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ORIGINAL ARTICLE

Effect of Levothyroxine Therapy on Hypothyroidism-induced Dyslipidemia

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ABSTRACT

Objective: The aims of the present study were to determine the prevalence of hypothyroidism, both subclinical hypothyroidism (SH) and overt hypothyroidism (OH), its correlation with dyslipidemia, and whether replacement therapy with levothyroxine has an effect on plasma lipid profile, i.e., total cholesterol (TC), triglyceride (TG), low-density lipoprotein (LDL), high-density lipoprotein (HDL) of hypothyroid patients.

Materials and methods: A prospective, open-label, observational, clinical study was conducted by the Department of Pharmacology in collaboration with the Department of Medicine, Rohilkhand Medical College & Hospital, for a period of 10 months. A total of 50 patients, age 18 to 65 years, of both genders, who were newly diagnosed cases of hypothyroidism with dyslipidemia (Adult Treatment Panel III National Cholesterol Education Program guidelines) were recruited for the study. Levothyroxine replacement therapy was administered and the patients were reassessed at 6 and 36 weeks for an effect on lipid profile and body mass index.

Results: In cases of OH, baseline TC, TG, LDL, and HDL were 231.01 ± 27.84, 148.18 ± 10.72, 149.07 ± 12.38, and 35.42 ± 6.73 mg/dL, which was reduced to 177.33 ± 23.17, 123.15 ± 29.50, 118.44 ± 29.85, and 47.86 ± 8.53 mg/dL after 36 weeks of levothyroxine therapy ($p < 0.05$).

Conclusion: In cases of OH associated with dyslipidemia, levothyroxine therapy achieved a favorable lipid profile in significant number of cases.

Keywords: Dyslipidemia, Hypothyroidism, Levothyroxine therapy.

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INTRODUCTION

Thyroid hormones play a pivotal role for normal growth and development. These have marked effect on lipid, carbohydrate, and protein metabolism. Triiodothyronine (T_3) and thyroxine (T_4) increase basal metabolic rate by stimulating cellular metabolism and resetting of the energy stat. Besides, thyroid hormones also govern some important functions in the physiology of cardiovascular system, gastrointestinal system, skeletal system, hematopoietic system, and reproductive system.

Dysfunction of thyroid hormone secretion can present as hypothyroid or as hyperthyroid state. Hyperthyroidism means the disorders resulting from the overproduction of T_3 and T_4 by the thyroid gland itself, while thyrotoxicosis results from ingestion of excessive quantities of thyroid hormone (e.g., while treating hypothyroidism) rather than from overactivity of the thyroid gland.[1]

Hypothyroidism is a syndrome resulting from deficiency of thyroid hormones. Hypothyroidism in infancy or childhood is commonly known as cretinism, while in older child or adult it is known as myxedema. Patients having low T_3 and T_4 and high thyroid-stimulating hormone (TSH) value than normal have OH and those with normal T_3 and T_4 but elevated TSH level have SH.[2]

Thyroid disease is being increasingly diagnosed with greater awareness and is one of the chronic noncommunicable diseases affecting women more than men. It is estimated that about 200 million people are at risk of iodine deficiency disease in our country.[3] A study was conducted in India in eight major cities, namely Bangalore, Chennai, Delhi, Goa, Ahmedabad, Hyderabad, Kolkata, and Mumbai and the prevalence of hypothyroidism in the overall study population was found to be 10.95%.[4] Another study conducted in Meerut and nearby area (western Uttar Pradesh) also showed a high prevalence of abnormal thyroid hormone levels (OH was 8.2% and SH was 8.4%) with female preponderance.[5] Hypothyroidism accounts for about 2% of all cases of hyperlipidemia and is second only to diabetes mellitus as a cause of secondary hyperlipidemia.[6] Hypercholesterolemia and hypertriglyceridemia are very commonly found in patients of myxedema and in these cases atherosclerosis is accelerated because of hypertension, increased lipids, and reduced level of homocysteine.[1]

It is well known that disorders of the thyroid gland (mainly hypothyroidism) result in changes in the composition and transport of lipoproteins.[7-9] In general, OH and SH are associated with hypercholesterolemia mainly due to elevation of LDL cholesterol levels, whereas HDL cholesterol concentration is usually normal or even elevated.[9-11]

Correction of hypothyroidism rectifies the lipid abnormalities.[12] Thyroxine (levothyroxine sodium) is the hormone of choice for thyroid hormone replacement therapy because of its consistent potency and prolonged duration of action. The daily replacement dose of levothyroxine is usually 1.5 µg/kg (typically 100–150 µg). The dose is adjusted based on the TSH levels, with the goal of therapy being a normal TSH.

