Clinical study evaluating β-blockers use and fracture risk in patients with primary osteoporosis.

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Abstract

Introduction: Osteoporosis is a disease identified by low bone mass, in parallel with an intensification of bone fragility. Several observational studies suggested that users of beta-blockers (BB) had higher bone mineral density (BMD) and/or reduced fracture risk. Other studies, on the other hand, found no effect of BB on fracture risk or improving osteoporosis disease state.

Objective: To investigate the relationship between the use of selective and non-selective BB and fracture risk in male and female osteoporotic patients.

Methods: This is a randomized, controlled, parallel, prospective study that involves fifty osteoporotic patients of both sexes with osteoporosis. These osteoporotic patients are treated with (osteoporosis standard therapy) and were divided into three groups: control group (CG) contained 10 patients, non-selective beta-blocker group (NSBB), and cardio-selective beta-blocker group (CSBB) each BB group containing 20 patients. Then, the effect of BB on T-score, bone mineral density (BMD), fracture risk (FR), and bone turnover markers were studied.

Results: A significant difference was noticed between mean values of T-score among the three studied groups after six months of follow-up. BMD was statistically significantly higher in (NSBB & CSBB) groups compared to the CG group. The fracture risk was statistically significantly lower in both (NSBB & CSBB) groups in the three types of fracture risk region. Moreover, there was a drop in bone turnover markers (BTM) in both groups (NSBB or CSBB) compared to the control group.

Conclusion: The usage of BB either (NSBB or CSBB) improves osteoporosis disease state by increasing BMD, lowering FR, and decrease BTM.

Key words: Osteoporosis, Beta-blockers (BB), Bone mineral density (BMD), Fracture risk (FR), Bone turn over markers (BTM), Non-selective beta-blockers (NSBB), Cardio selective beta-blockers (CSBB).

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Introduction

Osteoporosis is a bone disorder affecting millions of people worldwide [1]. Low bone mineral density and deterioration in bone tissue are the most common features of osteoporosis [2]. It is mainly diagnosed with bone mineral density (BMD) T-score 2.5 or more standard deviations below peak bone mass, according to the World Health Organization (WHO) criteria [3]. Osteoporosis can be categorized into primary osteoporosis, which involves postmenopausal osteoporosis (type I) and senile osteoporosis (type II), and secondary osteoporosis, which occurs due to malabsorption, medications such as glucocorticoids, and some diseases such as hyperparathyroidism [4]. Osteoporos is fracture is a severe outcome of osteoporosis that eventually causes high risk of mortality and morbidity. Moreover, management of osteoporosis and osteoporosis fracture placed an intolerable burden due to their cost and the need for qualified manpower and material resources. Therefore, identifying risk factors to avoid osteoporosis has been one of the great magnitude topics.

Age, gender, smoking, drinking coffee, coronary heart diseases, diabetes, essential hypertension, and decreased estrogen level are risk factors for osteoporosis. Hypertension is one of the major risk factors for osteoporosis and both of them are age-related diseases and consequences of the interaction between genetic and environmental factors. Nevertheless, there is still controversial theory whether a correlation occurs between hypertension and osteoporosis. Several studies had indicated that hypertension is negatively correlated with bone mineral density [5,6].

A prospective study done by Cappuccio F P and his colleagues on more than 3000 women, found an association between high blood pressure and increased bone loss at the femoral neck. They hypothesized that more calcium loss associated with hypertension might contribute to hip fractures. On the other hand, other studies showed no correlation between hypertension and bone density. where the BMD percentage of patients with both osteopenia and osteoporosis was the same in those with and without hypertension [7, 8].

