

A Comparative Study of Homocysteine, Cyanocobalamine, Folate, Lipid Profile and Serum Creatinine Level in Hypothyroid Subjects before and During Treatment

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Abstract: *Introduction:* Hyperhomocystenemia is a disease involving abnormal homocysteine metabolism and is characterized by increased level of total homocysteine concentration (normal 5-15 $\mu\text{mol/L}$). Many factors like dietary folate, cyanocobalamine deficiency or thyroid disorder are the most common causes for increased homocysteine level. This present study was planned to delineate the usefulness of levothyroxin, supplementation of folate and cyanocobalamine in patients of hypothyroidism to evaluate change in homocysteine level before and during treatment. Also to find out correlation between levothyroxin, cyanocobalamine and folate with homocysteine. *Material and Method:* The present study was conducted on 75 patients of hypothyroidism of either sex in department of biochemistry, J.L.N. medical college and hospitals, Ajmer. Serum homocysteine, cyanocobalamine, folate level was measured by ELISA while thyroid function test were evaluated by RIA method. *Result and discussion:* There was highly significant change in homocysteine, cyanocobalamine, folate, total cholesterol, HDL, VLDL and LDL in hypothyroid subjects before and during treatment ($P < 0.0001$). This emerging evidence suggest that these parameters are influenced by levothyroxine used in treatment of hypothyroid disorder and usefulness of supplementation of cyanocobalamine and folate for significant improvement of serum lipid profile. *Conclusion:* It is concluded that supplementation of levothyroxin, cyanocobalamine and folate in hypothyroid patients can cause significant decrease in level of homocysteine and significant improvement of serum lipid profile, which decreases risk of coronary heart disease in hypothyroid patients.

Keywords: Homocysteine, cyanocobalamine, folate, levothyroxine, serum creatinine, lipid profile

1. Introduction

Thyroid disorders are most common endocrine abnormalities encounter in clinical practices. Thyroid function affects the activity of MTHFR gene, its activity reduced in person with underactive thyroid. Hypothyroidism can also disturb the conversion of riboflavin to FAD, which can equally affects the activity of MTHFR gene. Even other enzyme such as cystathionine β synthase or methionine synthase, a vitamin B12 dependent enzyme may be affected. Furthermore, a change of kidney functions may have an effect; lower glomerular function rate (GFR) is found in patients of hypothyroidism, with increase serum creatinine level.

Homocysteine is metabolite of amino acid methionine. Hyperhomocystenemia is a disease involving abnormal homocysteine metabolism, is characterized by increased total homocysteine concentration (normal 5-15 $\mu\text{mol/L}$). This can be result of a dietary folate or cobalamine deficiency and thyroid dysfunction. Several studies have concluded that moderate hyperhomocystenemia is powerful independent factor for arteriosclerosis.

Aims and objectives:

To estimate plasma homocysteine, serum cyanocobalamine, folate, lipid profile and serum creatinine in control and hypothyroid subjects before treatment and in hypothyroid

patients during treatment to find out correlation between thyroxin and cyanocobalamine, folate with homocysteine, lipid profile and serum creatinine in hypothyroid patients.

2. Material and method

The present study will comprise of 75 diagnosed patients of thyroid dysfunction (hypothyroidism) attending OPD of Medicine / Surgery of J.L.N. Medical College and Hospital, Ajmer. Diagnosis would be finalised after thyroid profile estimation.

Seventy five healthy subjects of either sex of similar age group will be included in the study, as the control group.

Exclusion Criteria:

Uncontrolled diabetes mellitus, Cardiovascular disease, Pregnancy, Patient on drug like methotrexate, fenofibrate, l-dopa, cholestyramine, Renal failure, Chronic alcoholism.

Blood samples will be collected by venipuncture by aseptic technique, Serum / plasma will be subjected to following estimations:

- 1) Plasma homocysteine – By ELISA method.
- 2) Serum cobalamin – By ELISA method.
- 3) Serum folate – By ELISA method.
- 4) Serum cholesterol – By enzymatic CHOD-POD, end point method (Allian CC; 1974).

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- 5) Serum triglycerides – By enzymatic GPO-POD, endpoint method (Fossati P, 1982).
- 6) Serum HDL cholesterol – By phosphotungstic acid, endpoint method (Finley PR, 1978).
- 7) Serum LDL cholesterol – Calculated from the Friedewald's formula.
- 8) Serum VLDL cholesterol – Calculated from the Friedewald's formula.
- 9) Lipoprotein (a) (Lp-a) – Latex turbidimetry method (Gaubatz JW, 1983).

3. Result

75 patients suffering from hypothyroidism (24 males and 51 females), and 75 healthy control subjects (24 males and 51 females) were studied for thyroid function test, serum homocysteine level, serum folate, serum cyanocobalamin, serum lipid profile and serum creatinine.

