

Effect of Thyroid Hormone Replacement Therapy on Lipid Profile in Primary Hypothyroidism

AZAM ALI, ABDUS SATTAR*, AMIR MUHAMMAD**, ABDUL HAMEED***, MUHAMMAD FAROOQ****,

ABSTRACT

Aim: To study the effect of thyroid hormone replacement therapy on lipid profile in primary hypothyroidism.

Methods: Eighty subjects were recruited for this study. 40 patients (patient group before treatment G₁) were treated with gradually increasing doses of “thyroxine” (50,100 and 150µg/day “doses adjusted by the treating physician”), each for 20 days to achieve a euthyroid state. Then 100-150 µg/day of thyroxine was given as maintenance dose for 30 days until the post therapy fasting blood sample from the same patients (patient group after treatment G₂) was drawn. In control group (Group CG), 40 subjects age and sex matched euthyroid were selected. Study subjects were selected from the individuals who were referred to Atomic Energy Medical Centre (CENUM), Mayo Hospital Lahore. 40 subjects diagnosed as primary hypothyroidism (TSH >10µIU) with age range 18-40 years were selected. 40 with age and sex matched euthyroid subjects were selected as controls. The subjects having diabetes mellitus and ischemic heart disease were excluded. The individuals who were on any drug therapy that could alter lipid metabolism and thyroid function were also excluded. 10ml Antecubital venous blood samples were taken during morning hours (0800-1000), after an overnight fast (12-14 hours) and 30 minutes of supine rest. Serum was obtained for the thyroid profile.

Results: Serum T₃ level increased significantly in patients of primary hypothyroidism after treatment as it was compared with patient group before treatment. Serum T₄ level increased significantly in patients of primary hypothyroidism after treatment when comparing with the patient group. Serum TSH level decreased significantly in patients of primary hypothyroidism after treatment when comparing it with the patient group before treatment. Serum TC, LDL-c, TG levels decreased significantly in patients of primary hypothyroidism after treatment as compared with serum TC, LDL-c, TG levels before treatment.

Conclusion: Our results have proved the beneficial effects of L-thyroxine on the lipid profile of patients of primary hypothyroidism and showed the decreased TC, LDL-c & TG levels after treatment.

Keywords: Hypothyroidism, Cholesterol, LDL-c.

INTRODUCTION

Hypothyroidism is the generic term for exposure of body tissues to a subnormal amount of thyroid hormones. Hypothyroidism is a risk factor for atherosclerosis and coronary heart disease due to its potential association with atherogenic lipid profile. Hypothyroid conditions can even cause premature atherosclerosis¹. Overt hypothyroidism is associated with an increased risk of cardiovascular diseases. In humans untreated hypothyroidism is a frequent cause of reversible hyperlipidaemia. Moreover the thyroid hormones reduce oxidative modification of LDL-c and may act as natural antioxidant and an inhibitor of atherosclerosis. Hypothyroidism has so strong association with higher lipid profile that even

the patients of subclinical hypothyroidism present with hyperlipidaemia. L-thyroxine therapy has been advocated as the most effective way to treat patients of primary hypothyroidism. It has beneficial effects on clinical and biochemical parameters thus reducing cardiovascular risk factors due to its antiatherogenic effect (by lowering lipid levels) and to its antioxidant property².

METHODOLOGY

Eighty subjects were recruited for this study. 40 patients (patient group before treatment G₁) were treated with gradually increasing doses of “thyroxine” (50,100 and 150µg/day “doses adjusted by the treating physician”), each for 20 days to achieve a euthyroid state. Then 100-150µg/day of thyroxine was given as maintenance dose for 30 days until the post therapy fasting blood sample from the same patients (patient group after treatment G₂) was drawn. In control group (Group CG), 40 subjects age and sex matched euthyroid were selected.

*Assistant Professor Medicine, KEMU/Mayo Hospital, Lahore, **Associate Prof Pathology, Khyber Girls Medical College, Peshawar, ***APMO, DHQ Hospital, Muzaffar Ghar, ****Emergency Pathology Lab. SIMS/SHL, Lahore
Correspondence to: Dr. Azam Ali, Assistant Professor Biochemistry, KEMU, Lahore

RESULTS

The details of results are given in tables 1 and 2.