β-Adrenergic receptor antagonists (β-blockers) are one of the most well-known antihypertensive treatments via reducing cardiac output, the release of renin from the kidneys, and blocking the action of endogenous catecholamines on β-adrenergic receptors [9]. Recent findings demonstrated that β-blockers might affect the bone structure, metabolism, and fracture healing [9, 10]. Surprisingly, β -Adrenergic receptors have been detected on osteoblast-like cells [11, 12]. Osteoclast formation necessitates the existence of M-CSF and receptor activator of nuclear factor kappa-B ligand (RANKL) [13]. Stimulation of β -adrenoceptors enhances the expression of RANKL and triggers osteoclast-genesis activation in mouse bone marrow cells. In addition, a recent study found that β -blocker use was associated with a 30% reduction in fracture risk and BMD was higher among β -blocker users at the spine, total hip, whole body [14]. Another theory suggested that leptin signaling in the hypothalamus stimulated a positive sympathetic tone and targeting either leptin or its signaling pathway by β –blocker might be effective for osteoporosis [15]. Therefore, the current study was done to fill the gap in research regarding the correlation between β -blocker (either selective or non-selective) use and osteoporosis in primary osteoporotic patients.

Subjects and Methods

All study patients were informed of the study's purposes and with the anticipated adverse effects that recipients might experience. Informed consent was obtained from all individual participants included in the study. The study was conducted in conformity with the standards of good clinical practices and was approved by the Research Ethical Committee (REC) of College of Pharmacy, Tanta University; and Tanta University Hospital Institutional Review Board (IRB). The clinical trial number was NCT04704947.

Study design and patients population

This is a randomized, open-label, controlled, parallel, prospective study that involved fifty 50 osteoporotic patients of both sexes who were recruited from the Rheumatology and Rehabilitation Department, Tanta University Hospital, Tanta, Egypt. During the period from November 2017 to December 2019. Patients were screened for eligibility according to the following inclusion and exclusion criteria as shown in figure 1.

Inclusion criteria

Age ≥ 50 years old, Male & female osteoporotic patient, Hypertensive & normotensive patients, BMD T-score ≥ 2.5 or more SD below peak bone mass.

Exclusion criteria

- Patients on drugs that may improve osteoporosis disease such as: Angiotensin-converting enzyme inhibitor (ACEI), Angiotensin receptor blockers (ARBs), Thiazide diuretic, Nitrates, Spironolactone, and Statins.
- Patients on drugs that may worsen osteoporosis disease such as: Corticosteroids, Loop diuretics, Anticonvulsants, Antidepressants, Aromatase inhibitors, Thyroid replacement therapy, and Proton pump inhibitors.
- Patient refused or failed to give informed consent.

Study protocol

All eligible patients who met the above-mentioned criteria and agreed to participate in the study were asked to sign an informed consent before conducting the study. In the current study all recruited patients with osteoporosis are treated with Alendronate sodium 70 mg once/week (Fosamax)®, Calcium supplement 500 mg once daily, Vitamin D_3 1 mcg daily (osteoporosis standard therapy) and were randomized using a table of random numbers into:

Group A (control group) (CG): Ten patients with osteoporosis and attended to Rheumatology and Rehabilitation Department. They received Alendronate sodium 70 mg (Fosamax)® once/week, Vitamin D3 1 mcg once daily and Calcium supplement 500 mg once daily.

Group B (Non-selective beta-blocker Group) (NSBB): Twenty patients with osteoporosis and hypertension on the same treatment as (CG) in addition to starting propranolol (Inderal)® 10 mg once daily titrated up according to patient's response.

Group C (Cardio-selective beta-blocker Group) (CSBB): Twenty patients with osteoporosis and hypertension on the same treatment as (CG) in addition to starting bisoprolol (Concor)® 5 mg once daily titrated up according to the patient's response.

Patients were followed- up for six months to monitor & evaluate the difference in disease progression or regression as shown in figure 1.

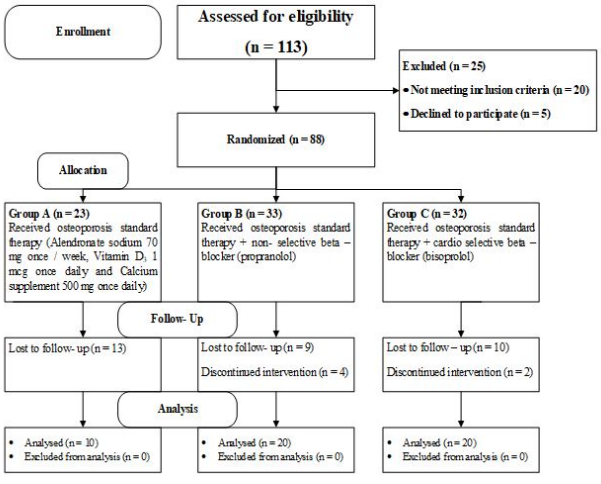

Figure 1. *Study design & flow chart of screened patients.*

All recruited patients were subjected to the following:

History taking with an emphasis on demographic characteristics such as age, sex, weight, and height of the patients, full medical and medication history. Past medicinal History with special emphasis on all types of fragility fracture which classified into three main groups: hip fracture, clinical

vertebral and non-vertebral fracture. Associated risk factors are Lifestyle factors (e.g. smoking, alcohol use, weight, and height of the patient), History of present illness.

