Original Research Article

A study on change in GFR and CPK levels with treatment of hypothyroidism

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Abstract

Background: Hypothyroidism is a clinical condition characterized by low thyroid hormone production. Primary hypothyroidism results when thyroid gland fails to produce adequate thyroid hormones. In secondary hypothyroidism the hypothalamopituitory thyroid axis works inadequately.
Aim: To assess the level of creatinine phosphokinase, serum creatinine and estimated glomerular filtration rate in hypothyroid patients on pre and post treatment conditions.
Objectives: To estimate the level of CPK, serum creatinine and eGFR levels in newly diagnosed hypothyroid patients and to assess the changes in serum creatinine, CPK and eGFR after control of hypothyroidism and to study the correlation of serum creatinine, eGFR and CPK with TSH and Free T4 levels.
Materials and methods: Present study was prospective experimental study with 6 weeks follow up. The study was conducted in endocrinology OP of Department of General Medicine, Pushpagiri Medical College Hospital, Thiruvalla. The study population was patients diagnosed with hypothyroidism. The period of study was 6 months from 26-09-2018. Total number of patients studied was 62 patients with diagnosed hypothyroidism.
Results: After evaluation of the study, out of the 62 patients, 56 had TSH and Free T4 levels became normal after 6 weeks of treatment, six patients had TSH between 5-10 µIU/L after 6 weeks of treatment the free T4 was normal in all patients. The serum creatinine and eGFR became normal in patients up to 50 years of age and showed improvement after 51 years of age.
Conclusion: Prolonged hypothyroidism leads to vasoconstriction and reduced blood flow to various organs. There is also reduced heart rate. The reduced blood flow results in reduction in GFR. The

muscular dystrophy and myopathy associated with hypothyroidism lead to increased CPK. This study showed that after controlling hypothyroidism the CPK, serum creatinine and eGFR improved.

Key words

Change, GFR, CPK, Hypothyroidism.

Introduction

Hypothyroidism is a clinical condition characterized by low thyroid hormone production. Primary hypothyroidism results when thyroid gland fails to produce adequate thyroid hormones. In secondary hypothyroidism the hypothalamopituitory thyroid axis works inadequately. The hypothalamic TRH stimulate pituitary TSH which in turn stimulate thyroid hormone synthesis and secretion. The thyroid hormones act via negative feedback through thyroid hormone receptor B2 (TR B2 Isoform) to inhibit TRH and TSH production. TSH is measured by immunoradiometric assay that are highly sensitive and specific [1].

Long standing hypothyroidism can cause reversible changes in metabolic parameters such as increase in serum creatinine [5, 8, 9]. There is thickening of skin, vasoconstriction and reduced blood flow. There is decrease in glomerular filtration and tubular functions and electrolyte and water homeostasis [12, 13, 14, 15].

Studies [2, 7, 10, 12] have been conducted to establish a relationship of creatinine phosphokinese (CPK) levels in thyroid disease. Serum CPK was first used as a diagnostic and important clinical marker of muscle damage. The serum CPK levels in healthy individuals depend on age, race, lean body mass and physical activity. Musculoskeletal disorders are more profound in overt hypothyroidism [3, 4, 6, 11].

Materials and methods

Study design

This was a prospective study with 6 weeks follow up. The period of study was 6 months from 26-09-2018.

Study population and site

Patients diagnosed with hypothyroidism. The study was carried out in Endocrinology OP Department of General Medicine, Pushpagiri Medical College Hospital, Thiruvalla. Sample size was 62 patients with diagnosed hypothyroidism.

Inclusion criteria

- Only OP patients.
- Both male and female patients with TSH $\geq$10 µ IU/L.
- Patients more than 18 years of age.

Exclusion criteria

- Pregnancy
- Pediatric patients
- Patients who are unable to give informed consent form
- Patients with preexisting chronic kidney disease

Brief procedure of the study

Informed consent was obtained from all patients. The level of TSH and Free T4 was obtained from medical records. For CPK and serum creatinine blood was collected and analyzed in the laboratory. The estimate GFR was calculated by MDRD formula (modification of diet in renal disease).

Analysis of data was done using SPSS Version 20.00 statistical software and mean I standard error of mean of different parameters were compared to determine the difference between two groups by paired ‘t’ test. The significant level were determined by p value < 0.05 was considered as significant.

Results

In the six months study, total 62 patients were enrolled as per inclusion exclusion criteria. In

this study, most of population falls under age group of 30-40 years. The mean age was found to be 39.41 (**Table – 1**). In this study, majority of patients were female, which was 44 (71%), males were 18 (29%).

Table – 1: Distribution of patients based on age group.

Age (Years)	Frequency	Percent	Mean	SD	Min	Max
Below 30	16	25.8				
30-40	23	37.1				
41-50	12	19.4	39.41	13.91	18	74
51-60	4	6.5				
Above 60	7	11.3				

Table – 2: Comparison of subjects with respect to TSH on consultation and after 6 weeks.

