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THYROID HORMONES AND CARDIOVASCULAR HOMEOSTASIS; A REVIEW

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ABSTRACT

Two iodinated hormones, 3,5,3-triiodothyronine (T3) and 3,5,3,5-tetraiodothyronine; also known as thyroxine (T4) are secreted by thyroid gland. Thyroid hormones interact with specific receptors on myocardial and vascular endothelial tissues to induce chemical changes and these tissues are very sensitive for a small fluctuation in circulating thyroid hormones. The obtained data from different experimental and clinical studies revealed significance of normal thyroid hormones to maintain the cardiovascular homeostasis. Even subtle fluctuation in the concentration of thyroid hormone as in subclinical hypothyroidism or hyperthyroidism could significantly affect the cardiovascular system. In this review article we will understand how thyroid hormones interacts with specific receptors on myocytes and induces many genomic as well as non-genomic alterations directly and indirectly including due to dyslipidemia, blood pressure changes and endothelial dysfunction.

Key Words: Hormones, Homeostasis, Cardiovascular, Hypothyroidism, Hyperthyroidism

INTRODUCTION

Thyroid gland is a type of endocrine glands that functions in producing, storing and releasing of hormones in the blood stream. In the endocrine system the only cells that assimilate iodine from ingested food and utilize it. Thyroxine (T4) and Triiodothyronine (T3) are the central hormones produce by integration of iodine and tyrosine by these cells.[1] Thyroid hormones have wide-reaching effects on whole body, particularly on heart. T4 also acts on neural tissues but primarily it is a pro-hormone.[2] 5-mono-deiodenation of T4 transformed it into physiologically active form T3 in kidney, pituitary gland, liver and skeletal muscles.[3]

Normal production of T4 and T3 by thyroid gland is 80% and 20% respectively however, T3 has four times more success than T4 hormone.[4] Essential functions of body including body weight, heart rate, cholesterol, muscle strength, peripheral and central nervous systems are performed by these hormones. Maintenance of proper level of T3 and T4 hormones within body is achieved by communication of pituitary and hypothalamus of brain. Hypothalamus send signal to pituitary gland for thyroid stimulating hormone which ultimately activate thyroid gland to express or suppress the level of T3 and T4. Decreased level of these hormones stimulates thyroid gland to produce more TSH or vice versa. The relationship between thyroid hormones and cardiovascular system was studied by an English physician, Caleb Hillier parry, before 200 years ago. He observed that a woman having palpitations and goiter and her every systole shook the thorax. This reveals that there is an association between thyroid gland and cardiac disorders. Thyroid diseases have severe effects on heart.[3]

Abnormalities in thyroid hormones change the normal functions performed by heart.[5] Remarkable increase in thyroid hormones causes hyperthyroidism and decrease causes hypothyroidism, although, both states have harmful effects on heart. Increase in thyroxin level (hyperthyroidism) in body enhances the heart activity to beat more forcefully enhancing heart rate called tachycardia. Severe form of tachycardia leads to palpitations in the patient. Palpitations also noticed in other heart diseases and if over activity of thyroid gland leads to palpitations it does not mean any heart disorder is present.[6]

Long stimulation of heart by thyroxin leads to improper coordination in transferring of electrical impulses in atrial fibrillation and heart.[7] When impulses are generated in right atrium then instead of transmitting into ventricles they form a short circuit result in atrial contraction and loss of regular functioning of ventricles ultimately leads to irregular heartbeat. Systolic hypertension or increase in blood flow rate results due to prolonged heart contraction. This condition doesn't increase the lower number of two blood pressures called diastolic pressure. Hypothyroidism is antagonistic to hyperthyroidism having low blood pressure and low activity of thyroid gland. Level of cholesterol increases and changes occur in metabolic system due to hypothyroidism.[8]

