The thyroid gland and the heart

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Introduction

Thyroid disease is a common endocrine disorder and is associated with significent short and long term adverse health outcome if left untreated.the cardivascular system (cvs) is a target for such changes which may affect structure and function of the system in the two major disorders of the gland, hyperthyroidism and hypothyroidism(1). Not only overt thyroid disorders but the subclinical forms of thyroid dysfunction are also reported to precipitate or predispose to heart disease (2). Subclinical thyroid diorders are defined as the association of an abnormal thyroid stimulating hormone (tsh) level and normal thyroxine (t4) level (3). This article is intended to discribe briefly such changes.

Hyperthyroidism

Excess thyroid hormones increases energy expenditure and heat production. This represents an exagerated physiolgic action of the hormones potentiating the sympathetic nervous system action and catecholamines on the heart (4). Alterations of cvs function result from increased circulation demands and the need to dissipate the excess heat produced by hypermetabolism. This is in addition to subtle changes in structure and function of muscle fibres and conducting system (5). At rest peripheral vascular resistance is reduced by vasodilatation and cardiac output is augmented by an increased stroke volume and heart rate. This is a direct inotropic and chronotropic effect mediated by alterations in the contractile cardiac muscle proteins and sinoatrial node (6). Tachycardia at rest is almost always present and an increased sleeping pulse rate of more than 90 beats / minute helps to distinguish tachycardia of hyperthyroid aetiology from that of psychogenic causes.

Widening of pulse pressure results from a rise in systolic blood pressure and a drop in the diastolic pressure. This produces the characteristic large volume collapsing peripheral pulse.

The increased force of cardiac contraction produces a diffuse forceful apex impulse and the heart will seem clinically enlarged. Echocardiographic studies however, are usually

unremarkable unless there is a superimposed chronic anemia or arterial hypertension. The heart sounds are loud and a systolic murmur may be appreciated over the mitral area.

Hyperthyroidism is associated with up to 10% increase in the incidence of cardiac arrhythmias (7) that is almost invariably of supraventricular origin and specifically atrial fibrillation (af). A simillar percentage of patients with otherwise unexplained aetiology of thier af are thyrotoxic. In a study of more than 2000 individuals 60 years of age or older, af is detected in 28% of those with a suppressed tsh serum level (8).

Af is the main cause of heart failure in patients with hyperthyroidism. The arrhythmic impact is augmented by a chronic increase in cardiac muscle work load. These challenges are usually tolerated in the young patients and those without a preexisting heart disease. The elderly patient may develop heart failure following subclinical hyperthyroidism (8, 9). Af is associated with a higher risk of thromboembolism that often involves the central nervous system. It is more common in males than females and incidence increases with advancing age and t3-toxicosis.

Conversion of af to sinus rhythm is unusual unless the thyroid function is well controlled and is maintained with any of the recognized strategies of management. This may include antithyroid medications, surgery, radioiodine therapy or any combination. Beta blocking agents are drugs of choice as the first step to initiate the control of ventricular rate . Calcium channel blockers such as deltiazm and verapamil can be used for long term control of ventricular rate when beta blockers are unsuitable. The response to digitalis is suboptimal in thyrotoxic patients. This is possibly related to increased metabolism of the drug. A larger dose may be required to obtain the desired clinical effect. Indeed resistance to digitalis in idiopathic af patients should alert the cardiologist to the possible diagnosis of hyperthyroidism.

Hypothyroidism:

The effect of hypothyroid state on the cvs is secondery to the slowing down of body metabolism and heat production. The cardiac output is decreased at rest because of reduction in heart rate and stroke volume. Peripheral resistance is increased and blood volume is decreased. There is narrowing of pulse pressure, prolongation of circulation time and decrease in tissue perfusion (10, 11). These changes produce the cold peripheries and cold intolerance in myxedema patients.

Electrocardiograms show low amplitude sinus bradycardia, flat p waves and qrs complexes. Rarely complete heart block is present. Echocardiographic studies show an increased incidence of septal hypertrophy and apparent obstruction of ventricular outflow tract. These structural and functional changes are often referred to as the myxedema heart. It is rarelyassociated with heart failure in the absence of other cardiac pathology. Changes are gradually reversible following appropriate thyroxine replacement.

There is considerable controversy as to whether hypothyroidism is a risk factor for atherosclerosis. Angina pectoris is unknown but in patients with a preexisting ischemic heart disease, angina may appear or worsen with enthusiastic thyroxine replacement therapy (10, 12, 13). This is of paramount importance in the old hypothyroid patient. A gradual titration of the thyroxine dose is required to avoid such effect.

The association of hypothyroidism and lipid metabolism as a possible confounding factor in patients with chd is well recognized. Prevalence of hypercholesterolemia increases as serum tsh increases in primary hypothyroidism and subclinical hypothyroidism (14). The hunt study from norway has shown a linear and significent increase in serum triglycerides, total cholesterol, and low density lipoprotein cholesterol levels as serum tsh rises within the normal range (15). Some authorities propose thyroid function testing as having an important role in the risk stratification of patients with chd. Maintenance of a normal level tsh will achieve homeostasis of plasma lipids and slow the progression of atherosclerosis in chd patients (16).tsh receptors were identified in many tissues capable of synthesizing cholesterol such as the adipocytes. Through these receptor proteins tsh is shown to upregulate the expression of hydroxy methyl glutaryl co a (hmg coa) reductase enzyme and increase cholesterol synthesis (17). Hmg co a reductase is the rate limiting enzyme in cholesterol synthesis.

