Assessment of renal function using Tc99m-DTPA renal scintigraphy in hyperthyroid patients before and after treatment of hyperthyroidism

Thesis submitted for Partial fulfillment of the MD degree of nuclear medicine

By

Heba Mounir Abdelhamed
Master degree of nuclear medicine

Supervisors

Professor Dr. / **Shawky El-Haddad**
Professor of Radiation oncology and nuclear medicine
Faculty of Medicine
Cairo University

Professor Dr. **/ Saleh Abdo**
Professor of Radioisotope - nuclear medicine
Faculty of Medicine
Cairo University

Professor Dr. / **Shahenda Salem**
Professor of nuclear medicine
Faculty of Medicine
Cairo University

Cairo University
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Dedication

My work is dedicated to:

Soul of my mother

My husband

My children

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First of all and last of all, thanks to ALLAH who was always with me, whose care has supplied me with much strength to complete this work.

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Abstract

The present study indicates that hyperthyroidism regardless the etiology equally affects the renal function in the form of hyperfiltration more than decreased GFR as there was no statistically significant difference in GFR between both groups. In this study; the mean GFR in both groups was in the high normal range before treatment (133 ± 15 and 138 ± 23 in group1 and group2 respectively) that decreased in the post treatment state but still also in the normal range (110 ± 7 and 114 ± 18 in group1 and group2 respectively) the decrease in GFR before and after treatment is statistically significant with p value <0.005 In this study, there was no significant influence to the type of treatment on the GFR Also the study revealed that Tc99m DTPA renal scan can detect early changes in the kidney especially hyperfiltration status as this condition can be missed by serum BUN and serum creatinine In this study the results of TSH receptor autoantibodies (TRAb) assay revealed that; in the group 1: 28(93.3%) patients had antibodies >1.5 U/L and 2(6.7%) patients had antibodies <1 U/L. So the test confirmed the initial diagnosis in 93.3% of patients. In the group 2: 26 patients (86.6%) with antibodies <1 U/L and 4 patients (13.4%) with antibodies >1.5 U/L. So according to this result we divided the group 2 patients into; (86.6%) pure toxic multinodular goiter and (13.4%) multinodular Graves' disease.

Key word

GFR- Tc99m-DTPA- hyperthyroidism- scintigraphy

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INTRODUCTION

Hyperthyroidism includes diseases that are a subset of thyrotoxicosis that are caused by excess synthesis and secretion of thyroid hormones by the thyroid gland **(Mittra et al 2008**). The overall incidence of hyperthyroidism is estimated between 0.05% and 1.3%, with the majority consisting of subclinical disease. **(Sisson et al 2011**)

The most common forms of hyperthyroidism include diffuse toxic goiter (Graves' disease) represents 80-90% of all causes of thyrotoxicosis in different regions of the world **(Douglas et al 2010)**

Toxic multimodal goiter is the second most common cause of hyperthyroidism in the Western world, after Graves's disease. (**Lado-Abeal et al 2008).**

Thyroid hormones in normal physiological condition stimulate various metabolic activities of most tissues. **(Dumont et al 2011)**

Hyperthyroidism and hypothyroidism induce significant changes in the function of different organs. The kidney is one of these organs, which is influenced by thyroid status. Many physicians studied the effect of hypothyroidism on renal function but there are little studies on the effect of hyperthyroidism on GFR in human compared to that which done on animals **(Hollander et al 2005)**

Hyperthyroidism results in increased RBF and GFR, the effect of thyroid hormones on RBF and GFR occurs at multiple levels, among the pre-renal factors, thyroid hormones increase the cardiac output by positive chronotropic and inotropic effects as well as a reduction in systemic vascular resistance; this indirectly contributes to an increase in RBF. There

is an increase in endothelial of nitric oxide (NO) in the renal cortex and medulla by induction of nitric oxide synthase, directly by the thyroid hormones. This is accompanied by a reduction in renal vasoconstrictor endothelin. Thus, an increased intrarenal vasodilatation and decreased vasoconstriction ensues, contributing to a net increase in RBF. **(Basu and Mohapatra 2012)**

The GFR increases by about 18–25% among hyperthyroid patients; this improvement in GFR is not solely due to an increased RBF. The activation of renin – angiotensin – aldosterone system (RAAS) also contributes to the increase in GFR **(Mariani and Berns 2012)**

Hyperthyroidism can result in chronic kidney disease (CKD) by several mechanisms. Firstly, hyperthyroidism results in intra-glomerular hypertension (increased filtration pressure) and consequent hyperfiltration. Secondly, hyperthyroidism predisposes to proteinuria, which is known to cause direct renal injury. Thirdly, hyperthyroidism-induced increased mitochondrial energy metabolism along with down-regulation of superoxide dismutase contributes to the increased free radical **2012** generation and consequent renal injury. The increased RAAS activity can accelerate renal fibrosis. **(Basu and Mohapatra 2012)**

GFR is widely accepted as the best index of kidney function in health and disease and accurate values are needed for optimal decision making in many clinical settings. There are two methods for GFR evaluation:

1-Estimated GFR based on endogenous substances example; serum creatinine is now widely reported by clinical laboratories.

2-Measured GFR using urinary or plasma clearance of exogenous filtration markers. **(Stevens and Levey 2009)**

In general gamma camera techniques using Tc99m DTPA where considered some what less accurate than in vitro measurement in estimating GFR, but gamma camera technique based on an ease performance, reproducible results and proven suitable for clinical renography. While plasma sampling clearance tests are more time consuming and much attention to in vitro technique is needed **(Gates 2006)**

AIM OF WORK

The aim of the study is the use of Tc99m DTPA renal scintigraphy in evaluation of the effect of hyperthyroidism on renal GFR with detection if there is difference in this influence between Graves' disease and toxic multinodular goiter, as a two main causes of hyperthyroidism. Also evaluation of GFR values before and after treatment.