Sample collection:

Venous blood samples and urine samples were collected from each patient at two time points where timing of sample collection includes the following:

- Serum - Morning (before 9 am) after an overnight fast.
- Urine - Either first or second morning void, with creatinine correction, after an overnight fast.

Baseline laboratory tests include the following:

- Serum chemistry panel, Liver function tests.
- Thyroid function test, 25-Hydroxyvitamin D level, Serum protein electrophoresis calcium/creatinine ratio, Testosterone, luteinizing hormone (LH) /follicle-stimulating hormone (FSH)
- Serum creatinine, Liver enzymes (ALT), (AST) were assayed before and after six months of treatment with bisphosphonates with or without BB
- Measurement of BMD by Dual Energy X-ray absorptiometry (DXA) which is currently the criterion standard for the evaluation of BMD.

Biochemical analysis

The samples were collected before and after six months of follow-up for assessment of Bone Turn over Markers (BTM):

- Serum C-telopeptide fragment of type 1 collagen (serum CTX).
- Urine cross-linked N-terminal telopeptide of type 1 collagen (urine NTX).
- Human deoxypyridinoline (urine DPD) all these markers measured by ELISA technique.

Biochemical methods for analysis

Determination of BTM by ELISA test

- **Serum (CTX-I) ELISA Test:** This test is used to assay (CTX-I) in the sample of patient's serum according to Chubb S (2012) [16].
- **Urine (NTX) ELISA Test:** This test is used to assay (urine NTX) in the sample of human serum, blood plasma and other related tissue liquid according to Kanakis I (2004) [17].
- **Urine (DPD) ELISA Test:** This test is used to assay the (DPD) in the sample of human's serum, blood plasma and other related tissue liquid according to Hamwi A (2001) [18].

Statistical analysis

The collected data were tabulated using Microsoft® Office Excel 2016, Microsoft Corporation. All statistical analyses were conducted using SPSS statistical package version 26.0, August 2019, IBM corporation software group, USA. Appropriate statistical analyses were done according to the type of data obtained for each parameter. Continuous variables were presented as mean (±SD) and were analyzed using the ANOVA test. A posthoc analysis using TUKEY'S Test least significant difference (LCD) test was conducted to compare each BB group with the control group. The Paired Samples t-test was used to compare the mean values of each parameter before and after six months of follow-up within each group. Categorical variables were compared using the Chi-square test. Pearson correlation was used to assess the strength of association between T-score and BTM. The level of significance was set at $P < 0.05$.

Results

Baseline demographic and clinical characteristics of the study population

The baseline features of the three groups were well matched as shown in Table 1. Gender distribution revealed that male patients were found to be 4 (8%) while female patients were 46 (92%). The smoker patients were 3 (6%) while non-smoker patients were 47 (94%). The patients have no previous fracture before the study was 11 (22%), while those having only one previous fracture before recruited in the study were 22 (44%), having two previous fractures were 16 (32%), and having three previous fractures were only 1 (2%). On the other hand, the mean (±SD) of age was 60.3 years (±5.1), weight was 82.5 kg (±15.1) and the height was 158.3cm (±20.2) as shown in Table 2. There was a statistically significant difference using Chi-square in gender distribution.