The mean value for serum homocysteine level was 8.15 ± 0.345 $\mu\text{mol/L}$, Folic acid (ng/ml) 6.494 ± 0.397 , cyanocobalamin 360.9 ± 10.18 pg/ml, serum creatinine 0.7604 ± 0.058 mg/dl, Total cholesterol 162.46 ± 6.584 mg/dl, triglyceride 124.1 ± 13.084 mg/dl, HDL 37.0 ± 1.884 mg/dl, VLDL 25.72 ± 2.347 mg/dl and LDL 99.74 ± 5.439 mg/dl in control subjects. For hypothyroid patients, the mean value of serum homocysteine level were 17.10 ± 3.09 $\mu\text{mol/L}$ and 10.81 ± 1.96 $\mu\text{mol/L}$, folic acid 7.49 ± 0.345 and 11.01 ± 0.396 ng/ml, cyanocobalamin (pg/ml) 328.4 ± 4.78 and 274.27 ± 3.94 , serum creatinine (mg/dl) 0.99 ± 0.83 and 0.8 ± 0.05 , serum cholesterol (mg/dl) 272.77 ± 17.13 and 215.9 ± 16.98 , triglyceride (mg/dl) 176.19 ± 5.94 and 161.36 ± 6.34 , HDL (mg/dl) 33.63 ± 0.95 and 35.37 ± 2.030 , VLDL (mg/dl) 25.72 ± 2.3 and 32.26 ± 1.272 , LDL (mg/dl) 204.13 ± 17.72 and 147.88 ± 18.02 before and during treatment respectively.

Table 1: Comparison of homocysteine, folate, cyanocobalamin, serum creatinine and lipid profile of control and hypothyroid subject before treatment

Parameter	Control Subjects (mean \pm SD)	Hypothyroid subject before treatment (mean \pm SD)	P value (mean \pm SD)
Homocysteine ($\mu\text{mol/L}$)	8.15 \pm 0.345	17.10 \pm 3.09	0.0001
Folic acid (ng/ml)	6.494 \pm 0.397	7.49 \pm 0.305	0.0001
Cyano cobalamin (pg/ml)	360.9 \pm 10.18	328.4 \pm 4.78	0.0001
Serum creatinine (mg/dL)	0.7604 \pm 0.058	0.99 \pm 0.83	0.0001
Total cholesterol (mg/dL)	162.46 \pm 6.584	272.77 \pm 17.13	0.0001
Triglyceride (mg/dL)	124.1 \pm 13.084	176.19 \pm 5.94	0.0001
HDL (mg/dL)	37 \pm 1.884	33.63 \pm 0.95	0.0001
VLDL (mg/dL)	25.72 \pm 2.347	35.40 \pm 0.97	0.0001
LDL (mg/dL)	99.74 \pm 5.439	204.13 \pm 17.22	0.0001

*P – value < 0.0001 highly significant (HS)

P – value < 0.001 significant (S)

P – value >0.001 non significant (NS)

