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EFFECT OF ALTERED LEVELS OF MICRONUTRIENTS ON LIPID PARAMETERS IN THYROID DYSFUNCTION

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ABSTRACT: Trace elements are extremely important for normal metabolism. Copper is one of the trace metals which has important physiological function in maintaining thyroid activity. Copper is known to effect lipid metabolism. Increase in serum copper level is associated with decrease in concentration of total cholesterol (TC). Thyroid hormone binding transcription factors, which are essential for modulation of gene expression, contain zinc bound to cysteine residues and also thyroid hormones influence zinc metabolism by affecting zinc absorption and excretion. Zinc is required for enzymes involved in lipid synthesis and lipoprotein excretion. The purpose of this study was to determine the effect of various levels of serum copper and zinc on total cholesterol, plasma triglyceride and low density lipoprotein cholesterol in subjects with thyroid dysfunction. 61 subjects were divided into three groups of 13 hypothyroid, 23 hyperthyroid and 25 euthyroid based on thyroid stimulating hormone levels. The correlation between serum copper and low density lipoprotein ($p < 0.01$) ($r = -0.842$), serum zinc correlated strongly negative and significantly with total cholesterol ($r = -0.564$) , low density lipoprotein cholesterol ($r = -0.666$) in hyperthyroid group. But the correlation in hypothyroid and euthyroid group differed and was not significant. Elevated levels of total cholesterol and low density lipoprotein cholesterol may be proatherogenic and increase the risk of cardio vascular diseases hence measures must be taken in correcting and maintaining levels of micronutrients in thyroid dysfunction.

Key Words: Thyroid dysfunction, zinc, copper, lipid parameters, pro-atherogenic,

INTRODUCTION

Thyroid disorders are the very common [1]. On the basis of countrywide study, it can now be estimated that total burden of significant thyroid diseases in the country is approximately 42 million[2]. The importance of thyroid gland in maintaining human health is well recognised and normal thyroid status is dependent on the presence of many trace elements for both the synthesis and metabolism of thyroid hormones Among the different trace elements copper and zinc are of the trace metals which are not only very much abundant in our body but it also has many important physiological functions and redox active element [3, 4]. Copper levels in serum can be influenced not only by its metabolism which can be influenced by hormone levels but also by change in its transport protein in blood1. It is known that hormones have been shown to influence trace metal metabolism at several levels, including excretion and transport of trace metals [3]. Copper is a catalytic component of numerous enzymes and is also a structural component of other important proteins. It is seen that deficiency of copper (Cu) has been observed to affect the endocrine system adversely [5].

Thyroid hormones are known to have actions on protein metabolism and lipid metabolism. Serum copper has been shown to increase in hyperthyroidism but no statistically significant difference was found in plasma Cu concentrations between control subjects and patients with other thyroid diseases (including hypothyroidism), though in an animal study serum copper level has been shown to be lower than that of the controls [6, 7]. Copper status have also been linked to decreased plasma T3 concentrations in animals and man [8, 9]. Copper is known to effect lipid metabolism. Increase in serum copper level is associated with decrease in concentration of total cholesterol (TC), this is due to down regulation of both biosynthetic enzymes and regulatory proteins. The levels of triglycerides (TG) are significantly reduced whereas the levels of low density lipoprotein cholesterol (LDL-C) remained unchanged in subjects with increased Cu concentration. But few authors have reported that copper enhance the formation of oxidized LDL-C due to formation of free radicals. Zinc is essential for many biochemical processes and also for cell proliferation. Thyroid hormones influence zinc metabolism by affecting zinc absorption and excretion. Also thyroid hormone binding transcription factors, which are essential for modulation of gene expression, contain zinc bound to cysteine residues [3]. Additionally it was reported that reduced thyroid function was strongly related to low serum zinc level. But controversy exist regarding thyroid dysfunction and serum zinc levels as few authors report otherwise. Hypothyroidism is associated with elevated low density lipoprotein cholesterol (LDL-C) and total cholesterol (TC). Effect of alteration of serum zinc levels on plasma lipids is still controversial as low serum zinc was reported to be associated with low TC and TG but no change on LDL-C but few authors have reported elevated levels of TC, TG [10, 11].

Objective: To compare and correlate the plasma levels of zinc and copper with that of serum low density lipoprotein cholesterol, total cholesterol and plasma triglycerides levels in subjects with thyroid abnormalities. To study the effect and importance of zinc and copper supplementation for dyslipidaemia in subjects with thyroid abnormalities and there efficacy in it

MATERIALS AND METHOD

We evaluated 61 subjects of which 13 were hypothyroid, 21 were hyperthyroid and 27 were euthyroid controls who would visit Kasturba Hospital. Hyperthyroid and hypothyroid patients were selected on the basis of serum thyroid stimulating hormone (TSH). TSH values between 0.30 mIU and 3.00 mIU (both inclusive) were taken to be within normal limits. TSH > 3.00 mIU were considered as hypothyroid and TSH < 0.30 mIU were considered as hyperthyroid. All the subjects were age and sex matched having excluded smokers, alcoholics, and subjects on lipid lowering agents, OCP users, pregnant females, diabetics, jaundiced patients and those diagnosed with thyroid carcinoma. The ethical clearance was duly obtained from the ethical review committee for the study.

