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To study the effect of taurine on the effects of vital bones and regulate the level of glucose in type II diabetes

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ABSTRACT

Taurine is sulfur containing semi-essential amino acid that has important roles in many biological processes, but its effect on glucose homeostasis, weight, growth and bone mineralization weren't well-deϑined. Objectives: the evaluation of oral Taurine effects has used for 3 months on bone mineralization biomarker, glycemic control and body weight in type ll diabetic patients. Methods: the interventional double-blind placebo-controlled study in which 80 patients with type 2 diabetes mellitus (age range 45-55) assigned in either control (n=40), or study group the (n=40) group. The last group has received a 1000mg capsule of Taurine once a day for three months. Parameters measured were serum calcium, 25(OH) vitamin D and osteocalcin, NTX-1 HbA1C% with fasting blood glucose before and after 3 months. Results: taurine led to signiϑicant ($p<0.05$) rise in osteocalcin, signiϑicant lowering in body weight, BMI and there were no signiϑicant changes in serum calcium, NTX-1, Vitamin D, HbA1C and fasting blood glucose, all as compared with the control value. Conclusions: the 3 months of oral Taurine are used in type II diabetic patients may modulate bone mineralization represented by elevation of osteocalcin and reduction of body weight, but has no signiϑicant effect on glycemic control and did not reduce HbA1C%.

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INTRODUCTION

Diabetes Mellitus is a pandemic metabolic health disturbance, which featuring by chronic hyperglycemia and induces many pathological complications among both sexes in a wide range of ages, so these complications include microvascular complications like nephropathy, retinopathy, neuropathy and macrovascular complications like acute coronary syndrome and stroke. Several studies in recent years approved that patients with type II diabetes mellitus are prone to osteoporosis, and they are at a

greater risk of developing bone fragility (Oei *et al.*, 2015). A main mechanism of osteoporosis is an imbalance between the activity of osteoblasts that form bone, and osteoclasts that breakdown bone leading to bone microstructure deterioration and fractures. The other mechanisms by which diabetes affect bone include hyperglycemia, oxidative stress and gathering of advanced glycation end reproducers (AGEs) (Dede *et al.*, 2014; Dhaliwal *et al.*, 2014; Rubin, 2015; Jang *et al.*, 2011). The uncontrolled blood glucose level in typeII, diabetic patients can affect bone metabolism, and its fragility directly or indirectly leading to change in the level of bone biochemical markers in blood or urine. The most sensitive markers include osteocalcin (OC), the bone formation marker measured in serum, other biomarkers can be recommended is N-terminal telopeptide (NTX) as a reference marker for bone resorption. The antidiabetic medications have variable effects on bone metabolism, maybe a positive or negative impact. The most known biguanide is Metformin, because it has a positive effect on osteogenesis, via activation of osteoblast-speciϑic Runx2(run–related transcription factor 2). And the activation of AMP-activated protein kinase (Molinuevo *et al.*, 2010; Schuller-Levis and Park, 2003; Hansen, 2001).

At the same time, it has a negative effect on the differentiation of osteoclast. Taurine is a semi-essential or conditional amino acid, which found in a large amount of human and animal tissues, but its endogenous production is insufϑicient. Therefore it must be provided by the diet or given as a supplement. The Taurine exhibit antioxidant and anti-inϑlammatory actions, as well as have many beneϑicial roles in diabetes because it is able to block toxicity, which caused by oxidative stress, it also has a role in osmoregulation, in counteracting inϑlammation and glucose homeostasis. The novelty of this study is that the effects of taurine 1000 mg orally for glycemic control, bone mineralization, and body weight have not measured in human patients before (Lampson *et al.*, 1983; Cherif *et al.*, 1998; Nandhini *et al.*, 2004; Ahmadian *et al.*, 2017).

Aims of the study

The evaluation effect of oral Taurine used for 3 months on bone mineralization biomarker, glycemic control and body weight in type II diabetic patient.

MATERIALS AND METHODS

Study design

Randomize, double-blind placebo-controlled study, this study was carried out from October 2017 to December 2018 in Al-Basra General Hospital. Basra city–southern Iraq. After an agreement of scientiϑic and ethical committees in the college of pharmacy and hospital.

