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Effect of Thyroid Replacement with Statin Therapy on Cognitive Functions and Lipid Profile in Hypothyroidism Patients.

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Abstract

Aim: To evaluate the effect of combination therapy on lipid profile in hypothyroidism patients.

Methods: A prospective observational study was conducted in a private hospital at Tiruchengode. Patients who were under the management of thyroid disorder and hyperlipidemia more than 10 years was screened and selected for the study. The patients were interviewed using a Mini mental state examination questionnaire and their cognitive skills were assessed. Independent samples T test was used to compare the complication of the management.

Results: There were 36 patients were included in the study and the patients who were on levothyroxine with atovastatin labeled as Group 1 and atorvastatin alone was labeled as Group 2. Combination therapy shows greater percentage of lipid profile reduction and significant $p<0.05$ cognitive impairment was found in the combination therapy.

Conclusion: Hyperlipidemia management with levothyroxine with atovastatin has an association on the managing lipid profile efficiently than the mono therapy of statins. Cognition impairment was high in the combination therapy of levothyroxine and atorvastatin.

Keywords: Hyperlipidemia, Hypothyroidism, Lipid profile, Cognitive impairment.

INTRODUCTION

Thyroid disorders, one of the most common endocrine diseases across the globe, affect an estimated 42 million people in India. Untreated hypothyroidism during infancy and childhood is well known to have significant detrimental effects on skeletal growth, sexual maturation, and cognitive ability. Much has been said and done regarding universal screening to diagnose neonatal hypothyroidism which essentially requires resources rather than clinical acumen. Diagnosing hypothyroidism, on the other hand, requires sound knowledge and clinical skills on part of the treating physicians. The clinical manifestations of hypothyroidism are highly variable, depending on the age at onset and the duration and severity of thyroid hormone deficiency. Classic signs and symptoms (e.g., cold intolerance, puffiness, decreased sweating, and coarse skin) may not be present as commonly as once believed. Thyroid hormones directly or indirectly, through erythropoietin, stimulate growth of erythroid colonies. In the deficiency of thyroid hormones, anemia frequently develops and may be normocytic, hypochromic microcytic, or macrocytic.

Untreated hypothyroidism leads to multiple complications like cerebrovascular accident, cardio vascular risk factors, neurodegenerative disorder resulting in bipolar disorder, depression, mood disorder and anemia. Complex hypothyroidism can be treated with the help of only few drugs like thyroxine, levothyroxine. Hypothyroidism associated with hyperlipidemia, but the magnitude is small in mild chemical hypothyroidism. Thyroid is intricately related to cardiovascular system, having possible direct indirect effect to the vascular origin. Serum concentrations of Thyroid stimulating hormone (TSH), Free Thyroxine4 (FT4), Total cholesterol, Triglycerides and High density lipoprotein were measured in 5786 randomly selected subjects. From this study they concluded there is no differences existed in lipid profiles between subclinical hypothyroidism and euthyroid subjects but there are correlations between serum FT4 and TSH and lipid profiles.[1]

Treatment of subclinical disease results in lipid profile improvement, but there is no evidence that this improvement is associated with a decrease in cardiovascular or all-cause mortality in elderly patients.

The relationship among LDL oxidation, TSH levels, and carotid intima-media thickness (IMT), a biomarker of subclinical atherosclerosis. Their findings showed that lipid peroxidation was higher in the significant SCH patients than in the euthyroid subjects, which suggested that qualitative as well as quantitative changes in serum lipids resulting from SCH may add to atherosclerosis risk. Thyroid hormones play a significant role in regulating cardiac, vascular, and metabolic physiology. Physiologic alterations from both overt and subclinical hypothyroidism have varied cardiovascular effects.[2]

Dyslipidemia changes in women with subclinical hypothyroidism. This was a case control study in which women with subclinical hypothyroidism (SH) and euthyroid women were enrolled. Their lipid profile, fasting blood sugar, T3, T4 and TSH levels were measured. In subclinical hypothyroidism, various parameters were compared. He concluded that subclinical hypothyroidism, the earliest form of thyroid failure, has negative metabolic effects on the affected subjects. SH could be one of the causes of secondary hyperlipidaemia and should be viewed as an independent risk factor for atherosclerosis, along with obesity, hypertension, diabetes, etc.[3] So in this study planned to compare the effect of Levothyroxine 50mcg with Atorvastatin 20 mg and Atorvastatin mono therapy in Cognitive skills and lipid profile.

