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Evaluating the Effects of Testosterone Replacement Treatment on Lipid and Glycemic Profiles of Male Patients with Late-Onset Hypogonadism

Nauman Wazir[1], Sohrab Khan*[1], Muhammad Ubaid[1]

[1] Department of Endocrinology, MTI Lady Reading Hospital, Peshawar- Pakistan

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Corresponding Author
Sohrab Khan
Department of Endocrinology, MTI Lady Reading Hospital, Peshawar- Pakistan.
Email:

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Abstract

Objective: The objective of this study was to determine the effect of Testosterone Replacement Treatment (TRT) on lipid and glycemic profiles of late onset hypo gonadal men in Pakistani population.

Methodology: This was an observational retrospective study carried out from August 2022 to August 2023. All the cases of late onset male hypogonadism, either with type 2 diabetes mellitus (T2DM) or in a non-diabetic status, who had received testosterone replacement treatment were included in the study. Repeated measures Anova was used to see to see any difference in baseline, 6 months and 12 months' post treatment with testosterone of Total Cholesterol (TC), LDL cholesterol, HDL cholesterol, triglycerides HbA1C, and PSA.

Results: Data of (n= 57) hypo gonadal men who received TRT was available. Mean and standard deviation for age was 51.2 ± 7.3 years, for FSH it was 11.3 ± 7.2 IU/L and for total testosterone was 1.7 ± 0.7 ng/ml. Thirty-four (59.6 %) patients were diabetic and 23 (40.4 %) patients were non-diabetic. There was a significant reduction of TC from 175 ± 19.9 mg/dl at baseline to 157 ± 16.2 mg/dl at 12 months ($p < 0.001$), LDL cholesterol from 126 ± 29 mg/dl at baseline to 119 ± 25.1mg/dl at 12 months ($p <0.001$), triglycerides from 163 ± 27.4mg/dl at baseline to 144 ± 23.4 mg/dl at 12 months ($p <0.001$). There was significant improvement in HbA1C of diabetic patients from 7.5 ± 2.6 at baseline to 6.7 ± 2.1 at 6 months ($p< 0.001$) with TRT. The change in HDL cholesterol was not significant. There was significant increase in PSA from 1.73 ± 0.56 ng/dl at base line to 1.74 ± 0.57 at 6months ($p <0.001$).

Conclusion: Testosterone replacement improves total cholesterol, LDL cholesterol and triglycerides and did not improve HDL cholesterol in patients with late onset hypogonadism. It also significantly improves glycemic profile in patients with T2DM.

Keywords: Hypogonadism, Testosterone, Cholesterol, Triglycerides, Glycated Hemoglobin, Prostate-Specific Antigen

Introduction

Male hypogonadism is a condition in which there is a low testosterone production. In international literature, prevalence of hypogonadism in four population-based studies in the US ranged from 2.1% to 12.8%.[1-4] In Pakistan, the overall prevalence of hypogonadism is still not published but hypogonadism is reported to be common in patients with type 2 diabetes mellitus (T2DM), with prevalence estimated at 24.8% in one Pakistani study.[5] In both T2DM and non-diabetic patient groups, testosterone replacement therapy (TRT) is the most common treatment used for improving symptoms of hypogonadism.[6] Although a few studies have demonstrated beneficial effects of testosterone replacement therapy on hemoglobin A1c (HbA1c) in male patients with T2DM,[7-9] some on the other hand have showed no benefit.[10,11]

Regarding the effect of TRT on lipid profile, studies have not been consistent. In patients with T2DM, some studies have shown no significant effect of TRT on lipid profile.[12,13] In non-diabetic patients, some studies have shown a reduction of HDL- and an increase of LDL-cholesterol levels,[14] others showed an increase in HDL-C and a reduction of LDL-C levels,[15] which is often associated with a reduction in levels of total cholesterol.[16]

To the best of our knowledge no local study has assessed the effect of TRT on lipid profile in both of the above hypo-gonadal groups (with and without T2DM). In this study, we therefore, intended to assess the effect of TRT on lipid profiles of hypo gonadal patients and the objective of the study was to assess the effect of TRT on lipid and glycemic profile of male patients with hypogonadism with both diabetic and euglycemic status.