Table 1. *Demographic data and baseline clinical characteristics of the three studied groups.*

Groups								**Chi-Square**	
Group A(n=10)		**Group B(n=20)**		**GroupC(n=20)**					
N	**%**	**N**	**%**	**N**	**%**	**X2**	**P-value**		
Sex	Male	3	30	1	5	0	0	8.56	0.014*
	Female	7	70	19	95	20	100		
Smoking	Non-Smoker	8	80	19	95	20	100	4.787	0.091
	Smoker	2	20	1	5	0	0		
Previous fracture	No	1	10	4	20	6	30	5.696	0.458
	One	4	40	11	55	7	35		
	Two	5	50	4	20	7	35		
	Three	0	0	1	5	0	0		

(Group A): osteoporotic patients treated with osteoporosis standard therapy, (Group B): osteoporotic patients treated with osteoporosis standard therapy + NSBB, and Group C:

osteoporotic patients treated with osteoporosis standard therapy + CSBB.

Table 2. *Demographic data and baseline clinical characteristics of the three studied groups.*

Groups					ANOVA
		Group A(n=10)	Group B(n=20)	Group C (n=20)	P-value
Age	Range	51 – 68	50 – 65	52 – 63	0.42
	Mean ±SD	60.1 ± 6.4	61.5 ± 4.7	59.3 ± 4.2	
Weight (kg)	Range	70 – 95	60 – 124	54 – 125	0.868
	Mean ±SD	82.4 ± 9.7	84.0 ± 17.9	81.2 ± 17.8	
Height (cm)	Range	150-170	147-174	145-170	0.05
	Mean ±SD	161.0 ± 6.7	159.9 ± 6.8	155.4 ± 6.6	

T-score, Bone mineral density, and 5 –Year (non-vertebral, Hip, and vertebral) fracture risk before and after six months of treatment among the three studied groups.

T-score is a very important tool for the diagnosis of osteoporosis and it is one of the primary outcomes in the current study. There was a significant difference between mean values of T-score after six months of treatment within the same group (B) & (C) [-3.1 vs -2.3 and -3.4 vs -2.5] additionally there was a significant difference between mean values of T-score after six months of treatment with BB between group A & B and group A & C as shown in Table 3 (P<0.05).

Although the mean value of bone mineral density (BMD) was almost the same in the three groups after six months, a significant difference between mean values of BMD was observed within the same group (B) & (C) after six months of treatment with NSBB and CSBB (0.6 vs 0.7 for both groups) as demonstrated in Table 3.

Concerning non-vertebral fracture risk (FR), after six months of treatment with NSBB and CSBB a significant decrease in the value of FR within groups B & C from 22.4 and 21.3 to 20.1 and 19.7, respectively (P<0.05) as shown in Table 3. Moreover, a significant difference between the mean values of non-vertebral FR between group A & B and group A & C after six months of taking the investigated drug BB as illustrated in Table 3.

Likewise, 5- Year hip fracture risk value declined significantly from 5.5 to 4.1 in group B and from 4.9 to 3.9 in group C after six months of treatment with NSBB and CSBB respectively as shown in Table3. A significant difference between mean values of FR between Group A & B and Group A & C after six months of taking the investigated drug BB (P>0.05) as revealed in Table 3.

The same pattern was shown for 5-year vertebral fracture risk where a significant decrease in the mean values of FR after six months of treatment with NSBB and CSBB within the same group (B) & (C) respectively as shown in Table 3. The mean values reduced from 8.5 and 7.9 to 7.2 and 7 in the group (B) and (C), respectively, and after treatment. Additionally, a significant difference was demonstrated between mean values of FR between group A & B and group A & C after six months of taking the investigated drug BB with P-value <0.05, respectively as shown in Table 3.

Table 3. *T-score, Bone mineral density, and 5 –Year (non-vertebral, Hip, and vertebral) fracture risk before and after six months of treatment among the three studied groups.*

