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Research Article

Effect of Hypothyroid State on Bone Metabolism and Renal Handling of Biochemical Parameters

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Abstract: Thyroid hormones (TH) are essential for a proper growth and development of the kidney. Hypothyroidism is one of the most common thyroid dysfunction causing remarkable changes in glomerular and tubular functions and electrolyte and water homeostasis. Hypothyroidism is found to be associated with decreased glomerular filtration, hyponatremia, and an alteration of the ability for water excretion. In turn, renal disease leads to significant changes in thyroid function. The present study was done to see the effects of hypothyroid state on body. This case-control study included total of 35 females and 15 males in the age group of 19-45years. The results were compared with 50 age and sex matched healthy controls. Patients suffering from hepatic disorders, renal disease, hyperthyroidism, any chronic illness and pregnant females were excluded from the study. All routine renal parameters were estimated in serum samples of these 50 newly diagnosed patients of hypothyroidism. The patients of hypothyroidism were found to be suffering from hyponatremia 68%, hypokalemia 37% and hypocalcemia 71%. It was also observed that the levels of urea, magnesium and creatinine were raised significantly as compared to controls. It was concluded that hypothyroid state is associated with marked derarrangements in biochemical as well as various endocrine and bone metabolic parameters. Therefore, regular monitoring of these parameters is important in patients of hypothyroidism.
Keywords: Thyroid Hormones, Hypothyroidism, Hyponatermia, Hypokalemia, Hypocalcemia.

INTRODUCTION

Thyroid hormones (TH) affect nearly every system of body including kidney. The interplay between kidney and thyroid in each other's functions is known for many years and. They are essential for the normal growth and development of the kidney, for the maintenance of water and electrolyte homeostasis. On the other hand, kidney is involved in the metabolism and elimination of TH, also a target organ of some of the iodothyronine's action especially T_3 [1, 2]. Hypothyroidism is found to be accompanied by a decrease in glomerular filtration, hyponatremia and an alteration in water excretion. The declined kidney function is accompanied by changes in the synthesis, secretion, metabolism, and elimination of TH. TH influence protein synthesis and cell growth. TH status affects the functional renal mass as hypothyroidism reduces kidney to body weight ratio by unclear mechanism. TH plays an important role during early embryogenesis. Children with congenital hypothyroidism are found to have increased prevalence of congenital renal anomalies. Severe hypothyroidism also results in protein break down and eventually renal atrophy [3-5]. Perinatal thyroid hormone status affects the mitochondrial energy metabolic enzymes in the cells of proximal convoluted tubules [6, 7]. Hypothyroid state is associated with slowing of metabolism and electrolyte and mineral disturbances, as there was much debate about effect of hypothyroidism on bone metabolism therefore, the present study was planned to study the bone metabolism along with the underlying mechanisms for the renal handling of biochemical parameters in hypothyroidism.

MATERIALS AND METHODS

It was a case control study conducted in Department of Biochemistry in Pt. B.D.S. PGIMS, Rohtak. The population of study was recruited from 19 – 45 year old patients who were suffering from hypothyroidism. To evaluate the effects of hypothyroid state a total of 50 patients suffering from hypothyroidism, out of which 35 were females and 15 were males formed the study group.50 age and sex matched healthy persons were included in control group. Patients suffering from hepatic disorders, renal disease, hyperthyroidism, any chronic illness and pregnant females were excluded from the study. All routine renal parameters were estimated in serum samples of these 50 newly diagnosed patients of hypothyroidism and healthy control persons using standard techniques.T3 and T4 were estimated by RIA and TSH by IRMA. Renal parameters were evaluated on Trivitron Konelab30i Autoanalyzer using Erba kits. Electrolyte estimation was done on Eschweiler

Combiline electrolyte Analyzer. The results were compared with the results obtained from healthy controls. Statistical analysis was done by using Student's t-test.

RESULTS

A total of 50 patients suffering from hypothyroidism, out of which 35 were females and 15 were males formed the study group. 50 age and sex matched healthy persons were included in control group. The mean age was found to be 38.14±12.31 in the hypothyroid patients and 39.02±13.57 in the controls. The T_3 and T_4 levels in patients of hypothyroidism were found to be significantly decreased ($p<0.001$) as compared to controls, whereas the level of TSH was significantly higher ($p<0.001$) in the hypothyroid patients as compared to controls (Table 1).

Table 1: Levels of Thyroid hormones in patients of hypothyroidism and healthy controls

Thyroid Hormones	Controls	Hypothyroid Patients	p value
T3 (ng/dl)	124.26±8.53	88.76 ±6.53	<0.001
T4 (µg/dl)	8.56±1.58	5.17±0.76	<0.001
TSH(µlU/ml)	2.76±0.43	6.86±1.16	<0.001

In this study the levels of Serum sodium and calcium in hypothyroid patients were found to be significantly decreased and magnesium levels were significantly increased (<0.001) whereas urea, creatinine and phosphate significantly increased ($p<0.05$) as compared to controls. Serum Potassium was decreased and uric acid levels were increased non significantly in hypothyroid patients as compared to controls ($p>0.05$) (Table 2).