Methodology

We performed this observational retrospective study on 57 male patients who presented with late onset hypogonadism and were put on TRT before August 2023 to august 2024 whose data was present in electronic Hospital Management Record Information System (HMIS), after approval from hospital ethical committee. Hospital medical record numbers were used for retrieval of previous data. Patient with symptoms and signs of testosterone deficiency (decrease morning erection, decrease libido, erectile dysfunction, body aches and low mood) due to age related decrease in testosterone with total testosterone less than 3 ng/ml (3 to 8 ng/ml) were defined as having late onset hypogonadism. Patients with HBA1C more than 6.5% were defined as having diabetes mellitus (American diabetes association). Male patients with late onset hypogonadism aged more than 30 years (age related testosterone decline started after 30 to 40 years) either diabetic or non-diabetic were included in study. Patients with hypogonadism and having pituitary tumor, hyperprolactinemia, Empty Sella, pan-hypopituitarism (secondary hypogonadism), patient with primary hypogonadism (hyper gonadotrophic hypogonadism), patient on lipid lowering therapy, or patients with contraindications for TRT such as polycythemia, obstructive sleep apnea, prostatic cancer and breast cancer and were not given TRT, were excluded from study. In all included patients Testosterone was replaced previously using monthly intramuscular injection of testosterone enanthate 250 mg (Normal adult replacement dose of testosterone. Full replacement dose of testosterone was started in late onset hypogonadism, as compared to gradual increase in testosterone dose for puberty induction). The parameters estimated at the time of diagnosis were Complete Blood Count (CBC), Luteinizing hormone (LH), Follicle Stimulating Hormone (FSH), Glycated Hemoglobin (HBA1c), Prostate Specific Antigen (PSA), Total cholesterol (TC), Low density lipoprotein (LDL), High density lipoprotein (HDL) and triglyceride(TGs). CBC, HBA1C, PSA, TC, LDL, HDL and LDL done at 6 months and 12 months after initiation of TRT were recorded from HMIS (Laboratory parameters assessed at baseline, 6 and 12 months is according to endocrine society guidelines on testosterone replacement therapy in hypogonadism. All the labs done is clinically justified and we routinely do these investigations on follow up of patient who is on testosterone replacement therapy). Side effects of testosterone like edema feet, gynecomastia and polycythemia were also gathered from the notes entered in HMIS at 6 and 12 months. LH (Normal range (NR) = 2 to 9 IU/L), FSH (NR = 2 to 12 IU/L), total cholesterol (NR = up to 200 mg/dl), TGs (NR = less than 150 mg/dl), LDL (NR= 100 to 130 mg/dl) and HDL (NR= 35 to 65 mg/dl) were all previously measured in hospital laboratory using enzymatic assays. All the information was recorded using Performa validated by the ethical review committee of our Institution. Data was analyzed using SPSS version 20. Mean and standard deviations were calculated for age, LH, FSH and total testosterone. Frequencies and percentages were calculated for diabetes, polycythemia, gynecomastia and edema feet. Base line, 6 months and 12 months' total cholesterol, TGs, LDL, HDL were analyzed using repeated measures Anova test. HBA1c and PSA done at baseline and six months were analyzed by doing the same test. p value less than 0.05 was taken to see the difference as significant.

Results

Mean and standard deviation for age was 51.2 ± 7.3 years, for LH it was 8.9± 5.9 IU/L, for FSH it was 11.3 ± 7.2 IU/L and for total testosterone was 1.7 ± 0.7 ng/ml. Thirty-four (59.6 %) patients were diabetic and 23 (40.4 %) patients were non-diabetic. Baseline mean and standard deviation of HBA1C as 7.5 ± 2.6. The effect of TRT on different parameters of lipid profile of hypogonadal men, either diabetic or non-diabetic, is shown in Table No. 1. Total cholesterol, Triglycerides, LDL significantly decreased with TRT at 6 month and 12 months. There was no significant effect of testos-

Table 1. Effect of TRT on different parameters of Lipid Profile

Parameter	Baseline (Mean ± SD) mg/dl	6 months (Mean ± SD) mg/dl	12 months (Mean ± SD) mg/dl	P value
Total Cholesterol	175 ± 19.9	163 ± 17.5	157 ± 16.2	< 0.001
Triglycerides	163 ± 27.4	149 ± 25.8	144 ± 23.4	<0.001
HDL-C	46 ± 6.0	45.8 ± 6.1	45.9 ± 6.1	0.488
LDL-C	126 ± 29	122 ± 26.6	119 ± 25.1	<0.001

Abbreviations: TRT=Testosterone replacement treatment, SD= Standard deviation, HDL-C= High Density Lipoproteins, LDL-C= Low Density Lipoproteins

Table 2. Effect of TRT on HbA1C and PSA

Parameter	Baseline (Mean ± SD) % for HBA1C, ng/ml for PSA	6 months (Mean ± SD) % for HBA1C, ng/dl for PSA	P value
HbA1C	7.5 ± 2.6	6.7 ± 2.1	< 0.001
PSA	1.73 ± 0.56	1.74 ± 0.57	<0.001

Abbreviations: TRT=Testosterone replacement treatment, SD= Standard deviation, HbA1C= Glycated Hemoglobin, PSA= Prostate Specific Antigen

terone replacement on HDL cholesterol with p value of 0.488. The effects of testosterone on HBA1C and PSA is shown in Table No. 2. HBA1C significantly improved with TRT in diabetic patients, and PSA level increased with statistical significance with testosterone replacement at 6 months.

Seven (12.3 %) patients developed edema feet, seven (12.3 %) patients developed gynecomastia and six (10.5 %) patients developed polycythemia with testosterone replacement at the end of 12 months.

Discussion

Our study showed that in both euglycemic and diabetic patients, TRT decreased total cholesterol, triglycerides, and LDL cholesterol while it had no significant effect on HDL cholesterol. Our finding of TRT reducing TC goes in line with other studies of TRT replacement in both euglycemic[16,18,23] and diabetic patients.[19,13,17] Other studies showed no improvement of TC by TRT in diabetic patients.[20,21] Our study also revealed that TRT causes a reduction in LDL cholesterol. This is again consistent with other international studies where subjects of TRT were both diabetic,[19,20,22] and non-diabetic.[23] But this finding is not consistent with results of numerous other studies having diabetic,[12] and nondiabetic status,[14] which didn't show any significant change in LDL cholesterol with TRT. Regarding HDL cholesterol, our study failed to show any significant change with TRT. Results of some of the international studies go in line with ours in this regard, especially in both the diabetic[12,19] and non-diabetic status,23 while others show improvement of HDL cholesterol with TRT in diabetic[20,21] and non-diabetic[14] patients. One study showed improvement of HDL cholesterol with TRT only in patients with high baseline testosterone levels.[14] Our study population had a very low baseline testosterone (1.7 ± 0.7 ng/ml). This could explain the contrast of results of our study in terms of HDL improvement with TRT with those of the cited studies, that showed the results to be otherwise. In terms of triglycerides, our study showed a significant reduction. This is in agreement with results of many international studies with non-diabetic[14] and diabetic[19,20,22] statuses. One study however didn't show a statically significant change in TG levels which was done in patients who did not have diabetes mellitus.[23]

HbA1C was recorded at baseline and at 6 months. Our finding was that of statistically significant reduction of HbA1C especially in those with T2DM. This go along with findings of other studies that showed improvement of HbA1C.[7-9,12,20,23] While result of some studies didn't show any improvement in HbA1C.[10,11,21] Regarding PSA, TRT is known to be associated with a rise in PSA and the published guidelines recommend testing for PSA levels longitudinally after TRT initiation.[24]

This study included only a limited number of patients which limit generalizability of the results. Since it was an observational study, there was no randomization of patients into control group. Effect of diet, physical activity and duration of diabetes on HBA1C and lipid profile were not taken into account. Multicenter study with large number of patients and control and consideration of other confounding factors like effect of diet and physical activity on lipid profile is needed to establish these effects.

Conclusion

Testosterone replacement improves total cholesterol, LDL cholesterol and triglycerides and did not improve

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HDL cholesterol in patients with late onset hypogonadism. It also significantly improves glycemic profile in patients with T2DM.

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Authors' Contribution Statement

NW contributed to the conception, design, acquisition, analysis, interpretation of data, drafting of the manuscript, critical review of the manuscript, and final approval of the version to be published. SK contributed to the design, acquisition, analysis, and interpretation of data. MU contributed to the analysis, interpretation of data, drafting of the manuscript, and critical review of the manuscript. All authors are accountable for their work and ensure the accuracy and integrity of the study.

Conflict of Interest

Authors declared no conflict of interest

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None

Data Sharing Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.