ANATOMY AND PHYSIOLOGY OF THYROID GLAND

The thyroid is a butterfly-shaped organ highly vascular, brownish-red gland located anteriorly in the lower neck, extending from the level of the fifth cervical vertebra down to the first thoracic. The gland varies from an H to a U shape and is formed by 2 elongated lateral lobes with superior and inferior poles connected by a median isthmus, with an average height of 12-15 mm, overlying the second to fourth tracheal rings. Occasionally, the isthmus is absent, and the gland exists as 2 distinct lobes**. (Colledge et al, 2010)**

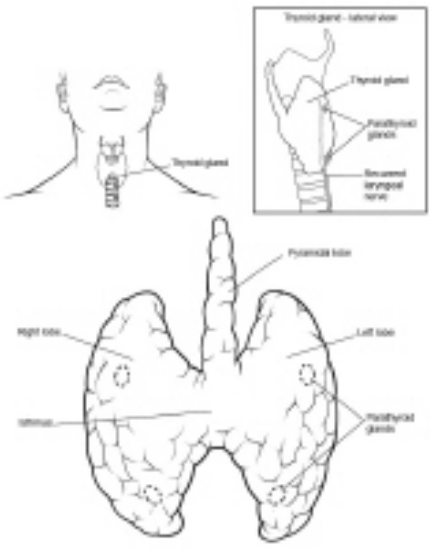

Figure (1): Thyroid gland anatomy

Each lobe is 50-60 mm long; the lower poles diverge laterally at the level of the fifth tracheal cartilage. Although thyroid weight varies, it averages 25-30 gram in adults (it is slightly heavier in women). The gland enlarges during menstruation and pregnancy. A conical pyramidal lobe often ascends from the isthmus or the adjacent part of either lobe (more often the left) toward the hyoid bone, to which it may be attached by a

fibrous or fibromuscular band. Remnants of the thyroglossal duct may persist as accessory nodules or cysts of thyroid tissue between the isthmus and the foramen caecum of the tongue base. Usually, 2 pairs of parathyroid glands lie in proximity to the thyroid gland. **(Andreoli et al, 2010)**

The main function of thyroid gland is the thyroid hormones synthesis; the synthesis of the thyroid hormones depend mainly on iodine which forms 65% of the product that is released into the blood stream**. (Moreno et al, 2008)**

Adult requires 150 microgram per day to replace the iodine lost from the body, mainly in the urine. In the alimentary tract; dietary iodine is converted into iodide which is readily absorbed from the stomach and upper part of the small intestine. Iodide is concentrated within the thyroid and several other tissues, normally in man the thyroid/serum iodide ratio is about 50/1. The iodine pump mechanism is located in the peripheral border of the follicular cells, the thyroid contains very little free iodide because iodide is very rapidly oxidized to iodine, a reaction depending on a peroxidase enzyme system in the follicular cells. The active iodine then combines with residues of the amino-acid tyrosine in the thyroglobulin (TG) at the periphery of the follicles. The compounds formed by the iodination of tyrosine are moniodotyrosine (MIT) and diiodotyrosine (DIT). Thyroxin (T4) is formed by the coupling of pairs of DIT molecules, while triiodothyronine (T3) by the coupling of MIT and DIT molecules. During synthesis and subsequent storage in the colloid T4 and T3 are bound to thyroglobulin. The hormones are liberated by the action of a proteinase system, which hydrolyses the peptide linkages of the thyroglobulin, and are then released into the circulation**. (Song et al, 2010)**

Control of thyroid activity

The most important regulator of thyroid function is thyroid stimulating hormone (TSH), which rapidly increases the rates of release and synthesis of thyroid hormones and stimulates the growth of the gland. The increase in secretion is almost immediate after binding to follicular cells TSH receptors; TSH activates adenyl cyclase that involved in the formation of cyclic 3', 5'-(AMP) Adenosine monophosphate. The latter then stimulates iodine trapping, iodination of tyrosine, iodothyronine synthesis, and release of the thyroid hormones, the activity of the TSH-secreting basophil cells in the pituitary gland is controlled by thyrotrophin releasing factor, which is secreted from the hypothalamus and reaches the pituitary gland via the pituitary portal vessels. So the level of TSH depends on the secretion of thyrotrophin releasing factor which depend on many factors; the most important one is the concentrations of free thyroid hormones in the circulation. **(Moreno et al, 2008)**

Over 99% of the thyroxine and triiodothyronine in the blood are bound to protein, mainly to thyroxine-binding globulin (TBG); this portion of thyroid hormones is inactive. The concentration of free T4 in the circulation is about three times that of T3, the most amount of T3 is formed due to peripheral conversion of T4. **(Moreno et al, 2008)**

Thyroid hormones stimulate various metabolic activities of most tissues, leading to an increase in basal metabolic rate. **(Dumont et al, 2011)**

Normal levels of thyroid hormone are essential to the development of the fetal and neonatal brain, in addition to normal child growth**.** **(Dumont et al, 2011)**

Effects of thyroid hormones on renal physiology

Thyroid hormones affect renal function by both pre-renal and direct renal effects:

1-Pre-renal effects are mediated by the influence of thyroid hormones on the cardiovascular system and the renal blood flow (RBF) **(Pothiwala and Levine 2010)**

2-The direct renal effects are mediated by the effect of thyroid hormones on glomerular filtration rate (GFR), tubular secretion and re-absorption processes**. (Fernandez-Reyes e t al. 2010)**