Patients Selection

Inclusion Criteria

Inclusion Criteria: adult patient with age range 45-55 years old, diagnosed with Diabetes Mellitus type 2, and each patient used medical diabetes, treatment no more than ϑive years.

Exclusion criteria

Diseases are included malignancy, thyroid problems, parathyroid, pregnancy or breastfeeding, medications use like vitamin D calcium supplements, and obesity medications or blends, steroids, bisphosphonates and insulin at least one month before starting study and to the next 3 months of study, (Alkholiϑi and Albers, 2015; Arrieta *et al.*, 2014).

Sample size determination

Was determined by using by G power V3.1 software assuming 1:1 subject division (control: study). The response within each subject group was normally distributed with standard deviation 5. If the true difference in the study and control means is 5, we will at least need to study 40 subjects for the study, and 40 control subjects to be able to reject the null hypothesis that the means of the study and control groups are equal with probability (power) 0.82. The type I error probability associated with the test of this null hypothesis is 0.05 (Bai *et al.*, 2016).

Study groups

Each diabetic patient, that fulϑilled the requirement of study, was asked to sign a written consent, then be randomly allocated, by using simple randomization, into either control or study group. Only 80 patients have completed the study successfully.

Study group: (n=40,age 48.8+3.1years, 22 males &18 females) received Taurine 1000mg capsule (Jarrow's formulas) orally once daily. There was no signiϑicant difference in average ages and male, the female ratio between groups. Hospital's pharmacist informed each patient about the goals of the study and function of taurine after signing of written consent. Height of the patient was registering at the beginning of the study, in addition to body weight and body mass index was measured to each patient before and after 3 months (Balshaw *et al.*, 2013; Chan *et al.*, 2013; Chen *et al.*, 2016; Chiang *et al.*, 2014).

Sampling

A venous blood sample was drawn from each participant, for measuring fasting blood glucose;

Table 1: shows the name and source of kits used to measure the parameters of the study

parameters	Kit	Source
Fasting blood glucose	Glucose Assay Kit (Colorimetric)	Cell Biolab, INC
Serum calcium	Calcium Assay Kit	BD Biosciences, USA
Osteocalcin	Osteocalcin (1-43/49) ELISA	ALPCO diagnostics
NTX-1 (N terminal telopeptidase of type1 collagen)	Human Cross-linked N terminal Telopeptides of type I collagen ELISA Kit	MyBioSource, US
Serum 25-OH-Vitamin D	25-OH-Vitamin D direct ELISA	IBL INTERNATIONAL GMBH

Table 2: Demographic data of patients in the study groups. Some of data expressed as Mean ± standard deviation

	Control group N=40	Study group N=40	P values
Age (years)	50.2 ± 3.7	48.8 ± 3.1	0.072
Male: female ratio	24:16	22:18	0.821
Weight (kg)	98 ± 14.5	95.8 ± 13.3	0.324
Height (cm)	172.6 ± 7.5	171 ± 6.2	0.326
Body mass index (kg/m2)	33.1 ±5.8	32.9 ± 5.1	0.821
Obesity ratio	30 (75%)	28 (70%)	0.802
Fasting Blood glucose (mg/dl)	121.5 ± 9.8	122.6 ± 12.2	0.544
HbA1c%	7.3 ± 0.6	7.5 ± 0.6	0.168
Diabetes duration (years)	2.7 ± 1.7	3.1 ± 1.6	0.342

P values<0.05 considered as signiϑicant values

Table 3: Comparison of bone mineralization biomarkers in both study groups; before and after treatment. Values are expressed as Mean ± standard deviation.