Non-genomic and genomic mechanisms of thyroid hormone influence the vascular system and heart.[9] In vascular smooth muscles and cardiomyocytes T3 bind with nuclear receptors to activate gene transcription that leads to formation of regulatory and structural proteins. Besides the regulation of proteins in heart thyroid hormones non-genomically and directly restrict the ion channels in cardiomyocytes that are accountable for change in cardiovascular parameters.[10] The recent finding associated to cardiovascular disorders and thyroid hormonal dysfunction reveals that heart disorders result in lowering of T3 levels. Cardiac tissue hypothyroidism has been confirmed by experiments conducted on animal models having hypertension, myocardial infarction and diabetes mellitus.[11,12]

Thyroid hormones and Cardiomyocyte Secretion and metabolism of Thyroid hormones

Two iodinated hormones, 3,5,3-triiodothyronine (T3) and 3,5,3,5-tetraiodothyronine; also known as thyroxine (T4) are secreted by thyroid gland. Thyroid hormone holds an important role in normal development, growth, neural differentiation, and metabolic regulation in mammals.[13,14] The thyroid gland is composed of small follicles in which thyroglobulin is iodinized at tyrosine residues to produce thyroid hormones in response to thyroid-stimulating hormone (TSH), another important hormone to control the circulating level of thyroid hormone level secreted by the anterior part of pituitary gland in response to feedback.[15] TSH released from pituitary gland acts on thyroid follicular cell on interacting with TSH receptor (TSH-R) to synthesized Thyroxin (T4) and 3,5,3´-triiodothyronine (T3).[16]T4 secreted by thyroid gland is transformed into T3 in different parts of body including kidney, liver and skeletal muscle.[17]

Both thyroid hormones T4 and T3 bind with specific receptors in responsive tissues to induce biological activities in the body. However, T3 have approximately tenfold higher affinity for these specific receptors than T4 so it is considered that T3 is biologically active hormone.[18] Although, for T3 production T4 acts as a pro-hormone,however, different issues have receptors where T4 act directly like blood vessels having plasma membrane integrin v3 receptors and indicating pro-angiogenic activity of T4.[19] Major part of T3 (>80%) is derived from T4 in extra thyroidal tissues after deiodination of a single iodine atom catalyzed by three selenocysteine enzymes called deiodinases (DIO1-DIO3). Type I iodothyroninedeiodinase (DIO1) is mostly present in the kidney and liver while type II iodothyroninedeiodinase (DIO2) activity is present in brain, heart, pituitary gland and in brown adipose tissues both enzymes are responsible for extra thyroidal production of T3 15-20% and two-thirds of total circulating T3 respectively.[20] The third type of enzyme deiodinase, thyroxine 5-deiodinase

(DIO3) is responsible for termination of T3 and T4 activity. In short, de-iodinase pathway is responsible for the regulation of thyroid hormone status both in serum and in intracellular tissues.[11]

Interaction of Thyroid hormone and cardiovascular cells. Interaction of thyroid hormones and cardiovascular tissues are vital for normal homeostasis of our body and are linked with the physiology of thyroid-induced heart disease and hypertension. Cardiac status is regulated by thyroid hormones through major three ways including direct genomic pathway, non-genomic pathway and through the effects of T3 and T4 on the peripheral circulation, which determines cardiac filling, systolic contractility and cardiovascular hemodynamics (Figure 1). Through genomic pathway thyroid hormones interact with specific nuclear receptors in the cardiomyocytes and influences the target genes expression while regulation of the ion channels present in the cell membrane of cardiomyocyte take place in non-genomic actions.[21] As thyroid hormones are hydrophobic in nature, so T3 in cardiomyocyte binds with its specific receptor in nucleus; there are two thyroid hormone receptors known as receptor-α specifically present in cardiomyocyte and thyroid hormone receptor-β; and then to target genes with response element of regulatory regions to control transcription.[22] One of the unique feature of thyroid hormone receptors is that in the absence of thyroid hormone it binds to thyroid hormone response elements to repress the gene expression so in cardiomyocyte transcription depends upon the presence of hormonal signal in the form of thyroid hormones.[23,24]