Groups					ANOVA
		Group A (n=10)	Group B (n=20)	Group C (n=20)	P-value
T. Score	Before Mean ±SD	-3.3 ± 0.5	-3.1 ± 0.9	-3.4 ± 1.0	0.575
	After Mean ±SD	-3.5 ± 0.6	-2.3 ± 0.8 a	-2.5 ± 0.7 b	0.001
	P. value	0.162	<0.001*	<0.001*	
BMD (g/ cm2)	Before Mean ±SD	0.6 ± 0.1	0.6 ± 0.1	0.6 ± 0.1	0.682
	After Mean ±SD	0.6 ± 0.1	0.7 ± 0.1	0.7 ± 0.1	0.06
	P. value	0.962	<0.001*	<0.001*	
5- year non-vertebral FR	Before Mean ±SD	22.8 ± 3.9	22.4 ± 3.7	21.3 ± 3.7	0.521
	After Mean ±SD	24.4 ± 3.9	20.1 ± 3.6 a	19.7 ± 3.8 b	0.007
	P. value	0.168	0.004*	0.011*	
5- year hip F.R	Before Mean ±SD	5.8 ± 2.4	5.5 ± 2.3	4.9 ± 2.3	0.525
	After Mean ±SD	6.7 ± 2.4	4.1 ± 2.1 a	3.9 ± 2.2 b	0.006
	P. value	0.168	0.005*	0.015*	
5- year vertebral F.R	Before Mean ±SD	8.7 ± 2.1	8.5 ± 2.0	7.9 ± 2.0	0.518
	After Mean ±SD	9.5 ± 2.1	7.2 ± 2.0 a	7.0 ± 2.1 b	0.008
	P. value	0.168	0.004*	0.010*	

- Group A (control group), group B (NSBB group), group C (CSBB group)
- Abbreviation: BMD= Bone Mineral Density, FR= fracture risk
- Statistically significant difference within groups B & C
- Statistically significant difference between groups A & B
- Statistically significant difference between groups A & C

Measurement of bone turnover markers (BTM) before and after six months of follow-up among the three studied groups (secondary endpoints): Serum (CTX), urine (NTX), and urine (DPD).

Surprisingly, there was a significant difference between mean values of s-CTX among groups A vs. B (86 vs. 44.9, respectively) and A vs. C (86 vs. 63.7, respectively) before treatment. After six months of treatment with NSBB and CSBB, a significant reduction in mean values of s-CTX within

the same group (B) & (C) from 44.9 and 63.7 to 38.5 and 52.7, respectively as shown in Table 4 (P-value < 0.001). Concerning urine NTX, a significant difference was demonstrated between mean values after six months of treatment within the same group (A), (B) & (C) as shown in Table 4. Thus, the mean values were 64.5, 64.6, and 64.9 and dropped to 57.6, 34.9, and 33.2 in the group (A), (B) & (C), respectively. Additionally, the mean values of urine NTX between Group A & B and Group A & C showed a significant difference (P-value <0.001) as illustrated in Table 4. Also, the mean values of urine NTX between the group A & B & C, demonstrated a significant difference using ANOVA, test as shown in Table 4. (P-value <0.001).

After that, there was a significant difference between mean values of urine DPD after six months of treatment with NSBB and CSBB within the same group (A), (B) & (C), respectively, as shown in table 4. The mean values of urine DPD between group A & B and group A & C showed a significant difference as presented in Table 4. Between-group A & B & C, there was a significant difference with (P-value <0.001) between mean values of urine DPD between the three groups as shown in Table 4.

Table 4. *Bone turn over markers (BTM) before and after six months of treatment among the three studied groups.*

		Group A(n=10)	Group B (n=20)	Group C(n=20)	ANOVA
					P-value
Serum CTX (ng / mL)	Before Mean ± SD	86.0 ± 25.9	44.9 ± 42.6 a	63.7 ± 43.1	0.036
	After Mean ± SD	71.2 ± 24.9	38.5 ± 36.6	52.7 ± 37.5	0.061
	P. value	0.020*	<0.001*	<0.001*	
Urine NTX (n. mol. /L)	Before Mean ± SD	64.5 ± 3.9	64.6 ± 6.9	64.9 ± 7.4	0.984
	After Mean ±SD	57.6 ± 3.1	34.9 ± 5.9 a	33.2 ± 3.7 b	<0.001
	P. value	0.001*	<0.001*	<0.001*	
Urine DPD(n. mol. /L)	Before Mean ± SD	27.8 ± 6.3	23.5 ± 6.4	26.1 ± 7.0	0.217
	After Mean ± SD	20.4 ± 6.4	13.1±2.9 a	14.9 ± 3.7b	<0.001
	P. value	< 0.001*	<0.001*	<0.001*	

Abbreviation for S-CTX= Serum c-telopeptide fragment of type 1 collagen, urine NTX= urine cross-linked N-terminal telopeptide of type 1 collagen, and urine DPD = Human deoxy pyridinoline.

