



SERUM TESTOSTERONE LEVELS IN CKD AND EFFECT OF ITS REPLACEMENT ON eGFR

Nephrology

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ABSTRACT

Background: Testosterone deficiency is common and impairs quality of life in patients with chronic kidney disease. However, there are very few studies about whether testosterone replacement therapy can improve quality of life in patients with chronic kidney disease. Therefore, the present study was designed to correlate the testosterone levels with the stages of chronic kidney disease and to observe the effect of testosterone replacement on eGFR.

Methods: This is a prospective study, conducted in Moti Lal Nehru Medical College, Prayagraj and Tejas Microdiagnostics, from September 2017 to August 2022. Adult male patients, who were diagnosed with chronic kidney disease, were included while patients with diabetes and patients on maintenance hemodialysis were excluded from the study.

Results: We included 100 diagnosed cases of chronic kidney disease however, 25 patients did not follow the study. Out of 75 patients 42.6% patients having serum testosterone level below 300 ng/dl, 42.6% were found to have serum testosterone levels in range of 300-400 ng/dl and 14.6% patients were having level above 400 ng/dl. Improvement in eGFR level of stage 3 and stage 4 were observed statistically significant (p-value 0.03 & 0.01 respectively). Staging of the disease improved after testosterone supplementation.

Conclusion: Present study clearly states that supplementation of testosterone in the patients with chronic kidney disease may leads to improvement in eGFR values and improves the staging of disease, consequently the quality of life. Further studies with more number of patients will clear the doubts about clinical benefit and adverse outcomes of the therapy.

KEYWORDS

Chronic kidney disease, Testosterone, Supplement, eGFR.

INTRODUCTION

Occurrence of testosterone deficiency is estimated to vary from 6% to 9.5% in community-dwelling men aged 40-75 years, rising to 15%-30% in diabetic or obese men [1-2]. In CKD this prevalence is much higher, with a prevalence of testosterone deficiency and insufficiency that was found to be 66% and 24%, respectively [3].

Chronic kidney disease (CKD affects the endocrine system, encompassing a wide variety of syndromes and clinical disorders. As a direct consequence, the uremic state is associated with abnormalities in the synthesis or action of many hormones, including the hypothalamic-pituitary-gonadal (HPG) axis [4-7].

Gonadal dysfunction is a common occurrence in patients with chronic kidney disease (CKD). Sexual dysfunction begins much before CKD-stage 5 and usually does not reverse with renal replacement therapy [8-9].

Moreover, because CKD can be neither cured nor improved but typically worsens over the long term, testosterone deficiency symptoms, too, may gradually worsen and affect quality of life (QoL) in most CKD patients [10]. Therefore, the present study was designed to correlate the testosterone levels with the stages of CKD and to observe the effect of testosterone replacement on eGFR.

MATERIALS & METHODS

This prospective study was conducted in Moti Lal Nehru Medical College, Allahabad and Tejas Microdiagnostics, from September 2017 to August 2022. Adult male patients, who were diagnosed with CKD without any other chronic illness, were included while patients with diabetes and patients on maintenance hemodialysis were excluded from the study. Consent was taken from all the patients and intramuscular injection of Testosterone undecylenate 250 mg (equivalent to testosterone 157.9mg) were administered at three month interval for a total of 2 doses. eGFR was calculated by using CKD-EPI 2009 equation.

All the patients were investigated for the radiological & pathological parameters like Complete blood count, Fasting blood glucose, Post prandial blood glucose, Liver function test, Renal function test, Serum electrolytes, Serum testosterone level, Estimated glomerular filtration rate (eGFR), and Serum prostate specific Antigen.

Statistical Analysis

Analysis was done using SPSS software version 19. Chi square test was applied for finding significant association between the categories of variables. Student's t-test was applied for finding the significant difference between mean values of variables. The numerical data was compared using t test for independent variables. The level of significance was considered at $p < 0.05$.

RESULTS

A total of 100 patients attended the nephrology OPD were included in the study. Since, fourteen patients were dropped after first follow up while 11 patients received only 1st dose of testosterone therefore, remaining 75 patients completed the study. The distribution of the patients according to the stages of disease is depicted in table 1 while Table 2 revealed the percentage of patients according to the level of testosterone.

Table 1: Distribution Of Patients By The Stages Of Disease.

CKD stage	No. Of Patients(n=75)	Percentage (%)
Stage 1	1	4.01
Stage 2	4	5.33
Stage 3	38	50.66
Stage 4	30	40

Table 2: Distribution Of Patients On The Basis Of S. Testosterone Levels.

S. Testosterone (ng/dl)	No. Of Patients(n=75)	Percentage (%)
<300	32	42.66
300-400	32	42.66
>400	11	14.66

Table 3: Effect Of Testosterone Supplementation On eGFR Values.

