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Hypertension in Hypothyroidism, A Response to Replacement Therapy With L-Thyroxine

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ABSTRACT

Objective: To study the association between hypertension and hypothyroidism and to see effect of thyroxine therapy on blood pressure after giving 6 months therapy

Patients and Methods: Hundred female patients enrolled in this study were selected from one hundred thirty four patient consulted the OPD and IPD of Rohilkhand medical college and hospital, Bareilly between period from January 2016 to August 2016 and presented with features of hypothyroidism. Each patient was interviewed, examined for body mass index and blood pressure measurements. Thirty four patients were excluded from the study fasting blood samples were analyzed to determine FT3, FT4, TSH and total cholesterol levels.

Results: The level of systolic and diastolic blood pressure in overt hypothyroidism in comparison to subclinical hypothyroidism showed a dramatic response to thyroxine replacement. Mean difference (95% CI after treatment with L-thyroxine for systolic (SBP) (16.74-29.09 mmHg) and (10.58-14.91 mmHg) for diastolic blood pressure (DBP) in overt hypothyroidism, while the mean difference (95% CI in subclinical form is (0.68-10.11 mmHg) for systolic (SBP) and (0.78-3.46mmHg) for diastolic (DBP) blood pressure.

Conclusion: Systolic and diastolic hypertension in hypothyroidism is a common association but the response of blood pressure to replacement with thyroxine was significant in overt hypothyroidism in comparison to subclinical hypothyroidism, while only systolic component had responded to replacement therapy in subclinical type.

KEYWORDS

INTRODUCTION

Hypothyroidism has long been considered as one of the secondary causes of hypertension.[1] The role of thyroid hormone in heart and vascular physiology has been investigated since the description of first cardiovascular symptom associated with dysthyroid patients. Arterial hypertension is associated with both hypo- and hyperthyroidism,[2] suggesting different working mechanisms in the two conditions. The most common type of hypothyroidism is that cause by primary thyroid gland failure. One of common clinical signs observed in hypothyroid and hyperthyroid patients is the changes in their blood pressure.[3] Many factors may contribute to these associations. [4,5] Arterial stiffness is an important determinant of arteriosclerosis and changes in arterial wall elasticity, and may occur before or during the early stages of atherosclerosis. Increased arterial stiffness of the central artery leads to an increase in systolic blood pressure but not diastolic part of the cycle of hypertension and this might explain the association between hyperthyroidism and wide pulse pressure but not for hypothyroidism. On the other hand, the increased systolic and diastolic BP could induce changes in the arterial wall, reducing elasticity and increasing stiffness. Adequate thyroid hormone replacement therapy successfully reduced BP, supporting the secondary cause of hypertension in patients with hypothyroidism.[6,7] 3,5,3'-triiodothyronine (T3) represents the metabolically active thyroid agent that possibly has a vasodilatory effect on the vascular muscle cells.[8] T3 deficiency is associated with peripheral vasoconstriction.[9] Thyroid hormones potentiate β-adrenergic response by increasing the number of β- adrenoreceptors with an opposite action on α- adrenergic receptors.[10] In the hypothyroid state, the density of α1-adrenoreceptors is increased while β-adrenoreceptors are reduced in vascular beds. Actions of α1-adrenoreceptors mainly involve smooth muscle cell contraction, causing vasoconstriction in the blood vessels.

Plasma vasopressin is found to be elevated in hypothyroid patients, that may explain the water retention that occurs in hypothyroid subjects.[11] Thyroid dysfunctions can interact with other systems involved in cardiovascular regulations.

In fact beside sympathetic activities, thyroid hormones can increase angiotensinogen,[12] atrial nitreurtric peptide level[13,14] and vasopressin levels.[15,16] More complex is the effects of thyroid hormone on renal function. Hypothyroidism leads to reduction in glomerular filtration rate and to a decrease in renal blood flow.[17,18] High serum prolactin and TSH concentrations, seen in patients with hypothyroidism, suggest a reduced dopaminergic activity in the central nervous system that could contribute to the development of hypertension by enhancing nor-epinephrine release. Normalization of central dopaminergic activity by thyroid hormone replacement therapy could be one factor responsible for reduction in blood pressure in the hypertensive hypothyroid patients.[19,20]

AIMS AND OBJECTIVES

- The study is to find the association between hypertension and hypothyroidism.
- To see the effect on blood pressure after 6 months of thyroxine therapy.

MATERIAL AND METHODS

This is a prospective cross sectional study carried on hundred elected patient who consulted Rohilkhand medical college and hospital, Bareilly between period from January 2016 to August 2016.

INCLUSION CRITERIA
134 female patients , age range from 15 to 58 years, with a mean 39 years were included in this study

EXCLUSION CRITERIA
Male patients, and patients with diabetes, ischemic heart disease, renal disease, smoker, pregnant women and morbidly obese were excluded.

34 patients were excluded from the study.
Each patient was subjected to full history and clinical examination including single observer arterial blood pressure measurement in seated position in both hands after five minute rest and elbow was slightly flexed and the highest result is considered abnormal using mercury type sphygmomanometer. Blood pressure of 140mm Hg or was considered abnormal for systolic (SBP) and equal or more than 90 mm Hg was considered abnormal for diastolic (DBP).

Anthropometric measures were made with the patients wearing light weight clothes with no shoes height. Body mass index (BMI) was calculated as weight in kilogram over squared height in meters. Serum concentration of TSH, free T4 and free T3 were measured using an automated immunoassay analyzer. Total cholesterol, was measured using standard techniques. All patients measurements were done in fasting state at baseline and after 6 months of thyroxine replacement therapy.