TSH	Mean TSH	P value
On consultation	38.92 µ IU/L	<0.001
After 6 weeks	1.8 µ IU/L	

Table – 3: Comparison of subjects with respect to Free T4 on consultation and after 6 weeks.

F T4	Mean T4	Mean	P value
On consultation	8.32 pmol/L	8.01	<0.001
After 6 weeks	16.34 pmol/L		

Table – 4: Comparison of subjects with CPK on consultation and after 6 weeks.

CPK		Mean Difference	P value
On consultation	243.75 IU/L	153.41	< 0.05
After 6 weeks	90.34 IU/L		

Table – 5: Comparison of subjects with serum creatinine levels on consultation and after 6 weeks.

Serum creatinine		Mean difference	P value
On consultation	1.61 mg/dl		
After 6 weeks	0.72 mg/dl	0.89	< 0.01

Table – 6: Comparison of subjects based on eGFR on consultation and after 6 weeks.

eGFR		Mean difference	P value
On consultation	65.89 Ml/mt/ 1.73^2		
After 6 weeks	120.4 ml/mt/1.73^2	54.52	< 0.01

Table – 7: Comparison of TSH on consultation and after 6 weeks with respect of age.

Age (Years)	TSH on consultation	After 6 weeks	P value
Below 30	49-55	2.21	<0.001
30-40	38.71	1.9	< 0.001
41- 50	22.66	1.59	< 0.001
51-60	41.04	1.61	< 0.005
Above 60	31.68	1.08	< 0.02

Table – 8: Comparison of Free T4 on consultation and after 6 weeks with respect of age.

Age (Years)	Free T4 on consultation	After 6 weeks	P value
Below 30	7.56	16.25	< 0.001
30-40	8.1	16.65	< 0.001
41- 50	9.2	15.83	< 0.001
51-60	7.4	15.75	< 0.006
Above 60	9.8	16.71	< 0.068

Table – 9: Comparison of CPK on consultation and after 6 weeks with respect of age.

Age (Years)	CPK on consultation	After 6 weeks	P value
Below 30	273.41	106.93	< 0.025
30-40	255.19	91.72	< 0.002
41- 50	168.51	80.7	<0.001
51-60	251.6	56.12	<0.007
Above 60	262.86	83.96	0.157

Table – 10: Comparison of serum creatinine on consultation and after 6 weeks with respect to age.

Age (Years)	S. creatinine consultation	After 6 weeks	P value
Below 30	1.44	0.71	< 0.004
30-40	1.6	0.76	< 0.001
41- 50	1.69	0.74	< 0.001
51-60	1.81	1.31	<0.155
Above 60	1.79	1.42	< 0.082

Table – 11: Comparison of eGFR with respect to age on consultation and after 6 weeks.

Age (Years)	eGFR	After 6 weeks	P value
Below 30	85	131	< 0.014
30-40	67.4	111.23	< 0.005
41- 50	46.98	117.77	< 0.001
51-60	45	71.7	< 0.076
Above 60	44	68.00	<0.096

Comparison of subjects with respect to TSH on consultation and after 6 weeks was as per **Table – 2**. Comparison of subjects with respect to Free T4 on consultation and after 6 weeks was as per **Table – 3**. Comparison of subjects with CPK on consultation and after 6 weeks was as per **Table – 4**. Comparison of subjects with serum creatinine levels on consultation and after 6 weeks was as per **Table – 5**. Comparison of subjects based on eGFR on consultation and after 6 weeks was as per **Table – 6**. Comparison of TSH on consultation and after 6 weeks with respect of age was as per **Table – 7**. Comparison of Free T4 on consultation and after 6 weeks with respect of age was as per **Table – 8**. Comparison of CPK on consultation and after 6 weeks with respect of age was as per **Table – 9**. Comparison of serum creatinine on consultation and after 6 weeks with respect to age was as per **Table – 10**. Comparison of eGFR with respect to age on consultation and after 6 weeks was as per **Table – 11**.

Discussion

This prospective study is used to find out the reversible changes of serum creatinine, creatinine phosphokinase and eGFR in hypothyroid

patients. This 6 months study was conducted in Endocrinology OP, Department of General Medicine at Pushpagiri Medical College Hospital, Thiruvalla. Total 62 patients were studied and a 6 weeks follow up was done in all patients after levothyroxine therapy. The level of TSH, Free T4, CPK and serum creatinine was estimated in the first part of study. eGFR is calculated by using MDRD formula. It was found that patients with significant hypothyroidism had decreased eGFR at diagnosis with the mean eGFR being 65.89. Significant cPK elevation was also seen in hypothyroid patients with a mean cPK of 243.75. The elevation of cPK was seen more in young patients, probably due to their higher muscle mass. After 6 weeks of levothyroxine replacement therapy the blood sample is again collected and CPK, serum creatinine TSH, free T4 are estimated. The eGFR also calculated the collective data was organized, tabulated and analyzed.