Thyroid hormone's induced changes in cardiovascular system. Myocardial contractility and systolic function are controlled by thyroid hormone activity in the cardiomyocyte. Expression of various genes including Na+/K+ transporting ATPase (sodium/potassium-transporting ATPases), myosin 6; encoded by MYH6 (myosin heavy chain-α), SERCA2; encoded by ATP2A2 (sarcoplasmic-/endoplasmic reticulum calcium ATPase 2) and negative regulation of myosin 7; encoded by MYH7 (myosin heavy chain-β) and PLN (phospholamban) (Figure 1).[25,26] The contractile apparatus of cardiomyocyte is composed of two myosin heavy chains.Release and reuptake of calcium from the sarcoplasmic reticulum for systolic contraction and diastolic relaxation of heart is regulated by SERCA2 and its inhibitor PLN. Hormones from thyroid gland enhanced the reuptake of calcium to promote ventricular relaxation, on increasing the expression of SERCA2 level and by lowering PLN level in the sarcoplasmic reticulum.[27] Direct inotropic effect on the heart is also regulated by thyroid hormone which regulates 1-adrenergic receptor gene expression in cardiomyocytes.[28]

Further, it was reported that in addition to above mentioned mechanisms the hormones secreted by thyroidglandalso affect the heart chronotropy. This affect is induced through both genomic and non-genomic alterations including by affecting adrenergic-receptor complex components, by influencing the channels of sodium, potassium, and calcium. Hyperthyroidism is manifested as bigger risk of atrial fibrillation (AF) and tachycardia while decreased cardiac contractility and bradycardia are the manifestations of hypothyroidism.[29] Activation of ions channel like sodium, potassium, and calcium, influence on the membrane of mitochondria and mitochondriogenesis, and regulating various signaling pathways of cardiac cells and vascular smooth muscle cells, increase in tissue metabolism, vasodilatation and thermogenesis are among the non-genomic effects of thyroid hormones induced both in cardiomyocytes and the systemic vasculature.[30] PI3K/ AKT (phosphatidylinositol 3-kinase/serine/threonine-protein kinase) signalling pathways are activated by thyroid hormone, which leads to the synthesis of nitric oxide in endothelial cells and a following decrease in the systemic vascular resistance.[31] As mitochondrial function is also control by thyroid hormones so a change in the blood thyroid hormones might influence bioenergetic status and function of cardiac cells (Table 1).[32,33]

Thyroid hormones also have many important roles to regulate the renin-angiotensin-aldosterone system as hemodynamic effects of thyroid hormones. As thyroid hormones induced the initial decrease in systemic vascular resistance, which results in kidneys perfusion decrease and ultimately leads to increase secretion of renin and aldosterone levels.[34] Plasma volume increases in the result of the activation of the renin- angiotensin-aldosterone system which results in escalation of cardiac pre-load and cardiac output, explain the role of thyroid hormone in cardiovascular homeostasis and many other cardiac protective effects of thyroid hormones summarized in table 1.

Figure 1: Effect of Thyroid Hormones on the Cardiomyocyte via Genomic and Nongenomic Actions Adopted and Modified from Jabbaret al., (1).