Table-1: T3, T4, TSH levels in control group and patients of primary hypothyroidism before and after treatment

Groups	T3	T4	TSH
CG(control)	1.78±0.3	114.1±24.2	3.4±0.8
G1(Before treatment)	0.6±0.3	19.9±8.1	109.3±23.9
G2 (After treatment)	1.7±0.3	113.0±29.7	3.63±0.61
Statistical			
CG VS G1	P<0.01 (HS)	P<0.01 (HS)	P<0.01 (HS)
CG VS G2	P>0.05 (NS)	P>0.05 (NS)	P>0.05 (NS)
G1 VS G2	P<0.01 (HS)	P<0.01 (HS)	P<0.01 (HS)

Table 2: TC, TG, HDL, LDL levels in control group and patients of primary hypothyroidism before and after treatment

Groups	Cholesterol	Triglyceride	HDL-C	LDL-C
CG(control)	178.5±12.9	125.9±11.2	44.6±5.7	106.3±13.6
G1(Before treatment)	304.9±45.4	209.5±43.8	47.5±12.1	213.1±41.7
G2 (After treatment)	183.2±17.5	130.2±14.9	45.7±9.1	107.1±19.4
Statistical analysis				
CG VS G1	P<0.01 (HS)	P<0.01 (HS)	P>0.05(NS)	P<0.01 (HS)
CG VS G2	P>0.05 (NS)	P>0.05 (NS)	P>0.05 (NS)	P>0.05 (NS)
G1 VS G2	P<0.01 (HS)	P<0.01 (HS)	P>0.05(NS)	P<0.01 (HS)

DISCUSSION

In the present study, serum total cholesterol (TC) was found to be increased in patients of primary hypothyroidism before treatment (group G₁). When compared with control group (CG), the difference between group G₁ and CG was highly significant statistically (p<0.001). The comparison of group G₁ vs G₂ showed decreased TC level in group G₂ (patient group after treatment) and difference was highly significant statistically (p<0.01). The findings of this study are consistent with results of Pazos et al (1995)³; Engler and Riesen (1993)⁴; Martinez et al (1998)⁵; Ness et al (1998)⁶; Petersson and Kjellstrom (2001)⁷; Morris (2001)⁸ who also observed increased TC level in patients of primary hypothyroidism before treatment and decreased TC level after treatment.

This increased TC in patients of primary hypothyroidism before treatment (group G₁) may be due to effect on LDL receptor protein. In hypothyroidism there seems to be decrease in the number and activity of LDL receptor protein. This decrease in number and activity may be responsible for decreased clearance of cholesterol leading to increased cholesterol level in patients of primary hypothyroidism.

The TC was found to be decreased in patients of primary hypothyroidism after treatment (group G₂) which may be due to increase in the number and activity of LDL receptor protein. This increase in number and activity of receptor may be responsible for decreased TC level after treatment (group G₂) (Pazos et al (1995)³; Engler and Riesen (1993)⁴. There is also increase in the transcription of LDL

receptor protein gene. So increased expression of LDL receptors genes may be responsible for increase in number of LDL receptors.

In the present study, serum LDL-c levels were found to be increased in patients of primary hypothyroidism before treatment (groups G₁). When compared with control group (CG), the difference between group G₁ and CG was highly significant statistically (p<0.01). The comparison of group G₁ vs G₂ showed decreased LDL-c level in group G₂ (patient group after treatment) and the difference was highly significant statistically (p<0.01). The findings of this study are in favour of results of Diekman et al (2000)⁹; Huesca et al (2002)¹⁰ who also observed increased LDL-c levels in patients of primary hypothyroidism before treatment and decreased LDL-c level after treatment.

This increased LDL-c in patients of primary hypothyroidism before treatment (group G₁) may be due to effect on the LDL-c receptor. Thyroid hormones regulate lipid metabolism through various mechanism but the key role may be played by the LDL receptor pathway. In hypothyroidism there may be decrease in the number and activity of LDL receptor. This decrease in number and activity may be responsible for the decrease clearance of LDL leading to increased LDL-c level in patients of primary hypothyroidism. In hypothyroidism LDL-c abnormalities may be mediated by the variation in activity and impairment of LDL-c clearance due to down regulation of cell surface LDL receptor.

The LDL-c was found to be decreased in patients of primary hypothyroidism after treatment

(group G₂) which may be due to an increase in the number and activity of LDL receptors. This increase in number and activity of LDL receptors seems to be responsible for decreased LDL-c level after treatment (group G₂). There is also increase in the transcription of LDL receptor protein gene. So increased expression of LDL receptors genes may be responsible for increase in the up regulation of LDL receptor.