Chronic pericardial effusion:

Chronic pericardial effusion is a known comlication of long standing untreated primary hypothyroidism. The exact mechanism of its development is not known but presumed to represent a serosal leak that resembles the subcutaneous collection of fluid producing the non- pitting oedema of that compartment. The fluid is typically rich in proteins and glycosaminoglycans. The effusion is rarely sufficient to cause tamponade. It reponds gradually and completely to adequate thyroxine replacement (18).

Amiodarone and thyroid disease:

Amiodarone is a potent anti arrhythmic drug that works efficiently to control both ventricular and supraventricular arrhythmias. It is rich in iodine with some structural homology with

thyroxine. It contains 37% iodine by weight. Standard maintenance therapy with 200 mg can provide more than 100 times the daily iodine requirement. It is highly lipid soluble and is concentrated in adipose tissue, muscle, liver and thyroid gland. Total body iodine stores remain elevated for up to 9 months after discontinuation of the drug. Thyroid abnormalities have been reported in 14 – 18% of patients receiving long term amiodarone therapy. The effect of amiodarone on thyroid function ranges from abnormal thyroid functions to overt thyroid dysfunction that may be either hyper- or hypothyroidism. Amiodarone impairs the deiodination of t4 to t3. It essentially inhibits thyroid hormone synthesis and secretion and reduces t3 binding to its nuclear receptors. Anti thyroid therapy may need to be added simultaneously to inhibit organification of the excess iodine and blocks any untoward effect of excess iodine (19,20,21).

References:

I – flynn rw, macdonald tm, jung rt et al. Mortality and vascular outcome in patients treated for thyroid dysfunction. Am j clin endocrin & metab 2006; 91: 2159-2164

2 – levasi g, molinaro s, et al. Association between increased mortality and mild thyroid dysfunction. Arch intern med. 2007; 167: 1526-1532

3 – bilezekian j, loeb j. The influence of hyperthyroidism and hypothyroidism on the alpha and beta adrenergic receptor system and adrergic responsive system. Endocrin rev 1983; 4: 378-388

4 – weber ka, thyrotoxicosis and the heart. 1992; 327: 94-98

5 – komiua n, isomoto s et al. Electrophysiologic abnormalities of the atrial muscle in patients with paroxysmal atrial fibrillation associated with hyperthyroidism. Clin endocrinol, 1998; 56: 39-44

6 – johnson pn, freedberg as, marshal jm. Action of the thyroid hormones on the transmembrane potentials for sinoatrial node cells and atrial muscle cells in isolated atria of rabbits. Cardiology; 1973: 273-289

7 – weber ka. Thyrotoxicosis and the heart. N engl j med. 1992; 327: 94-98

8 – sawin ka, geller a, wolf pa et al. Low serum thyrotropin concentration as a risk factor for atrial fibrillationin older persons. N engl j med. 1994; 331: 1249-1252

9 – forfar jc, miller hc, toft ad. Occult thyrotoxicosis: a reversible cause of idiopathic atrial fibrillation. Am j cardiol. 1979; 44: 9-12 (abstract)

10 – klein i, ojamaa k. Thyroid hormones and the cardiovascular system. N engl j med. 2001; 344: 501-509

11 – ladenson pw, sherman si, baughman kl et al. Reversible alterations in myocardial gene expression in a young man with dilatedcardiomyopathy and hypothyroidism. Proc natl acad sci usa. 1992; 89: 15251-15255

12 – keating fr, parkin tw, selby jb et al. Treatment of heart disease associated with myxedema. Prog cardiovasc dis. 1961; 3: 364-381

13 – compromise therapy in the patient with angina pectoris and hypothyroidism; a clinical assessment. Am j med. 1980; 69: 411-418

14 – mangeri d, santangelo a et al. Thyroid hormones and lipid metabolism in a group of of patients over seventy. Eur rev med pharmacol sci. 1999; 3: 211-216

15 – asvold bo, bjoro t, nilsen til et al. Thyroid levels and risk of fatal coronary heart disease.the hunt study. Arch intern med. 2008; 168: 855-860

16 - waterhouse df, mclaughlin am et al. An examination of the relationship between normal range thyrotropin and cardiovascular risk parameters. A study in healthy women.

Thyroid 2007; 17: 243-248

17 – lu s, guan q, liu y et al. Role of extrathyroidal tshr expression in adipocytes differentition and its association with obesity. Lipid health dis 2012; 11: 17-21

18 – hardisty ca, naik dr, munro ds. Pericardial effusion in hypothyroidism. Clin endocrinol (oxf) 1980; 13: 349-354

19 – tsadok ma, jackevkivs ca et al. Amiodarone induced thyroid dysfunction: brand name versus generic formulation. Cmaj 2011; 1839(12): 817-823

20 – ahmed s, van gelder ic et al. Determinants and outcome of amiodarone associated thyroid dysfunction. Clin endocrinol(oxf) 211; 75(3): 388-394(medline)

21 – mosher mc. Amiodarone induced hypothroidism and other adverse effects. Dimens crit care nurs. 2011; 30: 87-93 (medline)