After correction of hypothyroidism, there was significant improvement of eGFR with the mean eGFR improving from 69.85 to 120.4. cPK also showed a similar improvement from 243.75 to 90.35. Both the changes were more significant in the younger age groups (age less than 50).

Hypothyroidism is one of the most common endocrine disorders. The prevalence of hypothyroidism is influenced by sex and age. The thyroid disorders are more common in women than men in the study (females – 71 %, male – 29%). The level of TSH and free T4 is commonly used to reflect the severity of disorder.

Prolonged hypothyroidism leads to infiltration of body tissues by mucopolysaccharides and hyaluronic acid and chondroitin sulfate. There is thickening of tissues, vasoconstriction and reduced blood flow to kidneys and other organs. As a result there is reduced eGFR. There is also reduced heart rate myocardial contractilityand stroke volume is also reduced leading to reduced eGFR. There will be impairment of muscle functions with stiffness cramps and pain. These patients can develop proximal myopathies and pseudomyotonia. The creatinine phosphokinase and serum creatinine will be elevated in such patients.

Conclusion

In this study, uncontrolled hypothyroidism was seen to be associated with increased CPK levels and decreased GFR. Correction of hypothyroidism resulted in significant decrease in cPK and improvement is GFR. This was seen across all age groups and both males and females. This study suggests that hypothyroidism can reversible fall in GFR

References

1. Harrison's principles of Internal Medicine, 20th edition, McGraw Hill Education, Volume 2, 2018, p. 2692-2693.
2. Rashmi Ranka and Rati Mathur. Serum creatinine phosphokinase in thyroid disorders. Indian Journal of Clinical Biochemistry, 2003; 18(t), 10 F, 110.
3. Finsterer, J Stellberger, C, Grossege, Koroiss A. Hypothyroid myopathy with unusually high serum creatinine kinase. Hormone, 1999; 52(4): 205-208.
4. Wan Nazaimoon, W M Siano ES, Sheriff, I. H Faridah, I Khalid IA. Serum creatinine kinase an adjunct unit biochemical index of subclinical thyrotoxicosis, Ann. Clini. Biochem., 2001; 38 (Pt-1): 57-8.
5. Mahantesh BB, Shankar Prasad DS, SangappaVK, Sivanand G. Evaluation of serum creatinine in subclinical hypothyroidism. A case – control study. International journal of clinical biochemistry and research, 2015; 2(3): 182-184.
6. Mohammed Ali Imtiaz, Sushith, Prathima M, B. S. Reshma, Madangopal, Francis N P, Monteiro. Renal and muscular dysfunction in overt

hypothyroidism. Journal of evidenced based Med & Health care, 2015; 2(48).

7. Raju Panday, Suresh Jaiswal, Jay Prakash Sah, Krishna Bastola, Subadhradulal. Assessment of Serum Enzymes levels in patients with Thyroid Alteration Attending Manipal Teaching Hospital, Pokhar. Research and Reviews: A Journal of Life Sciences, 2013; 3(I): 324-333.
8. The National Academy of Clinical Biochemistry Standards of Laboratory Practice. Laboratory support for the Diagnosis and Monitoring of Thyroid Disease, American Association of Clinical Chemistry, 1996; 1-64.
9. Quhtan A. Rashead, Daniah M. Hamid. The effect of Thyroid hormone on some biochemical factors of kidney. International Journal of Advanced Research, 2015; 3(7): 290-297.
10. Archana Prakash, A.K. Lal, K.S. Negi. Serum Creatinine Kinase Activity in Thyroid Disorders. JK Science, 2007; 9(1).
11. Ahmad Mooraki, Behrooz Broumand, Fatemhneekdoost, Parham Amirmokri, Bahar Bastani. Reversible acute renal failure associated with hypothyroidism: report of four cases with a brief review of literature. Nephrology (carlton), 2003; 8: 57-60.
12. KMDS Panag, Getanjali, Sudeep Goyal. Evaluation of creatinine kinase a Diagnostic Tool for Thyroid Function. Indian Journal of Clinical practice, September 2012; 23(4).
13. Gopal Basu, Angali Mohapatra. Interactions between Thyroid disorders and kidney Disease. Indian Journal of Endocrinology and Metabolism, 2012; 16(2).
14. Babul Reddy Hanmayyagari, Mounika Guntaka, Sri. Nagesh. Hypothyroidism a reversible cause of renal dysfunction. Medical Journal of Dr. D.Y. Patil University, 2015; 8(1).
15. Laura H. Mariani, Jeffrey S Berns. The Renal Manifestations of Thyroid Disease. J. Am Soc Nephrol., 2012; p. 22-26.