- Statistically significant difference within groups A, B & C
- Statistically significant difference between groups A & B
- Statistically significant difference between groups A & C

The correlation between bone turnover markers (BTM) and T-score after six months of follow-up and taking the investigated drug (BB) in groups B & C.

There was a strong negative correlation between T- Score & BTM especially serum CTX and urine DPD with a p-value <0.001*, a good negative correlation between T-score and urine NTX with a P-value of 0.032*, after six months of follow-up and taking the investigated drugs BB as shown in table 5 & figure 2, 3 and 4.

Table 5. *The Pearson correlation between bone turnover markers (BTM) and T- score after six months of follow-up and taking the investigated drug (BB) in group B & C.*

Correlations		
Pearson Correlation	**T. Score After**	
	R	**P-value**
Serum CTX (ng/ml) After	-0.650	<0.001*
Urine NTX (n .mol./L) After	-0.339	0.032*
Urine DPD (n. mol./L) After	-0.550	<0.001*

- Abbreviation: BTM= Bone turnover marker
- Statistically significant difference among the studied groups

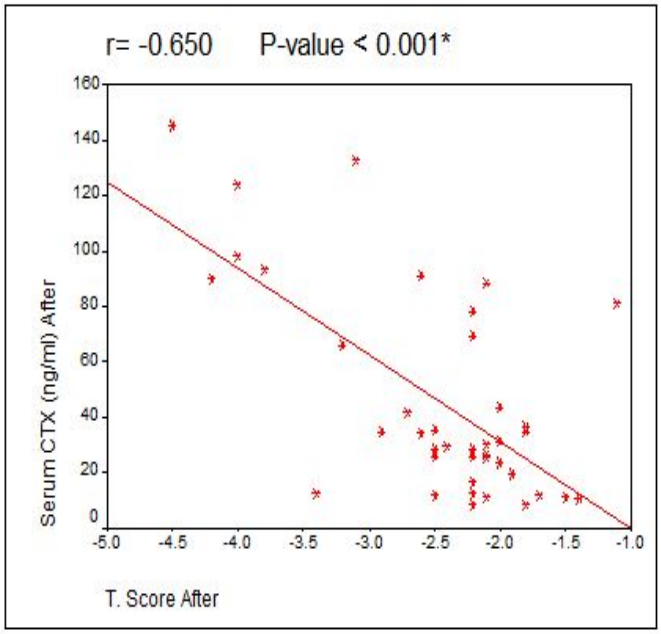

Figure 2. *The association between T-score and serum CTX after six months of follow-up.*

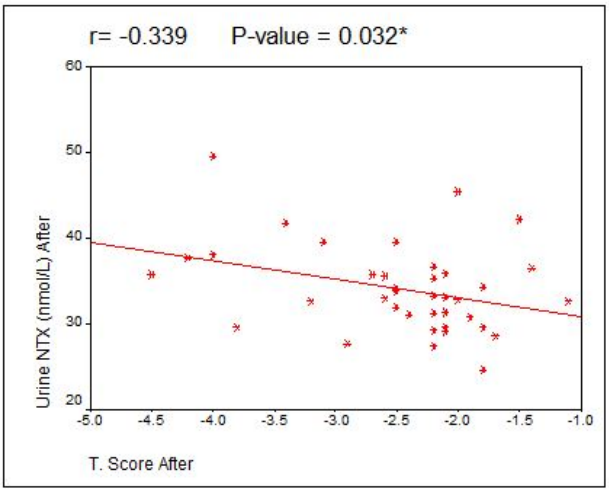

Figure 3. *The association between T-score and urine NTX after six months of follow-up.*