BIOCHEMICAL PARAMETERS

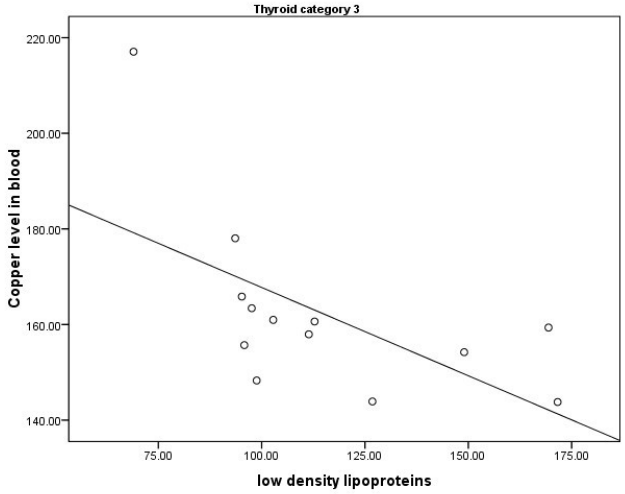
The various biochemical parameters were determined by auto analyser by enzymatic methods like CHOD – PAP method for TC [12], GPO – PAP [13] method for TG. Enzymatic method was used for determining LDL-Cholesterol. Serum copper levels were estimated colorimetrically using bathocuproin disulphonate method[14]. Serum zinc levels were estimated colorimetrically using kit method.

RESULTS

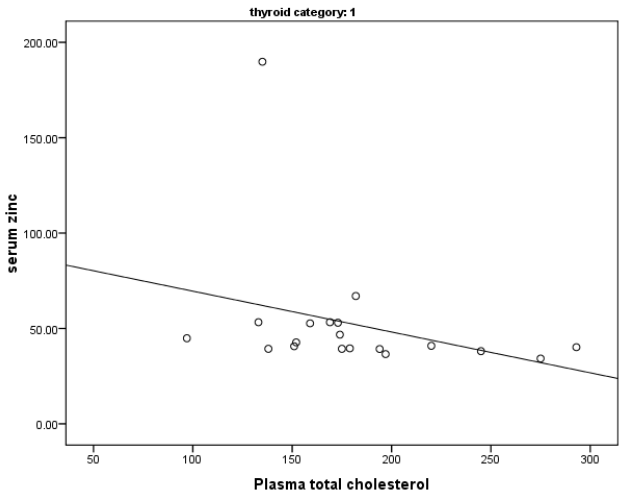
Full descriptive analysis of available data was performed using statistical package for social sciences (SPSS) version 17. The correlation analysis was done to test any possible correlation between plasma copper and serum zinc with that of total cholesterol, plasma cholesterol and low density lipoprotein cholesterol. The correlation between serum copper and TC was not significant statistically (p= 0.144) with strong negative correlation in hypothyroid group (r= -0.429) but it had no significance statistically with weak negative correlation in hyperthyroid and euthyroid group. The correlation between serum copper and TG had no statistical significance with weak negatively correlation in hypothyroid, euthyroid and hyperthyroid group.

The correlation between serum copper and plasma LDL-C levels in hypothyroid group were significant ($p < 0.01$) (Figure 1) which had very strong negative correlation ($r = -0.842$) (Table 1) but was not significant statistically with weak negative correlation in hyperthyroid and euthyroid group. The correlation between zinc and TC was found to be significant [$p< 0.05$] with strong negative correlation [$r= -0.564$] in hyperthyroid group [Graph 1] [Table 2]. The correlation between TC and zinc was not significant with weak negative correlation in hypothyroid [$r= -0.239$] and euthyroid [$r= -0.034$].