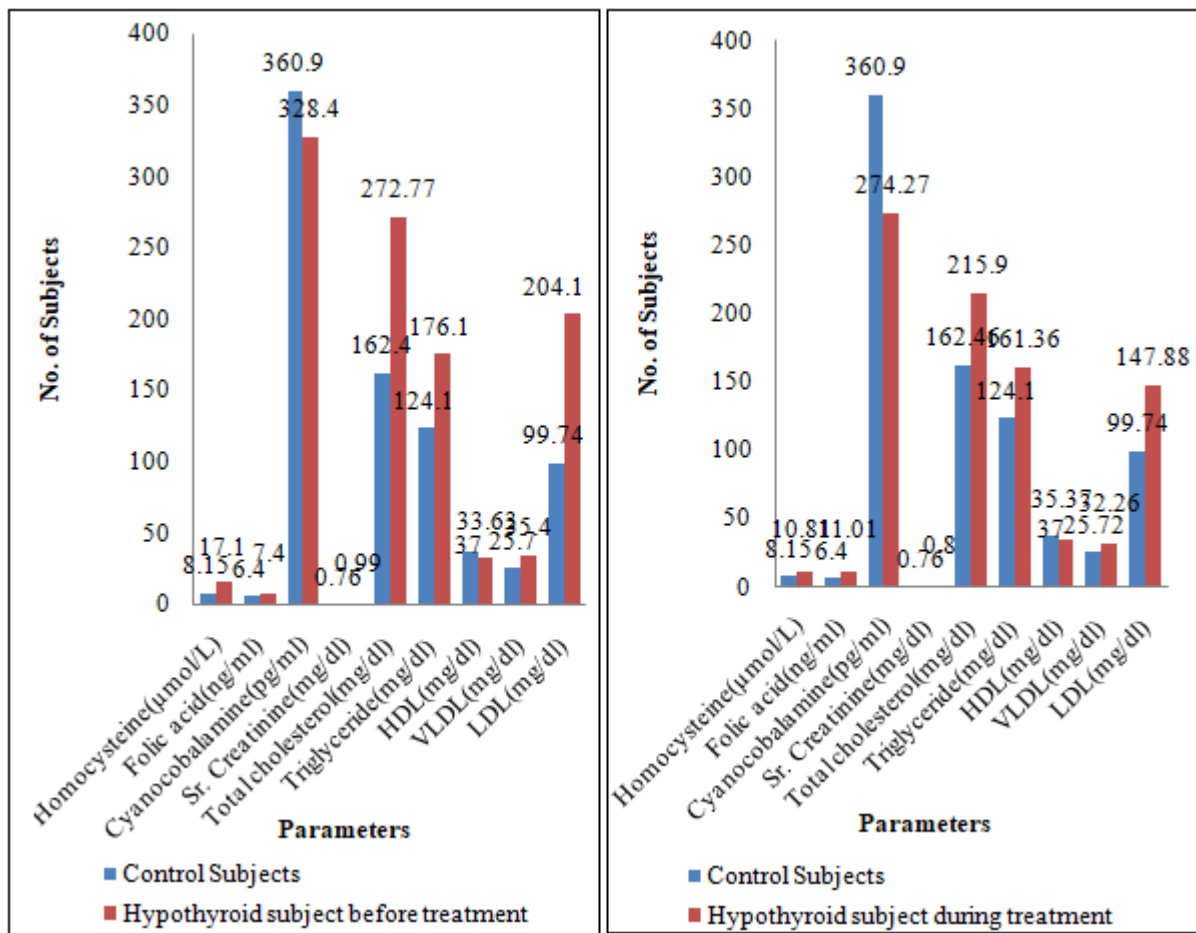
Table 2: Comparison of homocysteine, folate, cyanocobalamin, serum creatinine and lipid profile of control and hypothyroid subject during treatment

Parameter	Control subjects (mean \pm SD)	Hypothyroid subject during treatment	P value (mean \pm SD)
Homocysteine ($\mu\text{mol/L}$)	8.15 \pm 0.345	10.81 \pm 1.96	>0.0061 (NS)
Folic acid (ng/ml)	6.494 \pm 0.397	11.01 \pm 0.396	< 0.0001 (HS)
Cyano cobalamin (pg/ml)	360.9 \pm 10.18	274.27 \pm 3.94	< 0.0001 (HS)
Serum creatinine (mg/dL)	0.7604 \pm 0.058	0.8 \pm 0.053	>0.0017 (NS)
Total cholesterol (mg/dL)	162.46 \pm 6.584	215.91 \pm 16.98	<0.0001 (HS)
Triglyceride (mg/dL)	124.1 \pm 13.084	161.36 \pm 6.34	<0.0001 (HS)
HDL (mg/dL)	37 \pm 1.884	35.37 \pm 2.030	0.0002 (HS)
VLDL (mg/dL)	25.72 \pm 2.347	32.26 \pm 1.272	< 0.0001 (HS)
LDL (mg/dL)	99.74 \pm 5.439	147.88 \pm 18.02	< 0.0001 (HS)

*P – value < 0.0001 highly significant (HS)

P – value < 0.001 significant (S)

P – value >0.001 non significant (NS)



Comparison of Homocysteine, Folate, Cyanocobalamin, Serum Creatinine and Lipid profile of Control and Hypothyroid subject before and during Treatment

4. Discussion

Elevation of total plasma concentration of homocysteine (t-Hcy) is an important and independent risk factor for cardiovascular disease. Hypothyroidism is possibly also associated with an increased risk for coronary artery disease, which may be related to atherogenic change in lipid profile. Because hypothyroidism decreases hepatic level of enzyme involved in the remethylation pathway of homocysteine, we evaluated fasting t-Hcy in patients before and after recovery of euthyroidism. In univariate analysis, fasting Hcy was positively related to thyrotropin (TSH) and inversely related to folates, as thyroid hormone affects riboflavin metabolism and mainly by stimulating flavokinase and thereby synthesis of FMN and FAD which serve as cofactor for enzyme involved in metabolism of cobalamin, folate. MTHFR is FAD dependent enzyme is possible mediator of change in t-Hcy level according to riboflavin status.

Dyslipidemia is common finding in hypothyroid patients, explained by influences all aspect of lipid metabolism including synthesis, mobilization and degradation.

5. Conclusion

Hyper-homocysteinemia is a modifiable risk factor of atherosclerosis and can be prevented and treated by vitamin B12 and folic acid supplementation.

There is strong correlation of supplementation of thyroxin to patients of hypothyroidism which causes significantly decrease level of serum homocysteine and significant improvement of serum lipid profile which decreases relative risk of coronary artery disease in hypothyroid patients.

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