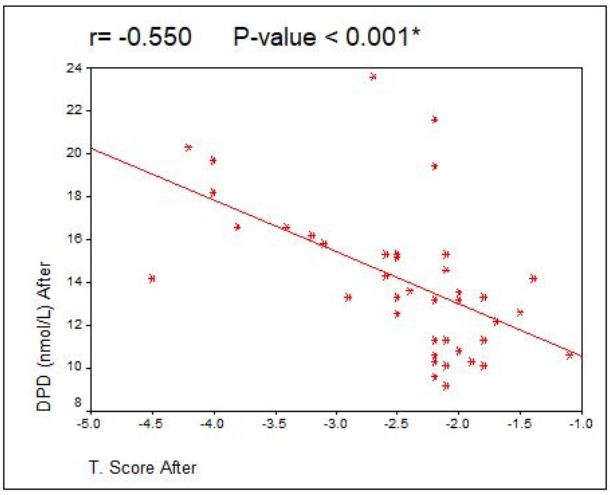

Figure 4. *The association between T-score and urine DPD after six months of follow-up.*

Discussion

Both hypertension and osteoporosis are age-related disorders that are caused by hereditary and environmental factors interacting [19]. Furthermore, hypertension has been linked to increased bone loss and the risk of fracture [20]. Despite important evidence of the sympathetic nervous system's role in bone construction via several pathways, the lack of sufficient clinical studies further confuses the topic. Additionally, the correlation between hypertension and osteoporosis is still a matter of debate. Cardiovascular illnesses particularly hypertension are a common therapeutic application of β -blockers, which may have a pathological basis with osteoporosis.

This study aimed to investigate the effect of β –blockers on osteoporosis as the data in humans are limited and conflicting results exist in the literature. In this study, we investigated the effects of non-selective and cardio-selective BB use on bone health in women and men over 50 years old. Firstly, T-score was significantly lower in group B after taking non-selective beta-blockers (NSBB) and group C after cardioselective beta-blocker (CSBB). These findings match with previous data where the lumbar and femoral total T-scores were better in the BB group compared with the control group [21]. Accumulating evidence suggested that the sympathetic nervous system had a regulating effect on bone mineral metabolism [12, 22]. Moreover, several data showed that BB increases bone mineral density (BMD) [14,23]. Concordant with this result, BMD was higher after NSBB and CSBB treatment in groups B and C compared to the control group. However, Levasseur and his colleagues could not detect any effect of BB on bone mass in postmenopausal female patients [24]. Moreover, after 6 months of BB treatment with either non-selective or selective BB; 5-year non-vertebral fracture risk (FR) declined in groups B and C in comparison to the control group. On the contrary, a recent study showed that selective BB use was associated with a reduction in fracture risk not with non-selective BB [25]. In addition, a systematic review and meta-analysis study found that there was a significant reduction of any fracture with the use of BB [26]. In agreement with these data, a significant reduction of 5-year hip and vertebral FR was observed after 6 months of BB treatment either selective or non-selective in the current study. As well as, the value of 5-year hip and vertebral FR was lower in groups B and C compared to the control group after 6 months of treatment.

Then bone turnover markers (BTM) were studied in the current study as they were known to evaluate the bone turnover rate and to observe osteoporosis therapeutic response. Concerning the effect of BB on BTM, there are a few studies in humans with conflicting results. A previous randomized controlled tria l done by Reid and his colleagues studied the effect of BB on bone markers. They observed a 20% reduction in serum osteocalcin after 2 weeks of propranolol treatment, however, no significant change in serum C-terminal telopeptide of type I collagen (CTX) [27]. In the same study, urine DPD (other BTM) showed a reduction after 6 weeks of propranolol treatment. They explained this contrast and hypothesized that DPD is produced in the kidneys as a consequence of the catabolism of the cross-linking telopeptides, and propranolol has a direct impact on the kidney [28]. However, CTX is released directly from bone as the end product of osteoclastic resorption [27]. In contrast, after 6 months of propranolol and bisoprolol use, CTX was decreased significantly in the present study. In addition, there was a decrease in other BTM (urine NTX, and urine DPD) within group B & C after six months of using BB and a significant reduction after 6 months between group A & B and group A & C.

Both BMD and BTM should be evaluated at the same time to determine the risk of fracture more precisely. BTM levels (s-CTX, u-DPD) were higher in the osteoporosis group than in the non-osteoporosis group [29]. Moreover, BMD declined as the postmenopausal period increased significantly [29]. Inconsistent with the previous results, a negative correlation present between bone turnover markers (BTMs) and T- score specifically after BB treatment. As BTM decreased after six months of BB treatment in parallel with increased T-score and

decrease osteoporosis. Although there are few controversial studies regarding the effect of BB on osteoporosis, in the current study, BB (selective or non-selective) showed a promising effect on decreasing bone resorption as they improved BMD, decreased FR and BTM.