Table 2: Renal parameters in patients of hypothyroidism and healthy controls

Parameters	Controls	Hypothyroid Patients	p value
Sodium(meq/L)	144.03±12.17	124.13±10.63	<0.001
Potassium(meq/L)	5.31±1.04	2.93±1.67	>0.05
Magnesium(mg/dL)	1.25±0.31	2.17±0.29	<0.001
Calcium(mg/dL)	8.76±1.26	6.78±1.49	<0.001
Phosphate(mg/dl)	3.73±1.95	7.50±2.53	<0.05
Blood Urea(mg/dL)	29.0±8.21	53.53±12.72	<0.05
Serum Creatinine (mg/dL)	0.81±0.19	1.52±0.39	<0.05
Uric Acid(mg/dL)	5.35±1.13	6.78±1.33	>0.05

DISCUSSION

As mentioned in table II serum sodium was significantly decreased ($p<0.001$), whereas potassium levels were decreased non significantly ($p>0.005$) in hypothyroid patients as compared to controls. From our study it was observed that the patients of hypothyroidism are suffering from hyponatremia (68%) andhypokalemia (37%). As TH affect tubular transport of sodium via action on sodium potassium ATPase pump and they also affect potassium permeability in proximal tubules.The principle abnormality appears to be inability to maximally suppress vasopressin (antidiuretic hormone or ADH) with normal fluid intake. Hypothyroidism causes a reversible increase in sensitivity of the collecting ducts, thus increasing free water reabsorption. The increased fluid retention, however, may not maximally suppress ADH in hypothyroidism [8, 9]. The resistance of pituitary response to increased fluid retention leads to continued ADH activity and further free water retention. Hypothyroidism results in low cardiac output which triggers the carotid baroreceptors and consequently increases the non-osmotic ADH secretion [10]. Glomerular filtration is also decreased causing diminished water delivery to the diluting segments. There is decreased sensitivity to β-adrenergic stimulus and decreased renin release along with decreased angiotensin II and resulting in loss of GFR. Also there is a structural constraint imposed by limited glomerular surface area for filtration due to renal parenchymal growth retardation in hypothyroidism. There is a reduced proximal tubular absorption and the net effect is impairment in water excretion and reduction in plasma sodium concentration by dilution [11].

Katyare *et al*. [12] conducted study on thyroidectomized rats and observed that tubular reabsorption of Na per gram of kidney tissue in rats was the lowest in thyroidectomized rats than in controls and was accompanied by a similar reduction of the specific activity of the Na-K ATPase pump. They also found that of the Na-K ATPase pump activity increased when the reabsorption of Na increased in euthyroid rats treated with triiodothyronine (T_3). Schwarz C *et al*. [13] in their study found that serum sodium was significantly lower in patients with high TSH levels that is cases. Also hypokalemia was more common in the group with elevated TSH which is in accordance to our study which states that serum sodium and potassium was lower in hypothyroid patients as compared to controls.

The hypothyroid patients in our study found to have significantly elevated levels of serum magnesium compared to the controls. McCaffrey *et al*. studied renal Calcium and Magnesium handling in rats with chronic thyroid hormone deficiency. According to their study thyroid deficient rats reabsorbed 15-30% more of the filtered magnesium at any given plasma concentration because the thyroid hormone has a direct effect on the tubule reabsorption and decreased level results in renal retention of magnesium [14]. As thyroxine normally regulates blood calcium levels by releasing calcium from the cells therefore in the hypothyroid state less calcium is realeased [15].

Hypocalcemia in hypothyroidism may also be due to the direct stimulation of bone resorption by TH. Hypothyroid state also cause decreased cortical osteoclastic resorption, decreased turnover of skeletal calcium and increased urinary excretion of calcium. TH modifies the size of calcium compartment and rate of flow to and from these compartments. As it occurs with sodium the reduction of TH activity at kidney level is accompanied by a decrease in the absorption of calcium at tubular levels. Decreased calcium levels may cause reciprocal rise of phosphate. Al Tonsi *et al*. [17] in their study found a significantly elevated phosphate levels in the hypothyroid patients which is in accordance to our study showing the same results. Further investigations in this field will provide new sights in our understanding of the biological significance of thyroid hormone changes on calcium and phosphate levels [16, 17].

In our study the levels of urea and creatinine were found to be raised significantly. Uric Acid levels were also increased. The mechanisms involved in hypothyroidism-associated kidney derangements are direct effects of TH on the cardiovascular system in the form of increased peripheral resistance and reduction of myocardial contractility and stroke volume and indirect effects through paracrine or endocrine mediators, such as insulin-like growth factor type 1 (IGF-1) and vascular endothelial growth factor whose expression is decreased [3, 18]. In hypothyroidism there is the generalized hypodynamic state of circulatory system resulting in decreased renal plasma flow and GFR which affects permeability across glomerular membrane leading to these effects. Finally different studies have shown that TH act on the regulation of kidney dopaminergic system [19, 20]. Elevation of serum creatinine develops rapidly and appears to be reversible in hypothyroidism. In our study the increased creatinine was found to be directly proportional to TSH levels. Therefore, evaluation of thyroid function may be useful in patients with isolated increased serum creatinine levels [21].

CONCLUSION

Renal and thyroid functions are interrelated through several mechanisms. The above results of our study showed that hypothyroidism is associated with significant derangements in biochemical parameters of renal function. The monitoring of renal function is important in patients of hypothyroidism and our study covers all the biochemical and bone metabolic aspects of the hypothyroid state. We would like to further extend our study to a large population to see the importance of electrolytes and minerals in the metabolism of thyroid hormones.

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