	Control group N=40		Study group N=40		P values
	Baseline	After treatment	Baseline	After treatment	
Osteocalcin (ng/ml)	17.4 ± 5.6	18.3 ± 5.9	17.7 ± 12.3	28.9 ± 10.7*a	0.00002
Serum Vit. D (ng/ml)	19 ± 5.3	20.3 ± 5.4*	18.8 ± 6.7	20.8 ± 6.8*	0.378
Serum Calcium (mg/dl)	7.1 ± 2	7.3 ± 1.9	7.1 ± 2.1	7.6 ± 2.5*	0.695
NTX-1 (ng/ml)	20.4 ± 7.1	20 ± 6.8	20 ± 8.9	18.3 ± 7.6	0.605

P values<0.05 considered as signiϑicant values
*signiϑicant (p<0.05) as compared to its baseline values
a- signiϑicant (p<0.05) as compared to control value

HbA1C%; serum calcium; Osteocalcin; Serum NTX (N- terminal telopeptide); 25-(OH)Vitamin D level; before and three months after administration their assigned supplement. Table 1 as follows,

Data Analysis

Data analyzed by using MedCalc® software V12, the data were expressed as mean + standard deviation. One – way ANOVA was used to find the significant (p<0.05) effects between the groups.

The independent sample t-test was used to the comparison between groups and paired t-test, was used to find the significant difference between pre-and after treatment values within each group, p-value < 0.05 was considered as significant (Coughlan *et al.*, 2016).

RESULTS AND DISCUSSION

Demographic data of patients (Czajka and Malik, 2016; Silva *et al.*, 2014; Luca *et al.*, 2015; Froger *et al.*, 2014)

As in Table 2 There were no significant (p<0.05) differences between control and study group. In age (50.2 ± 7 Vs. 48.8 3.1; p value= 0.072); male: female ratio (24:16 for control Vs. 22:18 for study; p value =0.821); weight (kgs) (98 ± 4.5 Vs. 95.8 ± 13.3 ; p value=0.324); Height (cm) (172.6 ± 7.5 Vs. 171 ± 6.2 ; p value =0.326), Body mass index (33.1 ± 5.8 Vs. 32.9 ± 5.1; p value = 0.821); obesity ratio (75% control Vs. 70% study. p value = 0.802); fasting Blood glucose (121.5 ± 9.8 for control Vs. 122.6 ± 12.2 for study group; p value= 0.544), Glycosylated hemoglobin (HbA1C%) (7.3 ± 0.6 for control Vs. 7.5 ± 0.6 for study group; p value= 0.168) and diabetes duration in years (2.7 ± 1.7 for control Vs. 3.1 ± 1.6 for study group; p value= 0.342)

Bone mineralization biomarkers (Furukawa *et al.*, 2014; Ginguay *et al.*, 2016; Ito *et al.*, 2012)

Osteocalcin raised significantly (p<0.05) in the study group after using Taurine for 3 months, as compared with its baseline value (28.9±10 .7) after treatment vs. 17.7±12.3 to baseline, also it was significantly (p<0,05) higher than the values of control group (28.9±10.7) after treatment to study group vs. 18.3±5.9 to control, as in Table 3.

Serum Vitamin D elevated significantly (p<0.05) in the study group, after using Taurine for 3 months as compared with its baseline value (20.8+6.8) after treatment vs. 18.8±6.7 to baseline, this elevation was not significant (p<0.05) as compared to control value (20.8±6.8) to study vs. 20.3 ±9 to control, as in Table 3.

Serum calcium: elevated significantly (p<0.05) in the study group, after using Taurine for 3months as compared with its baseline value (7.6+2.5) after treatment vs. 7.1+2.1 to baseline, this elevation was not significant (p<0.05) as compared to control value (7.6±2.5) to study vs 7.3 ±9 to control, as in Table 3.

N- terminal telopeptide (NTX-1) was not significantly(p<0.05) changed in both groups, even after treatment. As in Table 3.

Glycemic control markers (Hernández-Benítez *et al.*, 2012; Chen *et al.*, 2012; Jong *et al.*, 2012; Locke *et al.*, 2011)

Fasting Blood glucose was not significantly(p<0.05) changed in both groups, even after treatment as in Table 4.

Glycosylated haemoglobin (HbA_{1C} %) was not significantly(p<0.05) changed in both groups even after treatment, As in Table 4.

Effect on body weight (Junyent *et al.*, 2011; Zulli, 2011)

The per cent change in body weight was lowered significantly (p<0.05), in the study group after using Taurine for 3 months, as compared with a control value (-2.5±4.3 to study vs. 0.43±5.8 to control). And same to body mass index was (-2.4±4.3 to study vs 0.41±5.8 to control), as in Table 5.

Taurine contains the sulfur amino acid, that available in mammalian tissues. A lot of studies are talked about its function, and roles in many known biological processes, e.g. calcium metabolism, protein phosphorylation, energy extraction etc,. Despite the importance of Taurine in these biological functions, its interaction in the regulation of glucose homeostasis, weight, growth and bone metabolism remain not well defined.

In this study, Taurine supplement used for 3 months, in type 2 diabetic patients and used to study its effect on biochemical markers related to bones mineralization, diabetes control and effect on body weight (Puerta *et al.*, 2010).

Taurine administration as a supplement was able to raise the serum level of osteocalcin significantly(p<0.05), as in Table 3. This finding was different from results of many studies, that found the use of Taurine have not resulted in significant change, in the level of osteocalcin.

Taurine stimulates osteoblasts resulted in secreting osteocalcin. Due to oral supplementation, taurine probably was available in blood in sufficient concentration, to produce sustain raise in osteocalcin level in the blood of Taurine treated group, that reflected as significant rising as compared to control

Table 4: Comparison of changes in the percentage of glycemic control parameters in both study groups. Values are expressed as Mean ± standard deviation.

	Control group N=40	Study group N=40	P values
% change Fasting Blood Glucose	-0.4 ± 15.2	-0.2 ± 2.2	0.934
% HbA1c	1.1 ± 7.4	-1.5 ± 10.7	0.211

P values<0.05 considered as signiϑicant values.

Table 5: Comparison of percentage changes in Body weight & BMI for both study groups. Values are expressed as Mean ± standard deviation.

	Control group N=40	Study group N=40	P values
% change in Weight (kg)	0.43 ± 5.8	-2.5 ± 4.3	0.014
% change in BMI	0.41 ± 5.8	-2.4 ± 4.1	0.015

P values<0.05 considered as signiϑicant values

group (Kinney, 2005).

Taurine may enhance the intestinal absorption of fat-soluble vitamins, like vitamin D and studies found low Taurine dietary intake may compromise vitamin D absorption.in this study, Taurine supplement did signiϑicantly enhance intestinal absorption of vitamin D, so that serum level of 25 (hydroxy) Vitamin D, was elevated signiϑicantly in group used Taurine but unfortunately, these changes were not signiϑicant as compared to the control group (Udawatte *et al.*, 2008).

Serum calcium changes in this study were parallel to changes in vitamin D level.

In addition to that; blood N-terminal telopeptide, a bone resorption biomarker, that secreted by the activity of osteoclasts, was not signiϑicantly changed by Taurine supplement. This may indicate that Taurine may not stimulate osteoclast, probably not enhance bone turnover activities. The serum calcium was not also changed signiϑicantly, as compared to the control group (Choi and Seo, 2013; Yuan *et al.*, 2006).

Taurine may suppress insulin secretion in nondiabetic pancreatic islets and may serve as a regular factor to insulin secretion, and blood glucose level . enhancer to peripheral insulin sensitivity, and Taurine may have a hypoglycemic effect. There were no signiϑicant changes in the level of fasting blood glucose, or HbA1C% measures during studying this in agreement with (Zhang *et al.*, 2004) that found no signiϑicant change in fasting blood glucose, after 7 weeks from using the Taurine supplement in non –diabetic individuals. Although so, body weight and BMI index were signiϑicantly reduced after treatment with Taurine, but this was not signiϑicant as compared to the control group. This ϑinding was in agreement with (Zhang *et al.*, 2004).

CONCLUSIONS

Taurine 1000 mg orally use in type II diabetic patients may modulate bone mineralization represented by elevation of osteocalcin, and may reduce body weight but has no signiϑicant effect on glycemic control and did not reduce HbA1C%.

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The Contribution of authors

We declare that this work achieved by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne to the authors. Falah Hassan Shari, Hiba Dawood and Jubran K. Hassan conceived and designed the study. Qais A. Aljazaeari, Mazin A.A.Najim and Ahmad Salahuddin designed all the experiments and revised the manuscript. H. N. K. AL-Salman performed the experiments, collected, analyzed the data, and wrote the manuscript.

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