In the present study, serum HDL-c levels were found to be increased normal or decreased in patients of primary hypothyroidism before treatment (group G₁). When compared with control group (CG), the difference between G₁ and CG was non-significant statistically (p 0.05). The comparison of group G₁ vs G₂ showed increased, normal or decreased levels of HDL-c and the difference between group G₁ and G₂ was also non-significant statistically (p>0.05). The results of this study are consistent with the results of Erem et al (1999)¹¹ and Ascott (1994)¹² who also reported decreased level of HDL-c. However the normal HDL-c levels in this study are in favor of results of Verdugo et al (1987)¹³ who also observed normal HDL-c levels in patients of primary hypothyroidism.

In the present study, serum TG levels were found to be increased in patients of primary hypothyroidism before treatment (group G₁). When compared with control group (CG), the difference between group G₁ and CG was highly significant statistically (p<0.01). The comparison of group G₁ vs G₂ showed decreased TG level in group G₂ (patient group after treatment) and the difference was highly significant statistically (p<0.01). The findings of this study are consistent with the results of Martinez et al (1998)⁵ who also observed higher TG level in patients of primary hypothyroidism before treatment and decreased TG level after treatment.

REFERENCES

1. Asami T, Uchiyama M. Thyroxine inversely regulates serum intermediate density lipoprotein levels in children with congenital hypothyroidism. *Pediatr Int* 1999; 41(3):266-9.
2. Asami T, Kikuchi MD, Touru MD, Uchiyama M. Effect of L-thyroxine on serum lipid profiles in infants with congenital hypothyroidism. *J Pediatr*. 1995; 127:812-14
3. Pazos F, Alvarez JJ, Rubiespratt J, Varela C, Lasuncion MA. Long-term thyroid replacement therapy and levels of lipoprotein (a) and other lipoproteins. *J Clin Endocrinol Metab* 1995; 80:562-66
4. Engler H, Riesen WF. Effects of thyroid function on concentrations of lipoprotein (a) *Clin. Chem.* 1993; 39:2466-69
5. Martinez ML, Hernandez MA, Nguyen TT, Munoz ML, Pena H, Morillas. Effects of thyroid hormone replacement on lipoprotein (a), lipids, and apolipoprotein in subjects with hypothyroidism. *Mayo-Clin-Proc* 1998; 9:837-41
6. Ness GC, Lopez D, Chambers CM, Newsome WP, Cornelius P, Hardwood HJ. Effect of L-triiodothyronine and the thyromimetic an serum lipoproteins levels and hepatic low density lipoprotein receptor, 3-methylglutaryl coenzyme A reductase and apo A-I gene expression. *Biochem-Pharmacol.*1998; 1:121-29
7. Petersson U, Kjellstrom T. Thyroid functions tests, serum lipids and gender interrelations in a middle aged population. *Scand J Prim Health care* 2001; 3:183-85.
8. Morris MS, Bostom AG, Jacques PF, Selhab J, Rosenberg IH. Hyperhomocysteinaemia and hypercholesterolemia associated with hypothyroidism in the third US National Health and Nutrition Examination Survey. *Atherosclerosis* 2001; 1:195-200
9. Diekman MM, Anghelascu N, Endert E, Bakkar O, Wiersinga WM. Changes in plasma low-density lipoprotein (LDL) and high density lipoprotein cholesterol in hypothyroid patients are related to changes in free thyroxine, not to polymorphisms in LDL receptor or cholesterol ester transfer protein genes. *J Clin Endocrinol Metab* 2000; 85:1857-62.
10. Huesca GC, Franco M, Luc G, Montano LF, Masso F, Posactas RC et al. Chronic hypothyroidism induces abnormal structure of high density lipoproteins and impaired Kinetics of apolipoproteins A-I. *Metabolism* 2002; 51:443-50
11. Erem C, Deger O, Bastan M, Orem A, Sonmez M, ulusoy S. Plasma lipoprotein (a) concentrations in hypothyroid, euthyroid and hyperthyroid subjects. *Acta-Cardio* 1999; 2:77-81
12. Asami T, Ciomartan T, Uchiyama M. Thyroxine inversely regulates serum intermediate density lipoprotein levels in children with congenital hypothyroidism. *Pediatr Int* 1999; 41(3):266-9.
13. Verdugo C, Perrot G, Ponsin G, Valentin C, Brethezene F. Time-course of alteration of high density lipoproteins (HDLc) during thyroxine administration to hypothyroid women. *Eur J Clin Invest.* 1987; 17:313-16.