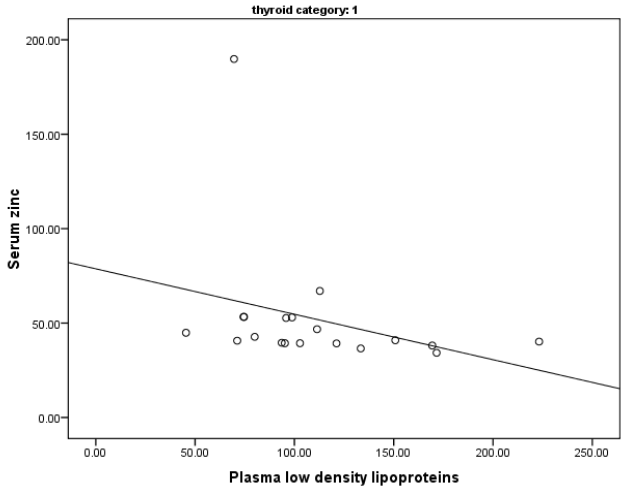
The correlation between zinc and LDL was significant [$p < 0.05$] with strong negative strength of correlation [$r = -0.666$] in hyperthyroid group [Graph 3] but was not significant with weak negative correlation in euthyroid [$r= -0.016$] and hypothyroid [$r= -0.265$]. Each small square represents a single observation and the best fit line has been drawn. From the graphs (1, 2 and 3) it is clearly visible that the correlation between serum copper and zinc levels are significant and negative with the levels of TC and LDL-C.



Graph 1



Graph 2



Graph 3

Table 1: Correlation between serum copper and TC, TG and LDL-C

TC	[r = - 0.429],p = 0.144	[r= - 0.242], p= 0.244	[r= - 0.302], p = 0.161
TG	[r= - 0.033], p= 0.915	[r= - 0.060], p = 0.774	[r = -0.040], p = 0.856
LDL-C	[r = -0.842], p < 0.01	[r = - 0.276], p = 0,181	[r= - 0.188], p = 0.391

Table 2: Correlation between serum zinc and TC f and LDL-C.

TC	[r= -0.564], p< 0.05	[r= -0.034], p= 0.276	[r= -0.239], p=0567
LDL-C	[r = -0.666], p< 0.05	[r= -0.265], p=0765	[r= -0.016], p=0886

DISCUSSION AND CONCLUSION

Thyroid disorders are the most common among all endocrine diseases in India. On the basis of countrywide study and other related studies, it can now be estimated that total burden of significant thyroid diseases in the country is approximately 42 million. Many micronutrients are associated with various biochemical function of which copper is one of the important essential micronutrient. Copper plays an essential role in human physiology. It serves as a cofactor of key metabolic enzymes and is required for embryonic development, neuronal myelination, radical detoxification, and numerous other physiological processes. Cu is a redox-active transition metal that may cause oxidative damage to lipids, proteins and DNA molecules. It has been reported by few authors that copper selectively up-regulates molecular machinery associated with the cell cycle and chromatin structure and down-regulates lipid metabolism, particularly cholesterol biosynthesis.It is known that the mean concentration of plasma Cu was significantly higher in patients with hyperthyroidism than in control or hypothyroid subjects. Zinc effects on thyroid hormones are complex and include both synthesis and mode of action. Thyroid hormone binding transcription factors, which are essential for modulation of gene expression, contain zinc bound to cysteine residues. Dyslipidaemia is commonly associated with thyroid dysfunction [12,13]. Zinc is required for enzymes involved in lipid synthesis and lipoprotein excretion. Zinc is also known to have lipid lowering action [14]. But effects of zinc on total cholesterol, HDL-C, LDL-C are still controversial with contrasting results and opinion [15, 16]. Our study demonstrated that relationship between serum copper and plasma TC varied in all three groups, it was not significant statistically in any group and correlated negatively but strength of correlation was different in all groups with strong negative correlation in hypothyroid group and weak negative in other groups.

Similar findings have been demonstrated in other studies too but not in subjects with thyroid dysfunctions [15].

In our study we observed that there was no significant change in levels of plasma TG in hypothyroid, euthyroid and hyperthyroid group. All the groups showed weak negative correlations which were not significant.

It is known that most of the cholesterol is carried in LDL-C and hence alteration in cholesterol metabolism may lead to varying levels p of LDL-C. We observed that the LDL-C levels in hypothyroid group had very strong strength of correlation which was significant statistically but showed weak negative strength of correlation which had no significance statistically.

Our study demonstrated that the relationship between zinc and TC differs in the three studied group. The effect of zinc on total cholesterol in hyperthyroid group was significant with strong negative correlation. Similar findings have been demonstrated in few other studies[17,18]. But the relationship of zinc to total cholesterol in euthyroid and hypothyroid group was not significant.

Previous studies have reported that zinc depletion per se produced no significant alteration in levels of LDL-C [6]. In our study the effect of zinc on LDL-C was significant with strong correlation in hyperthyroid group but not so significant in hypothyroid and euthyroid groups.

Conclusion:

Further it can be concluded that the serum zinc and copper levels significantly alter the levels of lipid parameters such as total cholesterol, triglycerides and low density lipoprotein cholesterol. In their deficiency the propensity towards proatherogenic and free radical damage of various tissue increases. To prevent it determining and correcting the levels of zinc and copper in thyroid dysfunction with dyslipidemia may be required. This can be proved only after further studies.

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