METHODS

Study design and sample

A prospective observational study was conducted in a private multispecialty hospital at Tiruchengode. The patients with hypothyroidism and hyperlipidemia with age group of 30 to 60 were inclusive criteria of the study. Totally 96 patients were screened and the patients who are according to the inclusive criteria and the proper follow up patients were finally included in the study. Chronically ill patients, Patients with multiple Drug therapy, improper availability of patients were excluded from the study. And the collected patients were separated into two groups. Institutional Ethical committee approval was obtained from the Vivekanandha medical care hospital. Informed consent was obtained from all the patients who were included in the study.

Group 1 Patients prescribed with levothyroxine 50mcg and Atorvastatin 20mg and Group 2 Atrovastatin 20mg alone. Separated groups were checked with lipid profile parameter like Total cholesterol (TC), Triglycerides (TG), High density Lipoprotein (HDL-C), Low density Lipoprotein (LDL-C) Cholesterol is one of the lipids found in the blood stream. A high level of cholesterol in the blood hypercholesterolemia is a major risk factor for coronary heart disease, which leads to heart attack. The enzyme cholesterol esterase is used to hydrolyze the cholesterol esters present in the serum to free cholesterol and free fatty acids. The enzyme cholesterol oxidase in the presence of oxygen to oxidizes the cholesterol to cholest-4- en-3one and hydrogen peroxide. Hydrogen peroxide oxidizes phenol and 4-aminoantipyrine to produce red color that can be measured spectrophotometrically and Mini mental state Examinations (MMSE) Score were calculated for the both the groups and data were compared and risk of cognition was assessed in this study. The MMSE is screening tool that provides a brief, objective measure of cognitive function. MMSE scores are very useful in quantitatively estimating the severity of cognitive impairment and also in serially documenting cognitive change. The measure from MMSE serves as one of the tests recommended by the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's disease and Related Disorders Association (NINCDS-ADRDA) to document the clinical diagnosis of probable Alzheimer's disease. The study population underwent a standardized assessment for cognitive function by using Folstein's Mini Mental State Exam (MMSE).[4] Any score greater than or equal to 25 points (out of 30) is effectively normal. Below this score indicates mild (21-24 points), moderate (10-20 points) and severe (<9 points) cognitive impairment.[5, 6]

Orientation: The object was asked the date, and then asked specifically for parts omitted. Registration: The names of 3 unrelated objects, clearly and slowly were said, about one second for each. The most commonly used were apple, table, and penny. After said all 3, subject was asked to repeat them.

Attention & Calculation: The subject was asked to begin with 100 and count backward by 7. Stop after 5 subtractions (93, 86, 79, 72, 65). Score the total number of correct answers.

Recall: The subject was asked to recall the 3 words that you previously asked Him/her to remember.

Data collection tool

Data were collected through specially designed data entry format in order to collect the details of the Patient details including name, age, sex, known allergy, educational status, I.P no/O.P no, date of admission, date of discharge and patient history including present complaints, past medical history, past medication history, social history and family history, Vital signs (Body temperature, Blood pressure and pulse rate), lipid profile (Total cholesterol (TC), Triglycerides (TG), Low density lipoprotein (LDL-C), High Density lipoprotein (HDL-C), Mini mental state examinations (MMSE), drugs treatment details were collected. The study was approved by the Human Ethics Committee of the study hospital. Written informed consent was obtained from the patients prior to interview.

Statistical analysis

Statistical Analysis was done using SPSS Version 16 software were used to compare the data in that Independent samples T test was used to analysis the study.

RESULTS AND DISCUSSION

There were 18 patients observed in each group and totally 36 patients were observed during the 8 months study period age, gender wise classification of patients were are detailed in Table 1 & Figure 1.