Conclusion

The administration of BB, whether selective or non-selective, increased BMD, a reduction in fracture risk, and a decrease in the three biological markers assessed in the current study (serum CTX, urine NTX, and urine DPD). When compared to the control group, the results were significant. As a result, we may conclude that the usage of BB may treat osteoporosis illness by improving BMD, lowering FR, and lowering BTM. Moreover, we found a strong negative correlation between BTM & T-score after six months of follow-up.

References

1. Pouresmaeili F, Kamalidehghan B, Kamarehei M, et al. A comprehensive overview on osteoporosis and its risk factors. Therap Clin Risk Manag. 2018;14:2029.
2. Akkawi I, Zmerly H. Osteoporosis: current concepts. Joints 2018;6:122-127.
3. Cosman F, De Beur SJ, LeBoff MS, et al. Clinician's guide to prevention and treatment of osteoporosis. Osteoporosis international: a journal established as a result of cooperation between the European Foundation for osteoporosis and the national osteoporosis foundation of the USA. 2014;25:2359-2381.
4. Rossini M, Adami S, Bertoldo F, et al. Guidelines for the diagnosis, prevention, and management of osteoporosis. Rheumat. 2016;68:1-39.
5. Yang S, Nguyen N, Center J, et al. Association between hypertension and fragility fracture: A longitudinal study. Osteop Int. 2014;25:97-103.
6. Cappuccio FP, Meilahn E, Zmuda JM, et al. High blood pressure and bone-mineral loss in elderly white women: a prospective study. The Lancet. 1999;354:971-975.
7. Javed F, Khan SA, Ayers EW, et al. Association of hypertension and bone mineral density in an elderly African American female population. J Nat Med Ass. 2012;104:172-178.
8. Zhang M, Li Y, Liu Y. Study on the influencing factors for bone mineral density among 24831 people in Changchun. Chin J Osteoporos. 2010;16:125-127.
9. Graham S, Hammond-Jones D, Gamie Z, et al. The effect of β-blockers on bone metabolism as potential drugs under investigation for osteoporosis and fracture healing. Expert opinion on investigational drugs 2008;17:1281-1299.
10. Khosla S, Drake MT, Volkman TL, et al. Sympathetic β1-adrenergic signaling contributes to the regulation of human bone metabolism. J Clin Inv. 2018;128:4832-4842.
11. Rodan SB, Rodan GA. Parathyroid hormone and isoproterenol stimulation of adenylate cyclase in rat osteosarcoma clonal cells Hormone competition and site heterogeneity. Biochem Biophys Acta. 1981;673:46-54.
12. Takeda S, Elefteriou F, Levasseur R, et al. Leptin regulates bone formation via the sympathetic nervous system. Cell. 2002;111:305-317.
13. Schoppet M, Preissner KT, Hofbauer LC. RANK ligand and osteoprotegerin: paracrine regulators of bone metabolism and vascular function. Arter Thromb Vascul Biol. 2002;22:549-553.
14. Pasco JA, Henry MJ, Sanders KM, et al. β-adrenergic blockers reduce the risk of fracture partly by increasing bone mineral density: Geelong osteoporosis study. J Bone Min Res. 2004;19:19-24.
15. Elefteriou F, Ahn JD, Takeda S, et al. Leptin regulation of bone resorption by the sympathetic nervous system and CART. Nature. 2005;434:514-520.
16. Chubb SP. Measurement of C-terminal telopeptide of type I collagen (CTX) in serum. Clin Biochem. 2012;45:928-935.
17. Kanakis I, Nikolaou M, Pectasides D, et al. Determination and biological relevance of serum cross-linked type I collagen N-telopeptide and bone-specific alkaline phosphatase in breast metastatic cancer. J Pharm Biomed Analys. 2004;34:827-832.
18. Hamwi A, Ganem AH, Grebe C, et al. Markers of bone turnover in postmenopausal women receiving hormone replacement therapy. