visual requirements of the patient's occupation or vocation.

It is also important to remember that best results occur with the multifocals when the patient has binocular vision with good stereopsis. Also two multifocal lenses are better than one.

Although this lens requires no change in surgical technique, it is important to have an intact capsular bag and secure placement of the IOL within the bag. We have the best results with a 3 to 3.5 mm incision and a 5 mm to 5.5 mm capsulorthexis.

The multifocal is not for every patient. Firstly, it is not for patients whose one eye is already implanted with monofocal lens. Along with this in mind it is also important to note that when the selection of patients is done properly, counseled appropriately and special attention to the IOL power calculation is paid, the results can truly be rewarding.

Surgical steps (important points)

1. Only Phaco surgeons should attempt.
2. Astigmatically neutral 2.8 – 3.0 mm clear corneal temporal incision.
3. 5.0 – 5.5 mm capsulorhexis.
4. Avoid multifocal in extended rhexis and PC rent.
5. Avoid putting in sulcus.

Dealing with pre-existing astigmatism

It has been realized that, spectacle free vision is nearly achieved by multifocal lenses, but the concern is pre-operative astigmatism. This remains the final borderline to be crossed when you put in a multifocal lens to give patient a spectacle free world. It is agreed that the temporal clear corneal incision is not be changed in any case and if there is an eye that does not have preoperative astigmatism, the temporal clear corneal incision uni-planar remains astigmatically neutral. Then, there is no need for further treatment. If the astigmatism is more than 1.5 to 2 D, then limbal relaxing incisions are the only choice to treat it.

Contradications

Ocular and systemic diseases (loss of contrast sensitivity)

1. Foveal impairment e.g. maculopathy, diabetic retinopathy etc.
2. Glaucomatous optic neuropathy and other ON anomalies.
3. Corneal disorders (dystrophy, degenerations, scar, dry eye)
4. Amblyopia.
5. Vitreous opacities.
6. Multiple slerosis, Pakinson's diabetes.

Other conditions

1. Astigmatism >1 D
2. Pupil diameter < 2mm
3. Certain professionals (night drivers, painters etc)
4. Very old, debilitated persons.
5. Patients with unrealistic expectations.

Post operative problems faced by the patient

1. Problem of Glare and Halos: During night driving, if patient complains of it, then very diluted Pilocarpine 0.25% to 0.125% put in the evening will solve the problem.

2. Adjusting for New Vision: Initially patients may have some problem in adjusting for new vision just as for progressive spectacles but with time patient is comfortable, proper counseling is also a must.

3. PCO: If meticulous cortical clean up is done chances of PCO are very less with these materials even if it occurs than a Nd:YAG posterior capsulotomy of at least 2.5mm is done after careful retinal check up,

4. IOL Exchange: In very rare circumstances, if a patient is extremely dissatisfied with glare and halos, then IOL exchange with monofocals is the only choice.

In conclusion the key to any refractive surgery is careful patient selection, meticulous pre-operative work and perfect Phaco surgery. These together can give remarkably superior results and contented patients.

Conclusion

The multifocal IOL offers patients sufficient functional vision to enable them to perform common daily tasks comfortably. Compared with monofocal subjects, multifocal IOL patients expressed higher overall satisfaction with their ability to see without spectacles.

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National Board of Examinations is introducing Prof. V G Appukutty Gold Medal for best DNB candidate in Anesthesia

Late Prof. V G Appukutty was born in a middle class family on 15th June 1932. He did his under graduate degree MBBS from Govt. Stanley medical College, Madras and qualified in 1958. He completed his D.A. in 1962 and passed his M.D. in Anesthesia in 1969 from Madras Medical College. Dr V G Appukutty served the Govt as Tutor and as Asst. Professor of Anesthesia in various medical colleges from 1959 to 1973. From the beginning of his carrier as an anesthesiologist his focus was on the Pediatrics speciality and particular attention on the Neonatal Anesthesia. During his service period as Prof. and Head of Pediatric Anesthesia and Chief Anesthetist of the Institute of Child Health and Hospital for Children Chennai, from 1973 to 1990, he trained many young anesthetists in the Speciality. He was popular as pediatric anesthetists who initiated and perfected for the first time in those years, Induced Hypo- tension in children and Spinal Anesthesia in Neonates in India. He retired as Professor and Head of the Department of Anesthesiology Madras Medical College and as Chief Anesthetist Govt. General Hospital Madras in the year 1990.

He was Member Editorial Board, Indian Journal of Anesthesia; Member Editorial Board Journal of Anesthesiology and Clinical Pharmacology; Trustee, Vision Research and Child Trust Research Foundations Madras '87; Hony. Director, The Child Trust Hospital Madras 1990-1992; President, Indian Society of Anesthesiologists 1990; Received the prestigious "Life Time Achievement" award posthumously by the Indian Society of Anesthesiologists 2000; Prof. V G Appukutty delivered in the Indian Society of Anesthetists prestigious 'Dr Venkat Rao' oration in 1986. He has delivered more than 100 scientific papers and lectures. He was one of the first anesthetists in the country to start induced hypotension in children, anesthesia for scoliosis surgery and spinal anesthesia in neonates in India. He was the founder Managing Trustee of Anesthesia Foundation started to create public awareness about anesthesia, to organized CME Programmes for the benefit of young trainees, private practitioners and to conduct Memorial Orations to remember the past teachers.

Primary Cemented Total Hip Arthroplasty -An Indian Experience

Analysis of long-term results of any operative procedure is important for the establishment of the outcome of the procedure. This outcome then serves as a basis for comparison of the results of newer procedures and of non-operative treatment. Because the rates of survival of the implant and the outcomes associated with the various designs and procedure for total hip arthroplasty have changed over time, the long term follow up of series of patients is important to determine the durability and the functions of implant over time.

In the current study, a series of patients in whom Charnley total hip arthroplasty with cement had been performed were followed up for a minimum period of 5 years with a mean of seven years. The purpose of the study was to establish the long term durability of total hip replacement with cement using mechanically sound prosthetic design and a hand packing technique for application of cement. We believe a longer follow up with a large number of patients is required as a basis for comparison of outcomes of newer devices and techniques of total hip replacement.

Materials and methods

Between years 1996 to 1999, forty-seven patients had fifty total hip replacements at Sassoon General Hospital, Pune. There were forty men and ten women in this series. The average age of patients at the time of index arthroplasty was sixty-five years (range fifty to eighty years). The pre-operative diagnosis was osteonecrosis of head of femur in 39 (78%) cases, rheumatoid arthritis in 5 (10%) cases, ankylosing spondylitis in 4 (8%) cases, post-traumatic arthritis of hip in one (2%) case and osteoarthritis in one (2%) case. The arthroplasties were equally distributed between left and right hips. The Harris Hip Score was calculated in each case preoperatively. It indicates function of the hip joint. The maximum score is of 100 points. Points are given for pain, functional capacity, range of movement and absence of deformity. More the score better the function of the hip. This score was compared with the postoperative score to find the improvement after arthroplasty. The indication for the surgery was pain. All patients underwent total hip replacement only after conservative line of management in the form of analgesic drugs, weight reduction, use of support for walking failed to relieve pain. The Charnley hip prosthesis was used in all patients. A stainless steel stem with head diameter of 22 millimeter and an acetabular cup made of ultrahigh molecular weight polyethylene with 22 millimeter inner diameter and varying outer diameter were inserted with polymethyl methacrylate radio-opaque bone cement.

All procedures were performed using posterolateral approach to the hip in lateral position without doing osteotomy of greater trochanter. After splitting the fibres of gluteus maximus the gluteus medius is retracted to expose short external rotator muscles of the hip. These are divided close to their insertion and an inverted T shaped incision is made on the joint capsule. Hip is dislocated and femoral neck is osteotomised with oscillating power saw. Retracting the osteotomised neck anteriorly exposes acetabulum. Exposed acetabulum is reamed using reamers of increasing size. Cement fixation holes are drilled in the acetabulum followed by saline irrigation and roller gauze packing. Femoral canal is gradually reamed with the rasps. Trial prosthesis is used to ensure fit. Trial reduction gives idea about the stability and range of movement. Acetabulum followed by femur is prepared for insertion of components using manual cementing technique. After reduction range of motion and stability are checked. Short external rotators are reattached to femur with drill holes. Closure is carried out over the drain. Postoperatively intravenous antibiotics were given for one day and drain was removed after fortyeight hours. Aspirin was used as prophylaxis for deep vein thrombosis. Average duration of the surgery was two hours and average blood loss was 400ml.

Postoperative protocol was carried out as per the recommendations of Internal Publication No.27, Nov.1970 (John Charnley Writhington Hospital). The limb is kept in abduction over a pilow. The breathing exercises and static exercises of calves, quadriceps and gluteal muscles are taught to patients preoperatively and carried out from the first day. Patient stands out of bed twice daily from the second postoperative day.

Patients walk with the help of walker from third postoperative day. Range of motion exercises – adduction, abduction, flexion are taught after 3 days. The patient is discharged after complete rehabilitation. At the time of discharge radiograph of the hip –anteroposterior and lateral views are taken. Patient is followed monthly for three months, three monthly for a year and six monthly thereafter. At each follow-up visit patient is examined clinically to calculate Harris Hip Score and radio logically to find out aseptic loosening.

Radiographic evaluation

Observations were based on anterioposterior radiographs of pelvis and lateral radiograph of the operated hip with the femur that has been made early postoperatively and at the latest follow up evaluation for all patients. In addition interval radiographs were used to determine the time that various radiographic changes had occurred. Loosening of the femoral component was defined according to criteria of Harris et al. It included subseidence of femoral component, fracture of cement or stem and presence of radioleucent line of greater than two millimeter that had not been seen on the immediate postoperative radiograph at the interface of prosthesis and cement. Subsidence of femoral component was determined using the Loudon and Charnley method. The distance between tip of the trochanter and the tip of the stem was measured and compared with earlier radiographs to find out subsidence. Any bone loss in the periacetabular region that appeared cystic was recorded, as was any localized loss of endosteal cortex of femur. The position of the stem (varus, valgus or neutral) was recorded on each radiograph. Heterotopic bone when present was graded according to classification of Brooker et al. Radioleucent lines between cement and bone, as seen on anterioposterior radiograph were recorded on the basis of the three acetebular zones described by Delee and Charnley and the seven femoral zones described by Gruen et al.

Results

At the follow up evaluation, the average age of the patient was seventy years (range fifty-seven to eighty-eight years). All patients were alive till latest follow up. The minimum follow up period was 5 years and the mean follow up was 7 years. A deep infection had developed in one (2%) of the fifty hips and two (4%) hips had dislocated at the time of latest follow up. The patient with deep infection underwent excision arthoplasty of hip and was excluded from the follow-up. None of the patients had undergone revision surgery. Before the index arthroplasty all patients had pain. All patients had excellent relief of pain after the total hip replacement and this was well maintained during the course of the follow up. Only two (4%) patients have moderate pain at the follow up. Preoperatively 45 (90%) patients used support for walking. Of these thirty (60%) patients used stick and fifteen (30%) used crutches. After surgery only ten (20%) patients use stick for walking. Deep vein thrombosis, heterotopic bone formation occurred in none of the cases. Radiolucent lines were seen at the bone cement interface on acetabular side in two (4%) cases and on femoral side in three (6%) cases. These were of less than two-millimeter width. But none of these patients complained of pain. Subsidence of cement prosthesis or fracture of cement or stem did not occur in any of the hips. The average preoperative Harris Hip Score in patients having osteonecrosis of head of femur was 43 and it went up to 88 postoperatively. In rheumatoid hips the score improved to 82 from a preoperative average value of 45. In cases of ankylosing spondylitis the average preoperative score was 49 and the postoperative score was 83. In cases of osteoarthrosis the average preoperative score was 47 and it improved to 87 after total hip replacement.

Discussion

The present study was undertaken to know the vital role of cemented total hip replacement in cases of osteonecrosis of head of femur and arthritic hip joints. Osteonecrosis of head of femur (39 cases) was the major indication in this series followed by rheumatoid arthritis (5 cases) and ankylosing spondylitis (4 cases). The results obtained in this series are comparable to those obtained worldwide. In 1971,Eftekhar followed up 205 case for 8 years (1962-1970). The sepsis rate was 3.6% and 1.4% had loose sockets. In present study the sepsis rate is 2% and none of the patients have clinically significant loosening. In 1972, Charnley published the results in 338 cases (1962-1965) followed up for 5 years. Postoperative hip scores improved over the preoperative ones. The sepsis rate was 3.8% and 1% had loose sockets. In 1973, Cupic published follow up of 185 cases for 10 years (1962-1972).The scores improved and the sepsis rate was 5% and 2% had loosening. Wroblewski studied 15 –21 year follow up of Charnley Low Friction Arthroplasty in 93 patients. 85% were painfree. 29% showed subsidence of stem cement complex. 78% had full range of movement. 36 hips showed socket demarcation. It may be inferred that the results are similar to other studies and are highly encouraging. All the patients are very well adjusted to the changed life style required after total hip replacement. The patients were crippled because of the pain, loss of movements and inability to carry out day to day activities. All the

patients have shown significant improvement in relief of pain, range of movement and deformities. Most of the patients have resumed their jobs and satisfied. Total hip arthroplasty is boon to the patients crippled because of arthritis of hip, as life is movement.

Table 1 Sex distribution

Sex	Number	Percentage
Male	40	80
Female	10	20

Table 2 Indications

Indication	Cases
Osteonecrosis	39
RA	5
AS	4
OA	2
Total	50

Table 3 Harris Hip Score

	Preoperative Score	Postoperative Score
Osteo-necrosis	43	88
RA	45	82
AS	49	83
OA	47	87

Table 4 Complications

Complication	%
Infection	2
Dislocation	4
Acetabular radiolucency	4
Femoral radiolucency	6
DVT	0
Heterotopic ossification	0

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Guidelines for Writing of DNB Thesis

Title- Should be brief, clear and focus on the relevance of the topic.

Introduction- Should state the purpose of study, mention lacunae in current knowledge and enunciate the Hypothesis, if any.

Specific Objectives- Should be specific, quantifiable, measurable and achievable.

Review of Literature- Should be relevant, complete and current to date.

Material and Methods- Should include the type of study (prospective, retrospective, controlled double blind) details of material & experimental design procedure used for data collection & statistical methods employed; statement of limitations ethical issues involved.

Observations- Should be Organized in readily identifiable sections having correct analysis of data be presented in appropriate charts, tables, graphs & diagram etc. These should be statistically interpreted.

Discussion- Observations of the study should be discussed and compared with other research studies. The discussion should highlight original findings and should also include suggestion for future.

Summary and Conclusion

Bibliography- Should be correctly arranged in Vancouver pattern.

Appendix- All tools used for data collection such as questionnaire, interview schedules, observation check lists etc should be put in the annexure.

Please ensure that there is a functional Thesis Committee and the Ethical Committee in your hospitals, which should meet frequently to assess the thesis progress of each DNB candidate.

Case Report

Mr. Y.N. Das, 55 yr. old hypertensive, smoker, male presented with complains of breathlessness class III and orthopnoea for last three months. He was keeping well, when about three months back he had severe excruciating pain in chest and in the back in the interscapular region and he reported to a local hospital where he was diagnosed and treated as acute coronary syndrome on the basis of symptoms and ST-T changes in the ECG. Gradually his pain lessened and was discharged on antianginals. However, he continued to have poorly controlled blood pressure and subsequently developed gradually progressive breathlessness and orthopnoea. Examination revealed a pulse of 100/mt regular in both upper limbs. Femoral pulses in both lower limbs were feeble and pulsations in popliteal, dorsalis paedis and posterior tibial vessels were barely palpable. However, there was no evidence of limb ischaemia. His blood pressure was found to be 220/110 mm of Hg. There were bilateral fine crepts in chest and S_4 gallop. ECG showed LVH and ST-T changes consistent with strain pattern. Chest X-Ray revealed a CTR of >50%. TTE showed mild concentric LVH with a normal LV function and no regional wall motion abnormality. Based on history, pulse deficits, severe hypertension, and absence of evidence of coronary artery disease, dissection of aorta was suspected and contrast enhanced CT scan was carried out which revealed dissection of aorta beginning from below the origin of left subclavian artery and confined to thoracic aorta with intimal flap blowing into the true lumen and causing its substantial narrowing. A diagnosis of distal chronic dissection of aorta; Type III DeBakey was entertained and in view of threatened lower limb perfusion he was referred for surgical management after appropriate medical management.

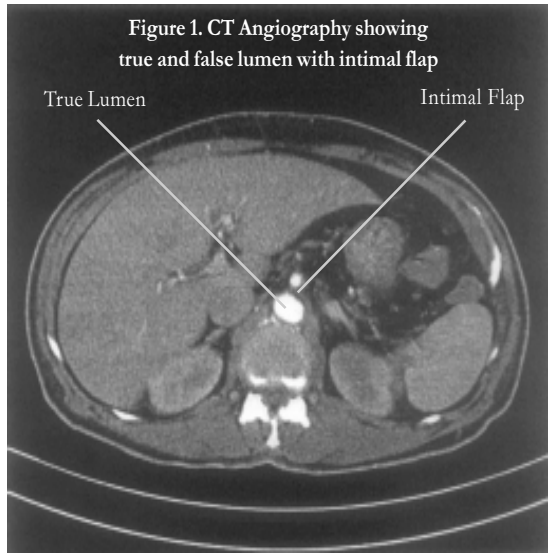

Figure 1. CT Angiography showing true and false lumen with intimal flap

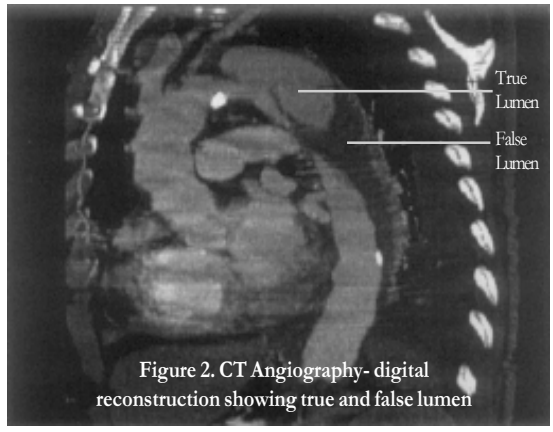

Figure 2. CT Angiography- digital reconstruction showing true and false lumen

Discussion

Pain is present in 96% of patients with dissection of aorta and an interscapular location of pain is consistent with involvement of descending thoracic aorta. Pulse deficits are typically associated with aortic dissection and should be actively sought in suspected cases. Differentiation from acute coronary syndrome or associated underlying aortic dissection, especially in Inferior Infarcts is vitally important; otherwise the consequences of thrombolysis may be catastrophic. However it must be recognized that the diagnosis of aortic dissection cannot be made on the basis of clinical findings alone. Contrast enhanced CT scan/ Spiral CT is currently the gold standard for the diagnosis.

TEE has comparable sensitivity and specificity and has advantage of easy bedside availability in unstable patients. A chronic dissection can be managed medically unless there is evidence of vital organ or limb ischaemia. Endovascular stenting is a growing viable option. Long-term medical therapy to control blood pressure and reduce dP/dT determines outcome in late follow up.

S.K. Mishra & A.K. Thakur
Heart Hospital, Patna

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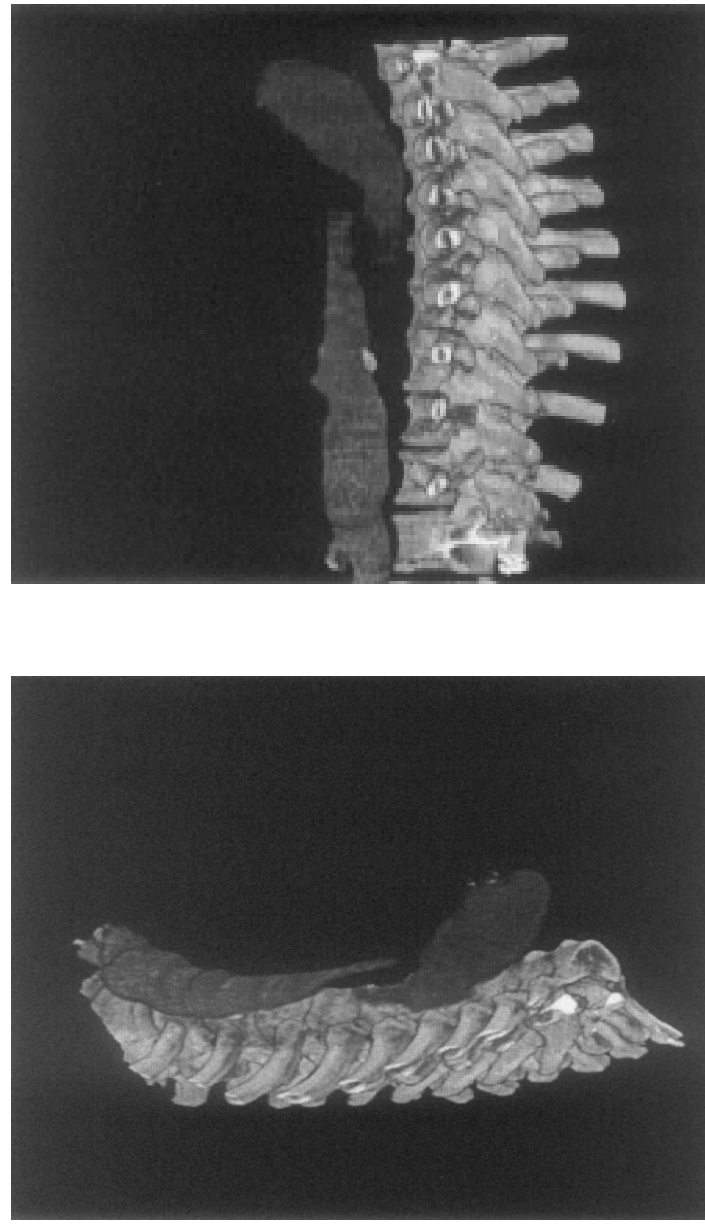


Figure 3. CT Angiography- Spiral(Hellical) reconstruction showing a virtual cut off Aorta due to distended bulging intimal flap into the lumen.

Sarcoma vagina causing APH in a young primigavida - a case report

Haemangio-endothelio-sarcoma of vagina is extremely rare tumor. This case is being reported to its rarity.

Case report

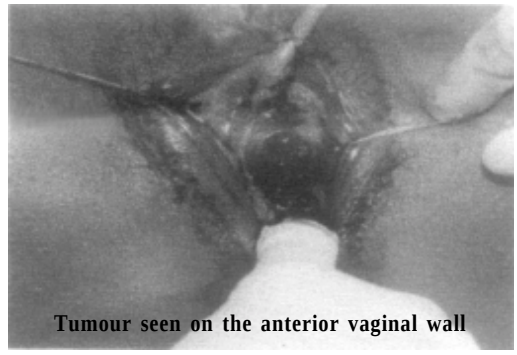
Mrs. Babli, 23 year old primigravida, unbooked, married for 9 months was admitted in CSS Hospital labour room on 2.8.2003 with H/o 7½ months amenorrhoea with profuse bleeding P/V, since early morning and spotting for last 2 days.

On general examination- She was moderately pale, pulse 98/mt, B.P. 100/60 mm Hg. noedema, no varicose veins.

Systemic examination- NAD, P/A examination- uterus 30-32 weeks, relaxed, cephalic presentation, free, FHS-132/mt, regular. Bleeding was causeless and painless. Patient was kept on conservative line of management.

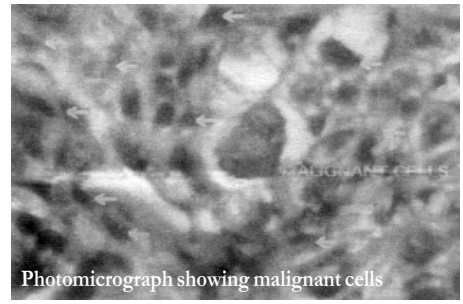
Investigations- Hb%- 7gm%, Hematological profile normal, Urine- NAD, USG revealed placenta in upper segment with no retro placental clot, liquor adequate, BPD 31 weeks + 7 days, no congenital abnormalities.

Treatment- Two Units of blood transfused, bleeding stopped on 5.8.2003. Patient was kept for P/S examination. An ill-defined soft (about 5 cm x 6cm) swelling was seen on anterior vaginal wall just below the external urinary meatus, tortuous, dilated blood vessels present on the surface. On introducing the Sim's. Speculum profuse bleeding started from the lower part of growth. Immediately decision for excision of swelling taken. 2 Units of blood arranged. Hematological and coagulation profile sent. Under epidural anesthesia-indwelling catheter put, growth was excised, packing done. Post operative recovery uneventful. On 10.08.2003 she developed facial palsy and severe pain in left ear. Haematoma on left tympanic membrane was diagnosed by ENT surgeon. Coagulation profile normal. On 11.8.2003 again bleeding P/V started. Manning's Biophysical score (BPP) was 6/10. Decision of immediate C- section taken. On opening the abdomen



Tumour seen on the anterior vaginal wall

large blood clots were seen in the peritoneal cavity, increased vascularity was noticed on uterine surface. A healthy premature male baby weighing 1.75 kg with APGAR score of 7 at 1 minute and 9 at 5 minutes was delivered by LSCS. Placenta normal weighing 385 gm, no retro-placental clot.



Photomicrograph showing malignant cells

On 3rd postoperative day she again started bleeding profusely. Histopathology of growth revealed- Haemangio-endothelio- sarcoma of vaginal wall with vascular embolisation. Knowing the report relatives of the patient took her to home, did not agree to go to higher centre. We were informed that patient died on 18.8.2003 due to severe haemetemesis & malena.

Discussion

Sarcomas represent less than 2% of all vaginal malignancies. In infants and adolescents rhabdomyosarcoma is the commonest type. While in middle-aged leiomyosarcoma is more common. Histologically the mitotic count is most important prognostic factor. Tumors with high mitotic count are uniformly fatal within 2 years of diagnosis. Other sarcomas reported in the vagina include malignant mixed mullerian tumors, alveolar soft part sarcoma, synovial like sarcoma, fibro sarcoma, neurofibro-sarcoma and angio-sarcoma. Angio-sarcoma arise from the endothelial cells of blood vessels. They tend to be highly haemorrhagic and deeply inva-

sive. Great variation in the appearance of the neoplastic endothelial cells are seen. In this case the cell cytology and the histological pattern indicated the diagnosis of haemangio – endothelio – sarcoma of vaginal wall. At places vascular embolisation of tumour cells was seen.

Due to rarity of sarcomas, no uniform standard of treatment has been developed. Treatment recommendation is based on the result of small studies and of experience with other types of squamous cell carcinoma. Our case had bleeding form several sites which could be due to DIC. The sarcoma of vaginal wall in out patient proved rapidly fatal probably because of younger age and pregnancy.

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Meerut

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Familial Methemoglobinemia - A Case Report

Methemoglobinemia should be suspected in a child with cyanosis, altered sensorium without any significant respiratory and cardiac findings.

RBC posses four hemoglobin chains each of which contain heme moiety. These hemoglobin chains transport and deliver oxygen to tissues. Methemoglobin can be found in RBC when there is oxidation of iron moiety changing normal oxygen carrying ferrous (Fe^{2+}) state to ferric state (Fe^{3+}) due to oxidant stress or deficiency of enzymes diaphorase I and diaphorase II thus reducing oxygen carrying capacity of blood and causing functional anemia. In addition methemoglobinemia shifts O_2 dissociation curve to the left thus impairing release of O_2 to tissue. It imparts a reddish brown colour to blood and causes cyanosis at fractions of 15-20%. We present a child admitted with unexplained sudden onset cyanosis and altered sensorium in whom the diagnosis was made on clinical grounds after excluding other causes and later confirmed by measuring methemoglobin concentration in blood.

Case report

An eleven year old child presented with sudden onset cyanosis, altered senses and fever. On arrival, the child had central cyanosis, shallow respiration and tachycardia corresponding to fever with altered sensorium. His chest was clear and heart sounds were normal. There were no signs of meningeal irritation or focal neurological deficits. Plantars were down going and fundus was normal. Clubbing was absent. His chest radiogram, ECHO and blood parameters were normal except mild leucocytosis ABG was normal except O_2 saturation which was slightly low. On direct questioning the relatives gave a history of similar cyanosis in his female sibling.

Based on the above findings, a provisional diagnosis of familial methemoglobinemia was suspected and blood was sent for Hb electrophoresis for methemoglobin and glucose-6- phosphate dehydrogenase levels. The child was started on intravenous Ascorbic acid, antibiotics and O_2.

Clinically child started improving by the end of 2nd day. He become conscious, started talking and cyanosis decreased but persisted. Later his reports confirmed the diagnosis of methemoglobinemia at 22%. Though methylene blue in dose 1-2 mg/kg is useful, it was not given in this child as G-6PD enzyme levels report came after 4-5 days by which time the child had clinically improved and was shifted to oral asorbic acid. His sister was also investigated on these lines and she was also found to have methemoglobinemia levels at 15%. Our patient was discharged on day 10 on oral ascorbic acid.

Disscussion

Methemoglobinemia also known as Blue Baby syndrome should be suspected in children who present with cyanosis without any evidence of anemia, sepsis respiratory and cardiac involvement. CNS and cardiovascular systems are the first systems to manifest toxicity. Oxygenated blood is red, deoxygenated blood is blue and methemoglobin is dark reddish brown in colour. This dark hue imparts clinical cyanosis when methemoglobin level is at 1.5 gm/dl (approx 10-15%). However, a level of 5 gm/dl of deoxygenated blood is required

for similar effects. Therefore when methemoglobin level are relatively low, cyanosis may be observed without cardiopulmonary symptoms. The primary erythrocyte protective mechanism against oxidative stress is the NADH system. Infants less than 4 months are specially prone as in them NADH methemoglobin reductase activity and concentration are low. Further GI infection may cause build up of systemic oxidants by an overgrowth of gut bacteria.

Normally methemoglobin fractions are 0-3%. At 3-15%, there is pale skin or slight blue discolouration. At 15-20% cyanosis is evident. At 25-50% there may be headache, confusion, dyspnoea, weakness, palpitation, chest pain, acidosis and cardiac or neurological ischemia. Drugs like dapsone, chloroquine, amyl nitrite, nitrates, nitrites, nitropusside, primaquine and sulfonamides as well as environmental agents like aniline dyes, aromatic amines may precipitate methemoglobinemia due to oxidant stress. It has to be differentiated from acute coronary syndrome, acute respiratory distress syndrome, anemia, anxiety asthma, CCF and pulmonary oedma, myocarditis and metabolic acidosis.

Acknowledgement

We are thankful to our Administrator and staff of Kurji Holy Family Hospital in helping us in literature review and completing the work.

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Superficial Ulnar Artery- A Case Report

Introduction

Normally the ulnar artery begins distal to the bend of the elbow as the larger of two terminal divisions of the brachial artery. Variation in the arterial system of the upper limb are well documented [Bergman RA et al 1988[1], Rochiguaz- Baega et al 1995[2] and Tountas CHP et al 1993[3]]. The variation and anomalies of the arterial system to the upper limb can best be explained on the basis of embryologic development of the vascular plexuses of the limb buds [Jurjus A et al 1986[4]]. The superficial ulnar artery is well known but very rarely encountered abnormality [Anil A et al 1996[5] and Nakatani T etal[6]].Superficial positions of the ulnar and radial artery make them more vulnerable to trauma and thus to hemorrhage but at same time more accessible for cannulation if necessary. If they are superficial to flexor muscles, the radial and ulnar artery may be mistaken for veins. Such misinterpretations can lead to intra arterial injections, wrong interpretations of incomplete angiographic images or severe disturbances of hand irrigation during surgical procedures on the arm or forearm.

Demonstration of patency of ulnar artery is very important before raising a free radial forearm flap which can be established by Doppler flowmeter. After such a flap, the blood supply of hand will depend entirely on adequate patent ulnar artery. Thus any abnormal course and division of ulnar artery is important in surgical and angiographic procedures related to that region.

Material and methods

100 randomly selected cadavers assigned to medical students for dissection were studied. All had been embalmed soon after death with mixture of 10% formaldehyde, glycerol, methylated spirits and 10% phenol in water. The topography of the upper arm arteries of all cadavers was examined during dissection and those showing anomalies were recorded and described.

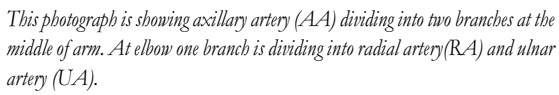
Results

In the left arm of this cadaver, just after giving origin to thoracoacromial artery in it´s second part, axillary artery divided into two branches at mid of arm (fig 1). At level of elbow one of the branches again divided to give origin to radial and ulnar artery. Both radial and ulnar artery were superficial to flexor group of muscles (fig 2). In the distal half of forearm, superficial ulnar artery lay between tendons of flexor carpi ulnaris and flexor digitorum superficialisand finally established the superficial palmar arch. Radial artery ran it´s own normal course through the forearm and winded dorsally through the anatomical snuffbox. The other branch of axillary, from the elbow ran deep to flexor group of muscles, giving origin to common interosseous artery. . Thus this cadaver had two ulnar artery; one superficial and other deep.

Discussion

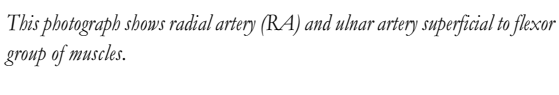
Morphologic variations in the arteries of the upper extremity are very important from the surgical point of view in relation to procedures in this area. Thus we have tried to study literature on variations in this area. Mc Cormack et al 1953[7]

Fig 1



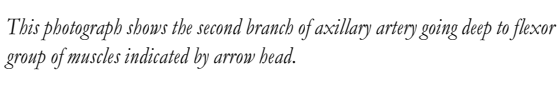
This photograph is showing axillary artery (AA) dividing into two branches at the middle of arm. At elbow one branch is dividing into radial artery(RA) and ulnar artery (UA).

Fig 2



This photograph shows radial artery (RA) and ulnar artery superficial to flexor group of muscles.

Fig 3



This photograph shows the second branch of axillary artery going deep to flexor group of muscles indicated by arrow head.

published a study of 750 dissected upper extremities where the percentage of major arterial pattern variations was 18.53% of total. They reported high origin of radial as largest group of variations and represented an occurrence of 14.27% of all specimens.the high origin of ulnar artery from the brachial artery and from axillary artery was 1.33% and 0.93% of the total respectively.

In a dissection of 451 upper limbs Weathersby 1956[8] found high origin of ulnar artery in 0.67% case. The ulnar artery arose from brachial artery in two cases and from superficial brachial artery in third case. In our case, we found dual ulnar artery . The superficial ulnar arose from brachial artery at level of elbow joint and deep ulnar artery took origin from axillary artery high up in arm. Superficial ulnar artery has been reported by Fadel 1986[9], Anil A 1996[5] and Gölshan Görmûs et al 1998[10]. Some authors have also reported bilateral case of superficial ulnar artery [Yazar Fet al 1999[11] and Jacquemin G et al 2001[12]]

A model of development of the arteries of upper limb in 5 stages has been proposed [Senior HD 1926[13] and Singer E 1933[14]. This states that an axial system appears first while other branches develop later from this axial system. Thus in the adult , this axial system includes axillary artery, brachial artery and anterior interosseous artery. The median artery branches from the later [stage 2]. Afterwards the ulnar artery branches from the brachial artery[stage 3]. Next , a superficial brachial artery develops from the axillary and continues as the radial artery [stage 4]. Regression of the median artery and an anastomosis between the brachial artery and the superficial brachial artery with regression of the proximal segment of the latter, gives rise to definitive radial artery.

The model of development of radial

artery is not unanimously accepted. Though Gruber 1867[15] and Meckel 1816[15] agreed with it. Adachi 1928[16] and Mrazkova 1989[17] considered that radial artery branches directly from the interosseous artery. Poteat 1986[18] modified Singer´s model and proposed a sandwich of stage 2 and 3, making ulnar artery the second artery to appear in arm. The present anomaly is thus explained by the persistence of embryological vessels which may be due to hemodynamic persistence of superficial system over deep system at the origin of ulnar artery . Genetic influences seen to be prevalent cause of such variation, although other factors like foetal position in utero, first limb movement or unusual muscular development can not be completely excluded.

Vascular anomalies occurring in common surgical sites tend to increase the likelihood of damage during surgery. Owing to unusual course of superficial ulnar artery, it would be particularly vulnerable to different surgical procedures. Thus it is important for surgeons and radiologists to be aware of the possible arterial variations in order to prevent complications during surgical and diagnostic procedures.

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Book Review

Mastering the Techniques of Lens Based Refractive Surgery (Phakic IOLs)

Editors: Ashok Garg; Jorge L Alio; Dimitrii Dementiev & Antonio Marinho

Publisher: Jaypee Brothers

Edition: 2005

The Book consists of 33 chapters and is contributed by 39 authors, 11 from different states of India and remaining 29 are from USA, UK, France, Germany, Japan, Egypt, Greece, Switzerland, Italy, Spain and Portugal.

The book has foreword by I Howard Fine Eugene, USA emphasizing it an extremely useful book for all the ophthalmologists interested in refractive lens surgery. The book is a real masterpiece illustrating innovative ideas and experiences of the authors. The CD of the video recorded surgical techniques of phakic refractive surgery and accommodative aphakic surgery is available with it. The book imparts the knowledge about phakic IOLs which is useful to the postgraduate students and more so to the aspiring general ophthalmologists to upgrade their services to their patients. It is a revelation for the general ophthalmologist globally except for those who are already on the task.

Chapters of interest incorporated:- Artiflex (Antonio Marinho, Portugal), Iris Claw (Sanjay Chaudhary, India), ICL^{tm} STAAR (Birgit Lackner, Austria), PRL^{tm} (Maria I Kalyvianaki, Greece) Phakic IOLs for lens refractive surgery including high myopias and high Hypermetropia with special reference to Toric Phakic IOLs(Antonio Marinho, Portugal) for correction of existing astigmatism . The Chapter on Humanoptics Accommodative IOLs (Sunita Aggarwal, Amar Aggarwal , Ashok Garg, India) is the current advancement of the century and is a novelty of its own kind. Lens filling procedure using plugs and imagining futuristic lens for refractive lens surgery- an ever dream of the ophthalmologist is also nicely dealt with.

The book by and large motivates the aspiring general ophthalmologists to understand and take up the newer surgical modalities in their own setup in this era of advancement.

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