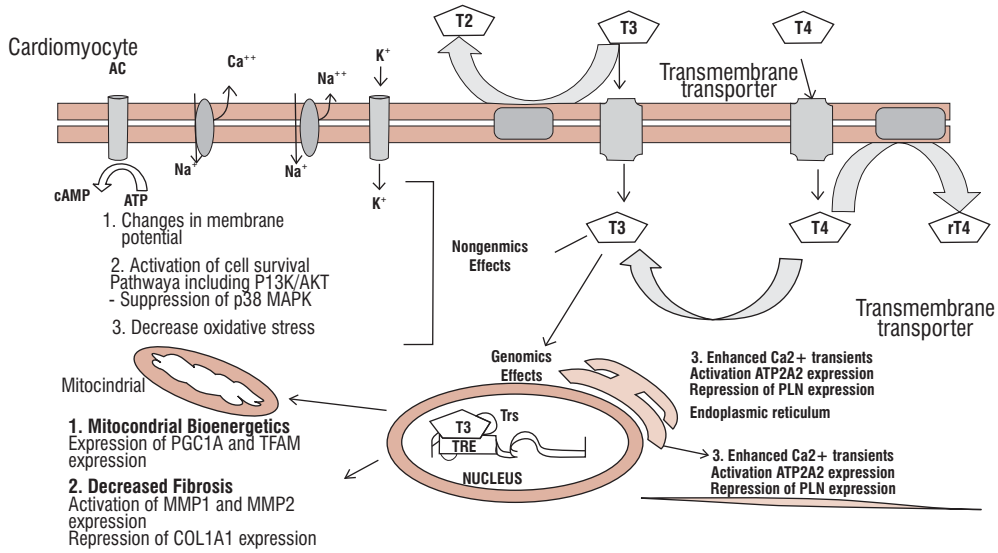

Table 1: Cardioprotective Effects of Thyroid Hormones on Cardiovascular System (1)

Cardioprotective Effects	Mechanism of action
Antiapoptosis	• PI3K/AKT and heat-shock proteins pathway activation • Decreased p53 signalling and p38 MAPK activation
Mitohondrial protection	• miR-30, PGC1A and TFAM expression Up regulation • Activation of mitoKATP channel and HIF1-α • Decreased p53 signalling
Cell growth and differentiation	• mir-208a and MYH6 expression Up regulation • mir-208b and MYH7 expression Down regulation
Induction of myocardial hypertrophy	PI3K/AKT/mTOR and GSK3signalling pathways Activation
Neoangiogenesis	Activation of ERK1/2 and HIF1- signaling
Antifibrosis	• MMP1 and MMP2 expression Up regulation • TIMP1 and TIMP4 expression Down regulation • miR 29c, miR 30c, and miR 133 Up regulation and Inhibition of TGF

Representing the cardioprotective mechanisms of thyroid hormones on cardiovascular system AKT, serine/threonine-protein kinase; ERK1/2, extracellular signal-regulated kinases 1/2; GSK3β, glycogen synthase kinase 3β; HIF1α, hypoxia-inducible factor 1α; MAPK, mitogen-activated protein kinase; mir, microRNA; mitoKATP, mitochondrial ATP-sensitive potassium channel; mTOR, serine/threonine-protein kinase mTOR; PI3K, phosphatidylinositol 3-kinase; TGFα, transforming growth factor-α.

HYPERTHYROIDISM

Hyperthyroidism cause palpitations as well as increment beat rate.[1] During the increment in thoughtful and degeneration of parasympathetic tone heart rate is altered.[35] Elevated heart rate has >90 beats/min called tachycardia while during workout the typical increment in heart rate is called exaggerated.[4] The heart rate of hyperthyroid patients is 50-300% high than normal people. This elevation is due to ascents in left ventricular contractility, lowering of systemic vascular resistance and increment in resting heart rate consolidated and ascent in blood volume.[36] After goiter, tachycardia act as secondary cause of hyperthyroidism as suggested by review of 880 patients of different ages.[10]

Studies in which organization of phenylephrine, blood vessel atropine and vasoconstrictors lowered the cardiovascular yield upto 34% and fringe blood stream having no effect on control subjects in hyperthyroid patients suggested the importance of less vascular systemic imperviousness to the extension of systemic blood stream.[37] Hyperthyroidism results in expansion of diastolic and systolic capacity of left ventricle in patients. In intra-ventricular weight amid systole both of aortic valve and left ventricular gets expanded due to discharge part the rate of blood stream.[36] Similarly, the rates of unwinding of assemblies of heart and left ventricular filling, ascertained as the stream over the mitral valve amid diastole, are expanded. In hyperthyroid patients the direction of flow rate is controlled by adrenergic receptor causing slow heart rate but it doesn't alter the performance of diastolic and systolic pressure.[38] It approves that heart muscles are directly affected by thyroid hormones.[1]

