The Effect of Testosterone Replacement Therapy on Glycemic Control in Hypogonadal Men with Type 2 Diabetes Mellitus

Nasrin Azad[1,2*]**, Nadia Sakla**[3] **and Gideon Bahn**[4]

[1]*Endocrinology Section, Edward Hines, Jr. VA Hospital, Loyola University, USA*

[2]*Endocrinology Section, Stritch School of Medicine, Loyola University, USA*

[3]*Department of Medicine, Research Service, Edward Hines, Jr. VA Hospital, USA*

[4]*Cooperative Studies Program Coordinating Center, Hines, IL, USA*

[*]**Corresponding authors:** Nasrin Azad, Endocrinology Section, Edward Hines, Jr. VA Hospital, Loyola University, Hines, IL, 60141, USA, E-mail: Nasrin.azad@va.gov

Abstract

Objective: The purpose of this study is to examine whether long term testosterone replacement therapy (TRT) improves blood glucose control in aged men with hypogonadism and diabetes mellitus.

Research design and methods: This is a retrospective and observational study using data from patients' Electronic Medical Record (EMR) at Hines Veteran Administration Hospital for 5 years, 2002-2007. The data were obtained from 129 out of 642 individuals with type 2 DM (T2DM) and hypogonadism, either receiving testosterone replacement therapy (TRT group) or not (control group) based on patient's personal decision.

Results: The overall mean HbA1c in the TRT group was lower by 0.25% compared to those of control group, 95% CI=0.016-0.49, p=0.037. After adjusting data by age, BMI, hemoglobin, and antidiabetic medications, HbA1c in TRT group decreased by 0.38%, CI=0.10-0.66, p<0.009. In a subgroup analysis, for the first time, we found that the mean HbA1c in TRT group decreased in those who received lower doses of antidiabetic, compared to those on control group: by 0.61%, CI=0.23-0.99, p=0.002 (oral agents) and by 0.27%, CI=0.011-0.52, p=0.041 (insulin). However, there was no association between TRT and glucose control in those patients who were on larger doses of antidiabetic. All the data were adjusted for age, BMI, and hemoglobin level.

Conclusion: TRT was associated with a modest but significant improvement of HbA1C in aged hypogonadal men with T2DM. Interestingly, the improvement of HbA1C was more significant in individuals whose blood glucose was controlled with less medications and no worsening of HbA1c was noted in TRT group who were treated with large doses of antidiabetic.

Keywords: Type 2 Diabetes mellitus; Glycemic control; Testosterone replacement therapy

Introduction

Presence of a complex interrelationship between testosterone levels and/or testosterone therapy on insulin level and insulin action, as well

Research design and methodology

Data collection:]s is an observational and retrospective study collecting data from Hines VA Hospital Patients' Electronic Medical Record (EMR) from 5 years: 2002-2007. e institutional Review Board of Edwards Hines Jr. VA Hospital had approved the study based on Helsinki declaration (1964).

Over the course of the study, we used this database to access all pertinent data such us provider's notes, medication prof les, labs (for various cofounders of this study), age, BMI, and information on subject's cardiac, renal, and other organ status. Moreover, the data was collected from the cohort of community dwellings who were self-su c]ent, living in their usual environment, like the general population. Because of this quality, the results of this study may be applicable to the similar community dwelling individuals.

First, we obtained data of 642 individuals with diagnosis of T2 DM, per ADA def n]t]on on either diet only, oral antidiabetic agents, and/or insulin and hypogonadism, primary or secondary, (total testosterone less than 9 nmol/L (260 ng/ml) and free testosterone less than 50 pg/ml). emwere either receiving testosterone replacement therapy (TRT group) or not receiving testosterone based on their personal decision to reject testosterone therapy (Control Group).

We used the following exclusion criteria to carefully choose those with very similar status of health without any spec]f c attention on the study arms. e exclusion criteria were: patients with untreated and/or active thyroid disorders, other endocrine disorders such as pituitary and adrenal gland, active malignancies, advance cardiac disease (NY heart association class III and IV), uncontrolled hypertension, renal]nsu c]encmftlef ned as a e GFR<40 ml/min/1.73 m^2, gastrointestinal problems that may cause malabsorption syndrome, liver disorders such as active or chronic hepatitis and cirrhosis of the liver (ALT, AST more than 2 times normal), polycythemia (Hg>18) and any hemoglobin disorders which may a ect HbA1c level, advance chronic obstructive pulmonary disease (COPD), on medication (s) which could decrease mobility, or steroids or any other medications which could a ect the hypothalamic-pituitary-testicular axis function. All the study data were available and obtained from the hospital Electronic Medical Record data base. Out of 642 patients a total of 129 patients met the study criteria, age 43-82 in TRT and 45-85 in control group and BMI 22.6-50 in TRT and 22.4-48.6 in control group (Table 1). Out of 129 patients, 63 received TRT (TRT group) and 66 patients in the control group who chose not to receive TRT.

Variables	Control Group	TRT Group	
HbA1C	56+10 (7.3+1.3)	53+7.6 (7+1)	P=0.18
Age	62.1+8.7	64.3+9.1	P=0.17
BMI	32.6+5.3	33.1+5.8	P=0.54
Hemoglobin	217.2+23.3 (14+1.5)	221.8+23.3 (14.3+1.5)	P=0.44

power with the difference of 0.25, standard deviation of 0.4 and alpha level of 0.05, age 43-82 in TRT and 45-85 in control group and BMI 22.6-50 in TRT and 22.4-48.6 in control group (Table 1). Of these 129 patients, 63 patients received testosterone replacement therapy (TRT group) and the remaining 66 patients chose not to receive TRT for the personal reasons (the control group). There were no significant statistical differences in baseline characteristics values for HbA1c, age, hemoglobin, and BMI between the two study groups (Table 1). As we have stated previously all the individuals were controlled with other cofounders that might have had any effect on data.

The Mixed random effect model for the longitudinal data was used to compare the overall HbA1c

reverse relationship in women, where higher testosterone levels were