Table 1: Demographic Characteristics of Patients

Variables	Levothyroxine 50mcg with Atrovastatin 20mg (n=18)	Atorvastatin 20 mg alone (n=18)	Total
Age in years,			
30-40	7	9	16
41-50	6	5	11
51-60	5	5	10
Gender,			
Male,	5	8	13
Female	13	10	23

Table 2: Lipid Concentration of Levothyroxine 50 mcg with Atorvastatin 20mg.

Parameter (mg/dL)	Baseline (mean±SD)	After 8 months (mean± SD)	P Value
TC	275.4±39.6	211.9±39.3	P<0.05
TG	209.4±34.7	148.3±34.9	
HDL-C	41.2±4.9	51.4±6.4	
LDL-C	192.3±27.7	130.9±25.9	

Table 3: Mean Lipid Concentration with Atorvastatin 20mg alone

Parameter (mg/dL)	Baseline (mean±SD)	After 8 months (mean± SD)	P value
TC	273±26.56	230±15.3	P<0.05
TG	220±39.34	179±33.08	
HDL-C	43±5.7	49±3.7	
LDL-C	186±26.28	144±13.62	

Table 4: Percentage of reductions in lipid profile between group 1 & group 2.

Parameter (mg/dL)	Levothyroxine 50 mcg with Atorvastatin 20mg	Atovastatin 20mg alone
TC	26	20.1
TG	34.16	20.1
HDL-C	22	13
LDL-C	38	25

Table 5: Mini mental state Examination score between group 1& 2

Drugs	MMSE Score after 8 months (mean±SD)	P Value
Levothyroxine 50 mcg with Atorvastatin 20mg	14±3.2	P < 0.05
Atovastatin 20mg alone	23±1.16	

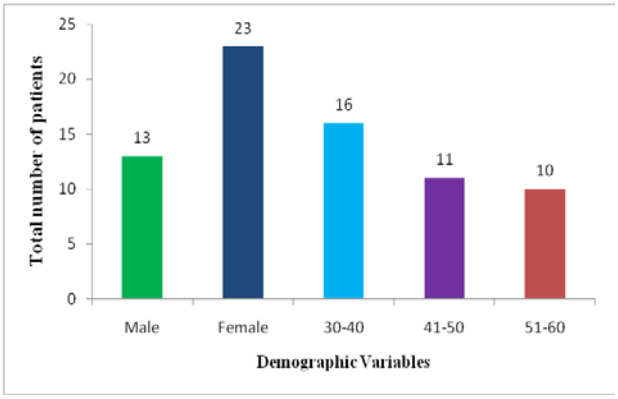

Figure 1: Demographic Characteristics of Patients

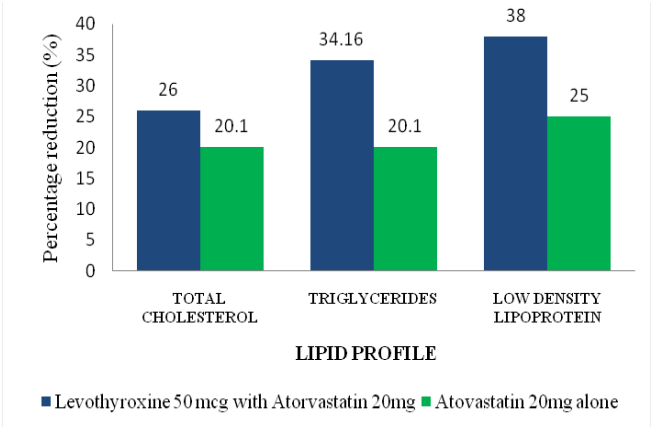

Figure 2: Percentage of reductions in lipid profile between group 1 & group 2.

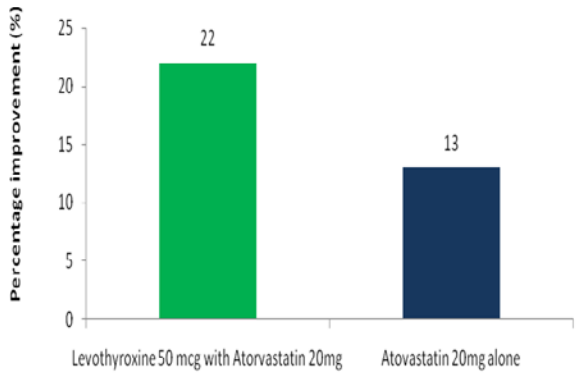

Figure 3: Percentage of HDL-C improvement between group 1 & group

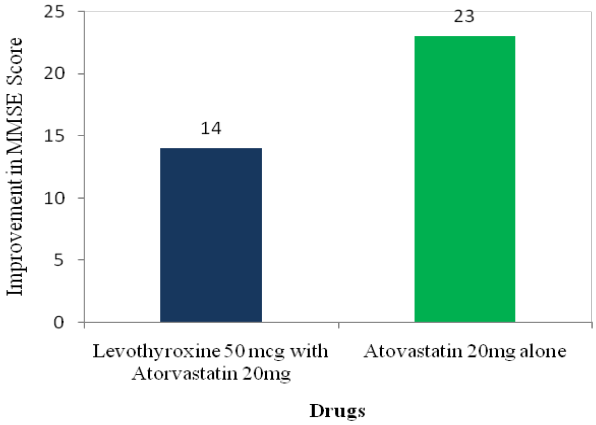

Figure 4: Mini mental state Examination score between group 1& 2

Patients were on the Levothyroxine 50 mcg with Atorvastatin 20mg therapy was labeled as (Group 1), Patients were on the Atorvastatin 20mg therapy was labeled as (Group 2).

Group 1 was checked with Total Cholesterol, Triglycerides, High Density lipoprotein, Low Density lipoprotein, was analyzed initial phase and after 8 months of therapy for the both the groups. The mean and standard deviation was calculated as mention in the Table 2.

Group 2 was checked with Total Cholesterol, Triglycerides, High density lipoprotein, Low density lipoprotein was analyzed initial phase and after 8 months of therapy for the both the groups. The mean and standard deviation was calculated as mention in the Table 3.

In the group 1 before and after 8 months of management with Levothyroxine and Atrovastatin shows significant reduction of Total Cholesterol, Triglycerides, Low density lipoprotein, and also shows significant improvement in High density lipoprotein (P<0.05). In the group 2 before and after 8 months of management with Atrovastatin shows significant reduction of Total Cholesterol, Triglycerides, Low density lipoprotein, and also shows significant improvement in High density lipoprotein (P<0.05) as mention in Table 4.

On comparison of both the groups not shows significant lipid profile reduction. Individual groups before and after treatment alone shows significant of lipid profile

reductions. On the percentage of reduction in lipid profile between both the groups identified that Levothyroxine 50 mcg with Atorvastatin 20mg shows greater percentage of reduction of lipid profile when compared to Atorvastatin 20mg mono therapy as mention in the Table 4 & Figure 2.
High Density lipoprotein shows greater percentage of improvement with the combination therapy of levothyroxine and atorvastatin when compared to mono therapy of atrovastatin. Hence it shows that effective management of lipid profile was attain with the combination of levothyroxine and atrovastatin and also it proves that cardiovascular risk was reduced significantly on the proper management of thyroid replacement therapy as mention in the Table 4 & Figure 3.
MMSE was also calculated using the tools initial phase and after 8 months of therapy and its mean and standard deviation and significance was identified. MMSE score shows extremely significant reduction ($P<0.05$) with Levothyroxine 50mcg with Atorvastatin 20mg when compared to Atorvastatin 20mg mono therapy. On combined management of both thyroid disorder and hyperlipidemia with levothyroxine and atovastatin respectively leads to significant cognition impairment when compared to atovastatin mono therapy as mention in the Table 5 and Figure 4.

CONCLUSION

The current study adds to the body of knowledge by confirming hypothyroidism management along with hyperlipidemia management has a association on the managing lipid profile efficiently than the mono therapy of statins. And the same time cognition impairment was high in the combination therapy of levothyroxine and atorvastatin compared to mono therapy of Atrovastatin. From this study recommended that cognition improvement management should be taken care during hyperlipidemia and hypothyroidism management.

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