Patients were classified in two groups;
Group A: Those with high level of TSH and significantly low FT3 and FT4.

Group B: Those patients with slightly elevated TSH and normal FT3 and FT4.

All patients in both groups received full dose of thyroxine in gradually building doses with informed consents.Patients were followed at monthly intervals and interviewed for symptoms. Recording of blood pressure and TSH estimations were made for six months and the final blood pressure record was considered the end result of the study. Data were fed on a computer and analyzed using the Statistical Package for Social Sciences.

The mean±SD was computed for comparing the results.The distribution of cases among various criteria was presented by their percentage. The comparison of means between two groups was tested by paired t-test. Results were considered statistically significant if P-value is less than or equal to 0.05.

RESULTS
Patients physical characteristics and anthropometric measures were presented in (Table-1). No difference between the two groups was found as they were carefully matched in physical criteria. Participants in this study belong to female gender as the disease is more common in female patients on one hand and male patients are excluded from study to exclude sex effects on blood pressure on the other hand.

Table 1.General characteristics of the study subject.

Variable	Group 'A' (n=50)	Group 'B' (n=50)	P-value
Age (Years)	39.00±9.07	40.61±9.13	0.523
Sex (female)	100%	100%	-
Body mass index (kg/m2)	30.96±6.83	33.58±4.73	0.106

Body mass index and age were matched for the same reasons. Overt hypothyroidism group showed markedly elevated TSH and suppressed FT3 and FT4 levels in comparison to marginally elevated TSH and normal levels of FT3 and FT4 in subclinical group (Table-2).

Table 2. Comparison of laboratory results between overt and subclinical hypothyroid groups.

Variable	Group 'A' (n= 50)	Group 'B' (n=50)	p-value
TSH (m.IU/L)	137.2 ±107.37	5.17 ±1.20	0.000
FT4 (IU/L)	2.09 ±2.16	4.26±0.42	0.000
FT3 (IU/L)	2.56 ±4.03	1.24 ±0.24	0.000
T.cholesterol (mg/dl)	210.5 ±36.5	200.2 ±40.2	0.1833

Total cholesterol levels were marginally increased in both groups, though statistically was not significant.

Both groups: overt group (A) and subclinical hypothyroidism group (B) showed an increase in systolic and diastolic blood pressure when first interviewed (Table-3) though overt hypothyroidism demonstrated diastolic and systolic predominance over subclinical group but it did not reach statistical significance.

However, the study demonstrated dramatic response of blood pressure in group A to replacement with thyroxine in both systolic and diastolic components (p-value <0.05). In comparison to the response of systolic component only in group B. However this difference was not statistically significant

Table 3.Comparison of mean systolic and diastolic blood pressure between overt and subclinical groups before and after thyroxine therapy.

Variable	Group 'A' (n= 50)	Group 'B' (n=50)	p-value
Diastolic B.P before(mmhg)	93.37 ± 4.28	91.50 ± 6.28	0.0850
Diastolic B.P after(mmhg)	80.62 ± 6.42	90.16 ± 4.24	0.000
Sysstolic B.P before(mmhg)	152.24 ± 14.52	144.32 ± 12.48	0.0043
Sysstolic B.P after(mmhg)	129.32 ± 16.54	138.92 ± 11.23	0.001

DISCUSSION
The main purpose of this study is to investigate the relationship between hypothyroid status and the blood pressure changes in the absence of known previous cardiovascular, renal disease and morbid obesity. Most of patients showed high reading blood pressure in both systolic and diastolic components and the increased in either systolic or diastolic component in minority of patients. This gives a strong evidence in that the clinical state of hypothyroidism is strongly associated with hypertension. Additionally, only patients without previous systemic diseases to reduce the effect on blood pressure as it is adversely affected by many systemic conditions or their therapy. The main finding in this study is that thyroid hormone replacement in highly deprived patients in overt hypothyroidism resulted in a dramatic response of both systolic and diastolic blood pressure which paralleled the clinical improvement. This gives a clue to the importance of thyroid hormones in reducing blood pressure, which is regarded as one of important secondary causes of hypertension. The mechanisms underlying this response are not fully understood, but increase in systemic\ vascular resistance (SVR) and arterial stiffness may accompany low thyroid function.[4,5,8] It has\ been shown that the thyroid hormone have direct vasodilator effect on vascular muscle cell.[7] On the other hand the response of only the systolic component of blood pressure which was statistically not significant and the absence of response in diastolic component in subclinical hypothyroidism, might support the fact that in this type, the patients are not actually deprived from thyroid hormones and the replacement, though full, does not produce dramatic result in decreasing the blood pressure. It might also support the possibility of other factors that may play a role such as hypercholesrolemia and hyperprolactinemia. [19,20] In the

Colorado study, total cholesterol levels were higher in subjects with subclinical hypothyroidism.[21] However no difference in total cholesterol in our subjects was found among groups suggesting qualitative changes that may include small density lipoprotein which is recognized to be proatherogenic. Thyroxine may modify cardiovascular risk and blood pressure through changes in lipid architectures.[22] This may explain the partial improvement in the subclinical type. This study in comparison with other studies showed close association between the replacement with L.thyroxine and blood pressure response in overt hypothyroidism, However, others have failed to demonstrate any association between blood pressure and subclinical hypothyroidism.[23]

Conclusion:

A parallel reduction of both systolic and diastolic blood pressure in overt hypothyroid patients was found after starting thyroxine therapy in recommended doses. This did not occur in patients with subclinical hypothyroidism. A large controlled trial may be needed to study whether the first group will continue in improvement or not.

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