CKD stage	No. of Patients (n=75)	Percent tage	eGFR before treatment	eGFR after 1 st replacement therapy	eGFR after 2 nd replacement therapy	P-value
1	3	4.01 %	108	110	118	0.98
2	4	5.33%	71.25± 2.85	73.25± 4.11	71.75± 11.41	0.937

3	38	50.66%	41.86± 6.16	43.86± 7.21	45.23± 7.32	0.033
4	30	40%	22.09± 4.47	24.34± 5.20	25.31± 5.41	0.011

- CKD stages in young and middle aged men. *Basic and Clinical Andrology*, 2015; 25, 9, doi:10.1186/s12610-015-0027-y.
13. Idan Goldberg, Ilan Krause. The role of gender in chronic kidney disease 1,2 *European medical journal*, 2016;12:58-64.

Out of 75 patients 42.6% patients were having S. testosterone level below 300 ng/dl, 42.6% were found to have S. testosterone levels in the range of 300-400 ng/dl and only 14.6% patients were having the level above 400 ng/dl. The effects of two doses of testosterone supplementation on eGFR values are revealed in Table 3.

Improvement in eGFR level of stage 3 and stage 4 of disease were found to be statistically significant (p-value 0.03 & 0.01 respectively). Staging of the disease improved after testosterone supplementation as revealed by the table mentioned above.

DISCUSSION

In the present study the mean age of the patients under study being was 59.40 + 9.075 which is consistent with the study of Carrero et al [11], who reported that the male population having CKD presented a median age of 63 years.

In our study, we observed low testosterone values in CKD patients. Out of 75 patients 42.6% patients were having S. testosterone level below 300 ng/dl, 42.6% were found to have serum testosterone levels in the range of 300-400 ng/dl and only 14.6% patients were having the level above 400 ng/dl. Hylander et al [12] reported significant decrease in total testosterone level and estimated free testosterone with CKD stages. Idan Goldberg [13] have explained that CKD is a common disease worldwide and is associated with high rates of morbidity and mortality. They have discussed several aspects of the relationship between gender and CKD. According to them although the prevalence of CKD tends to be higher in women, the disease is more severe in men, who also have a higher prevalence of end-stage renal disease. In our study we observed 90.6 % were found to be in either third or fourth stage of CKD.

Our study showed improvement in the staging of disease after testosterone supplementation. Testosterone supplementation has been associated with improvement in testosterone values and symptoms and signs of hypogonadism in previous studies.

Studies on testosterone replacement are few [10]. We have analyzed the effect of testosterone supplementation on eGFR value and testosterone levels. Values of eGFR improved significantly after second dose of testosterone supplementation in stage 3 and stage 4 of disease thereby (p-value 0.03 & 0.01 respectively).

CONCLUSION

Chronic kidney disease affects hormonal milieu of the body, also aggravates the age related decline in testosterone levels. Supplementation of testosterone in these men leads to improvement in eGFR values and improves the staging of disease but duration of improvement can't be commented on, but further studies with more number of patients will clear the doubts about clinical benefit and adverse outcomes of the therapy.

REFERENCES

1. Tostain JL, Blanc F. Testosterone deficiency: a common, unrecognized syndrome. *Nat Clin Pract Urol*. 2008;5:388-396.
2. Araujo AB, Esche GR, Kupelian V, et al. Prevalence of symptomatic androgen deficiency in men. *J Clin Endocrinol Metab*. 2007;92:4241-4247.
3. Gungor O, Kircelli F, Carrero JJ, et al. Endogenous testosterone and mortality in male hemodialysis patients: is it the result of aging? *Clin J Am Soc Nephrol*. 2010;5:2018-2023.
4. Andrade VA, Gross JL, Maia AL. The effect of methimazole pretreatment on the efficacy of radioactive iodine therapy in Graves' hyperthyroidism: one-year follow-up of a prospective, randomized study. *J Clin Endocrinol Metab*. 2001;86:3488-3493.
5. Foulks CJ, Cushner HM. Sexual dysfunction in the male dialysis patient: pathogenesis, evaluation, and therapy. *Am J Kidney Dis*. 1986;8:211-222.
6. Handelsman DJ. Hypothalamic-pituitary gonadal dysfunction in renal failure, dialysis and renal transplantation. *Endocr Rev*. 1985;6:151-182.
7. Holley JL. The hypothalamic-pituitary axis in men and women with chronic kidney disease. *Adv Chronic Kidney Dis*. 2004;11:337-341.
8. Finkelstein SH, Finkelstein FO. Evaluation of sexual dysfunction in dialysis patients. In: Nissenson AR, Fine RN, editors. *Dialysis Therapy*. 3rd ed. Philadelphia: Hanley and Belfus; 2002. p. 368-73.
9. Palmer BF. Sexual dysfunction in uremia. *J Am Soc Nephrol*. 1999;10:1381-8.
10. Yeo JK, Koo HS, Yu J, Park MG. Effects of Testosterone Treatment on Quality of Life in Patients With Chronic Kidney Disease. *Am J Mens Health*. 2020;14(3):1557988320917258.
11. Carrero J, Qureshi AR, Nakashima A et al: Prevalence and clinical implications of testosterone deficiency in men with end-stage renal disease. *Nephrol Dial Transplant* 2011; 26: 184.
12. Hylander, B., & Lehtihet, M. Testosterone and gonadotropins but not SHBG vary with