Symptoms associated with hyperthyroidism

Atrial Fibrillation

Symptoms associated with hyperthyroidism include exertional dyspnea and sinus tachycardia which is the rhythm unsettling influence in affected patients. Atrial fibrillation prevalence lies between 5-15% among hyperthyroid patients.[35] From the investigators of senior patients increased recurrence ratio has been takenhaving suspected or known heart disease.[23] According to extensive review it is suggested that 1% of new instances of atrial fibrillation is caused by hyperthyroidism. In spite of the fact in patients with hyperthyroidism the new onset of atrial fibrillation should be measured by checking serum thyrotropin so as to treat the infection as early as possible.[39]

Thirteen percent (13%) patients having secretive atrial fibrillation are hyperthyroid and it is confirmed by biochemical confirmation.[40] The anticoagulant treatment for hyperthyroid patients with atrial fibrillation is provoking. The risk of sleeping amid anticoagulant treatment to the risk of systemic embolization is still being weighed in every patient. In review investigation 610 hyperthyroid patients have hazard for embolization.[41] While in another investigation out of 11,354 patients, 6 had systemic embolization and 288 have atrial fibrillation.[38]

The age of these 06 (six) patients was above 50 years and they also have arterial fibrillation from six months while four patients have congestive heart disappointment. The treatment through anticoagulants has beneficial effects for young patients because they don't have any other coronary illness, free hazard element for embolization and hypertension.[42] Contrarily, in seasoned patients having a coronary illness and with endless atrial fibrillation the anticoagulant treatment should be started. Hyperthyroidism treatment is connected with inversion to sinus cadence as described in review of 163 patients 62% gets relieved from euthyroid state within 8-10 weeks of treatment.[43] Patients having or not atrial fibrillation and primary coronary illness the duration of sinus mood inversion is less without unconstrained inversion, electrical or pharmacologic cardioversion ought to endeavor simply after the patient's condition has been made euthyroid.[44]

Issue arises due to these consequences that patients having less serum thyrotropin either dealt with thwart atrial fibrillation or not. The treatment can be anti-thyroid medication, radioiodine and adrenergic-receptor rival. The latter is involved to moderate the rate of heart however in some patients with hyperthyroidism treatment was conducted by thyroxin and as a result it anticipated the atrial fibrillation. This discernment may be especially significant in hyperthyroid patients in which treatment is performed by thyroxin to stifle the emission of thyrotropin.[45]

Heart Failure

In spite of expanded contractile capacity of heart in hyperthyroid patients the advancement of heart disappointment has been astonishing and leads to creation of issues related to hyperthyroid cardiomyopathy.[46] As described already, in most of the hyperthyroid patients the level of cardiovascular yield becomes high like maximum increase in heart rate and bringing down vascular resistance as normally occur during exercise.[23]

High-yield disappointment expression was not fitting and the potential of heart in maintaining expansion of cardiovascular yield is very still and preserved in all practices.[47] Occasional hyperthyroid patients have less cardiovascular yield, low heart contractility, a third sound in heart, signs of heart improper functioning and formation of aspirator clog. These symptoms happen mostly in atrial fibrillation and tachycardia leading to heart failure.[48] Patients having coronary illness and hyperthyroidism the workload may exhaust heart functioning.[45] The proximity of hypertensive coronary illness and ischemic trades off the capability of myocardium to proceed the metabolic supplications of hyperthyroidism.[20]

Captivating management and quick acknowledgment of cardiac system and other organs in patients with age 50 years are critical and reveal that cardiovascular complications are the main reason of death in patients after taking treatment for hyperthyroidism. In patients with hearts related complications and hyperthyroidism from exertional dyspnea, sinus tachycardia to heart disappointment treatment should be conducted by incorporating αβ-adrenergenic- receptor rival (propranolol) and bi-adrenergenic-receptor (atenolol).[22]

To bring heart rate upto normal level is the main aim of this treatment.[32] Treatment results in tachycardia-intervened of the respective ventricular unevenness to increase, although the inotropic impacts of thyroid hormones are persevere.[49] The rapid onset of propranolol activity and following change in neuromuscular, cardiovascular and mental aspect of hyperthyroidism reveals that it should be given to most of the patients having unmistakable demonstrations. The complications caused by β-adregenic-receptor rival include asthma and albeit obstructive lung sickness. So, the decisive treatment can be accomplished by iodine-131 separately or by mixing with anti-thyroid medications.[39]

Subclinical Hyperthyroidism

Collet et al. elaborated that according to analysis of hyperthyroid patients the accommodations in cardio-vascular hemodynamics are considered in few but not in all.[50] Due to β-adrenergic-receptor rival treatment complications are developed like extension in heart rate as well as enhancement in left ventricle although positive inotropic reaction perseveres.[46] Patients having

hyperthyroidism lead to elevated level of atrial fibrillation.[51] Elderly people having a couple of alterations might give unexplained tachycardia or aggravations in cardiovascular musicality.[52] In patients having increased heart rate, systolic hypertension, atrial fibrillation, late onset of angina and ischemic heart disease the serum thyrotropin should be checked.[53]

Hypothyroidism

Hyperthyroidism and hypothyroidism share only few symptoms while other hemodynamic changes are opposite to each other. Most commonly identified signs include gentle hypertension, bradycardia, limited pulse pressure and debilitate movement examined by precordial analysis. The other trademark still non-specific inventions include elevated serum levels of creatine kinase and cholesterol (CK-MM isoform).[54] Patients with long lasting hypothyroidism have developed non-spitting edema and pericardial radiations.[55]

Lymvaioset al. explained that lowering of heart contractility, reduction in ventricular filling, less cardiovascular yield is commonly brought out by bradycardia. Resistance in systemic vascular system increases upto 50 percent.[56,57] The filling and diastolic unwinding is quite slow.[50] Heart disappointment is unusual and inspite of the fact that cardiovascular yield is normally appropriate to take care of requirement for fringe oxygen delivery.[40] Oxygen utilization in hypothyroid people is analyzed by positron-discharge tomography and it suggested that proficiency of myocardial work is less than in ordinary individuals. About 10-25% patients have diastolic hypertension and in it heart workload increases and vascular resistance also expands.[35]

However, hyperthyroid patients have uncommon ventricular ectopy and normal albeit atrial arrhythmias while hypothyroidism is antagonistic to it.[36] Hypothyroidism draw out QT interim and potential of cardiovascular system thus, this predispose the patients to ventricular touchiness and uncommonly acquire torsade de points.[52] These developments might appear at any rate to some range from administrative effect of triiodothyronine on statement of various particles directs in the heart.[57] All cardiovascular alterations of hypothyroidism are turned around by the thyroxin treatment.[58] Young individuals who have no confirmation of prevalence of coronary illness can be treated by giving dosage of thyroxin at early stage.

In older patients who either have suspected or known ischemic coronary illness should be treated with 25% of anticipated substitution measurement. The dosage should be increased in stepwise way after 6 to 8-week intervals.[59] During the investigation of hypothyroid individuals it is examined that patients have alteration in angina symptoms and rare occurrence of myocardial localized necrosis and angina at the initial stages of hormonal treatment.[46] The following discoveries strengthen the conceivably and essential aspects of thyroid hormone in influencing the efficiency of myocardial oxygen usage and also bring down the systemic vascular resistance.[10]

Subclinical hypothyroidism is 7-10% occur in most established ladies as a result the cardiovascular capability is less set apart then other patients with plain hypothyroidism. The diastolic and systolic contractility expanded when patients are treated with thyroxin.[60]

Due to relation of hypertension and hypercholesterolemia hypothyroid patients are characterized with rapid onset of atherosclerosis and coronary conduit malady.[37] However the exact proof of effects of plain hypothyroidism is deficient. According to an experiment conducted in 1149 postmenopausal females in Netherland and they may have elevated level of calcification in aorta and myocardial necrosis as checked in their background.[45] Whether the patients with hypothyroidism deal with this treatment is a topic of contradiction and in heart point of view this treatment has more advantages than risks.[47]