Various studies have been done showing the effect of levothyroxine in hypothyroid-induced dyslipidemia.[13-16] But research on this topic is lacking in India, particularly from Uttar Pradesh, so we planned to conduct this study in Rohilkhand Medical College & Hospital, Bareilly, Uttar Pradesh, India, to observe the incidence of hypothyroidism in Rohilkhand region, to assess the incidence of dyslipidemia in cases of OH, and also to evaluate the effects of levothyroxine therapy on plasma lipid profile in these patients.

MATERIALS AND METHODS

A prospective, open-label, observational, clinical study was conducted by the Department of Pharmacology in collaboration with the Department of Medicine, Rohilkhand Medical College & Hospital, for a period of 10 months. Institutional Ethical Committee clearance was sought before the commencement of the study. Informed consent was taken from the patient or his/her guardian.

Inclusion Criteria

A total of 50 patients, age 18 to 65 years, of both genders, who were newly diagnosed cases of hypothyroidism with dyslipidemia [Adult Treatment Panel (ATP) III National Cholesterol Education Program (NCEP) guidelines] were recruited for the study. Levothyroxine replacement therapy was administered and patients were reassessed at 6 and 36 weeks for an effect on lipid profile.

Exclusion Criteria

Presence of history of any other acute or chronic disease that would affect the study variables (diabetes mellitus, hypertension), pregnant and lactating females, child-bearing age group females using oral contraceptive pills, significant renal and liver disease, normal thyroid profile, postmenopausal women receiving hormone replacement therapy, patients receiving antihyperlipidemic drugs, and patients of thyroid carcinoma were excluded from the study.

Patients showing signs and symptoms of hypothyroidism were enrolled. Confirmed cases of OH showing high TSH and low T_3 and T_4 than normal were further evaluated and blood samples of these patients were drawn aseptically after 12 hours overnight fasting for lipid profile pertaining to TC, TG, HDL, and LDL. Levothyroxine replacement therapy was administered and patients of OH were reassessed at 6 and 36 weeks for an effect on lipid profile. Statistical analysis was done using paired t-test to evaluate the changes in lipid parameters before and after the initiation of levothyroxine therapy.

OBSERVATION AND RESULTS

During 10 months of study period, the patients were chosen among those attending the outpatient department (OPD) of Medicine of Rohilkhand Medical College & Hospital, Bareilly, Uttar Pradesh, India, and presenting with the clinical manifestations of hypothyroidism. A total of 50 patients, age 18 to 65 years, of both genders, who were newly diagnosed cases of OH with dyslipidemia (ATP III NCEP guidelines) were recruited for the study in which 8 patients dropped out from this study. Among these, the incidence of SH was 62% and that of OH was 38%. Out of 16 cases of OH (5 males and 11 females), greater number of hypothyroid patients belonged to urban population (35.71%) as compared with rural population (2.38%) (Table 1). It was observed that all the 16 patients of OH had associated dyslipidemia.

Table 2 shows that in OH, there was a statistically significant reduction in the mean values of TSH from baseline (68.45 ± 42.07) to first (48.56 ± 33.91) and second (7.42 ± 9.44) follow-up. Similarly, a statistically significant reduction in the mean values of TC from baseline (231.01 ± 27.84) to first (210.36 ± 27.42) and second (177.33 ± 23.17) follow-up is depicted in Table 3. Moreover, a statistically significant reduction in the mean values

Table 1: Distribution of patients of hypothyroidism according to habitat (n = 42)

Habitat	*SH no. (%)*	*OH no. (%)*	*Total no. (%)*
Urban	22 (52.38)	15 (35.71)	27 (64.28)
Rural	4 (9.52)	1 (2.38)	5 (11.90)
Male	10 (38.40)	5 (31.25)	15 (35.71)
Female	16 (61.51)	11 (68.75)	27 (64.28)
Total	26 (61.90)	16 (38.09)	42 (100)

Table 2: Thyroid-stimulating hormone in OH

Baseline TSH (mean ± SD)	*Follow-up TSH (mean ± SD)*	*t-value*	*p-value < 0.05*
68.45 ± 42.07	1st 48.56 ± 33.91	3.57	0.003
68.45 ± 42.07	2nd 7.42 ± 9.44	5.56	0

SD: Standard deviation

Table 3: Total cholesterol in OH

Baseline TC (mean ± SD) (mg/dL)	*Follow-up (mean ± SD)*	*t-value*	*p-value < 0.05*
231.01 ± 27.84	1st 210.36 ± 27.42	8.48	0
231.01 ± 27.84	2nd 177.33 ± 23.17	15.80	0

SD: Standard deviation

Table 4: Triglyceride in OH

Baseline triglyceride (mean ± SD) (mg/dL)	*Follow-up (mean ± SD)*	*t-value*	*p-value < 0.05*
148.18 ± 10.72	1st 130.91 ± 12.69	5.50	0
148.18 ± 10.72	2nd 123.15 ± 29.50	2.74	0.015