Thyroid function that coexist with heart disease

Depending upon chronic or severe heart diseases the thyroid hormone metabolism alters as well as in patients having non-thyroidal disorders. For example, the serum triiodothyronine level reduces up to 20% and serum free triodothyronine level is 40% in patients having myocardial infarction consisting of base after the fourth day of infarction.[61]

Evaluation of functional classification by New York Herat Association (NYHA) suggested that patients having heart malfunction leads to less serum triiodothyronine level and reduction is relative to stage of heart failure.[53] After the prospective study of 112 individuals by NYHA from class 2 to 4 of heart collapse it was resulted that 9% people have hypothyroidism, 6% have subclinical hypothyroidism and 31% have less serum triiodothyronine level.

In patients with heart failure the mechanism of changes in thyroid hormone metabolism help in obstruction of cardiovascular system is still unknown. This issue is described in two studies. In first case with complex heart failure 23 patients are given a single intravenous dose of triiodothyronine up to 58ug and after 2 hours of administration it will boost up the output of heart, reduce the systemic vascular hindrance and eliminating the myocardial ischemia.[62] In second case 20 patients having persistent heart failure are given with 0.1 mg of thyroxin for twelve weeks and enhance the cardiac index and lessen vascular resistance.[63]

Less concentration of triiodothyronine in serum in patients having non-thyroidal illness can alter the cardiac functioning and demonstration of cardiac genes.[55] For dealing this issue in animals the systolic and diastolic function of left ventricle is checked in which less serum level of triiodothyronine has been persuaded by caloric restriction.[64] Proper substitution

of doses of triiodothyronine influence the function of left ventricle and also normalized the expression of respective genes thus, giving the verifications of replacement of triiodothyronine for the amelioration of heart contractility in patients without thyroidal illness.[54] In an open label study out of 68 patients some have been treated by providing endogenous triiodothyronine when they have aortic cross-lump and some were suffering from coronary artery bypass are also given triiodothyronine treatment before surgery.[57]

Out of 142 individuals those who have been given with intravenous triiodothyronine during 24 hours after surgery by providing dose of 1.4ug/kg had lower systemic confliction and an elevated cardiac output. Analysis of following study suggested that after four days of surgery the incidence of atrial fibrillation becomes lower in patients however, in 73 individuals postoperative mortality has not been altered.[65]

Similar results also come from another study in which 211 patients were analyzed. In it dopamine or triiodothyronine were compared with placebo and ultimately there were no changes in outcome.[56] Triiodothyronine management had no any unfavorable impacts in these studies.[62] In children who are undergoing the bypass surgery for the enhancement of congenital heart disorders the triiodothyronine level in serum falls up to 60 percent and keeps it lower after eight days of surgery.[52] In those children who have more complicated procedures of surgery the decrease become more expanded.[59] Pharmacologic assessment of 28 children indicated that if they are given triiodothyronine in postoperative way the concurrence of hormone from circulation is immediate than anticipated from studies of normal children.[66] Infants suffering from cardiopulmonary bypass are studied and it reveals that repletion of triiodothyronine can be practiced safe and sound and it also improve cardiac functions.[67] Children having innate heart disorders are given with triiodothyronine to restore serum level to normal, cardiac output is increased up to 20% after vascular conflict and surgery and it reduced by 25% as compared to untreated children.[58]

CONCLUSION

Primary and secondary functions are performed by thyroid hormones on cardiovascular system and heart. Thyroid dysfunction in patients especially in hyperthyroid patients' symptoms showed the prevalence of cardiovascular hemodynamics. So, signs and symptoms occur in cardiovascular diseases indicates the dysfunction of thyroid hormones. Thyroid action is checked by measuring and diagnosing of serum thyrotropin level in patients having cardiovascular disorders. Even subtle fluctuation in the concentration of thyroid hormone as in subclinical hypothyroidism or hyperthyroidism could significantly affect the cardiovascular system.

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