SD: Standard deviation

Table 5: Low-density lipoprotein in OH

Baseline LDL (mean ± SD) (mg/dL)	*Follow-up (mean ± SD)*	*t-value*	*p-value < 0.05*
149.07 ± 12.38	1st 133.17 ± 9.09	7.56	0
149.07 ± 12.38	2nd 118.44 ± 29.85	4.33	0.001

SD: Standard deviation

Table 6: High-density lipoprotein in OH

Baseline HDL (mean ± SD) (mg/dL)	*Follow-up (mean ± SD)*	*t-value*	*p-value < 0.05*
35.42 ± 6.73	1st 46.45 ± 4.64	–6.97	0
35.42 ± 6.73	2nd 46.86 ± 8.53	–4.62	0

SD: Standard deviation

of TG and LDL was observed from baseline to first and second follow-up (Tables 4 and 5) respectively. But in contrast to the above lipid parameters, HDL showed a statistically significant increase in the mean values from baseline (35.42 ± 6.73) to first (46.45 ± 4.64) and second (46.86 ± 8.53) follow-up (Table 6).

DISCUSSION

The present study is done among hypothyroid patients attending a tertiary care hospital. In our study, a total of 50 patients were diagnosed as cases of hypothyroidism, of which 62% patients had SCH and 38% patients had OH. Moreover, SCH was found to be commoner than OH. Our findings with regard to incidence of SCH and OH are similar with other authors like Rezos et al,[17] Das et al,[18] and Shantha et al.[19]

Our study revealed that greater number of patients belonged to the urban population as compared with the rural population. Similar trend has been reported by Saxena et al.[6] In the present study, a predominance of females was noted in cases of hypothyroidism. Other studies like Shekhar et al[20] also reported that hypothyroidism was more prevalent among females than males.

It was observed that out of a total of 42 patients of hypothyroidism, dyslipidemia was found in 38 patients (90.47%). Out of the 26 SCH cases, 22 (52.38%) of them had associated dyslipidemia, whereas all the 16 patients of OH had associated dyslipidemia. In short, our study depicted that in hypothyroid cases lipid profile particularly TC, TGs, and LDL-cholesterol is elevated, whereas HDL-cholesterol (HDL-C) is decreased. Our findings are in line with other authors: Laway et al,[21] Das et al,[18] Saxena et al,[6] and Sharma et al.[22] Our study shows correlation between serum TSH level and lipid profile parameters of cases. Total cholesterol, LDL, and TGs were found to maintain significant positive correlation with serum TSH. But TSH was found to show no correlation with serum HDL-C. Our study findings were consistent with the previous studies done by Sharma et al,[22] regarding correlation of TSH with all the lipid parameters.

In OH, there was a statistically significant reduction in the mean values of TSH from baseline to first and second follow-up after treatment with levothyroxine. Our results are in concurrence with other authors.[6,17,18,21] Hypothyroidism leads to atherogenic lipid abnormalities as well as a number of other cardiovascular risk factors. Levothyroxine treatment may reduce serum cholesterol and thereby decrease the incidence of coronary artery disease, stroke, and peripheral vascular diseases. In our study, patients of OH showed a statistically significant reduction in the mean values of TC, TGs, and LDL from baseline to first (after 6 weeks) and second (after 36 weeks) follow-up after replacement therapy with levothyroxine. Various other authors (Monzani et al[23] and Akbar DH et al[24]) also reported significant reduction in the levels of lipid parameters following levothyroxine replacement therapy, thus supporting our observations. Ineck and Ng[25] and Meier et al[26] did not observe any change in TG levels following levothyroxine replacement therapy contrary to our findings. The response of HDL-C levels to thyroid substitution remains obscure. Few studies have shown an increase in HDL-C levels,[27] whereas others showed either no change or decreases.[28] Our study cohort also depicted a significant increase in mean HDL-C in OH cases following replacement therapy with levothyroxine. Our finding regarding increase in HDL was supported by Asranna et al,[29] who also observed a mild increase in HDL from mean pretreatment levels of 41.14 to 43.43 mg/dL after replacement therapy with levothyroxine. In contrast to our findings, Tanis et al[30] reported that HDL-C levels decreased in cases of OH.

CONCLUSION

The study has demonstrated and has further proved that hypothyroidism is an important cause of dyslipidemia. Therefore, patients presenting with dyslipidemia are recommended to be investigated for hypothyroidism.

Levothyroxine substitution therapy proves beneficial in normalizing the lipid parameters and hence, saves the patients from impending cardiovascular disorders. As our sample size was small and duration of study was limited, other studies with larger sample size and of longer duration are required.

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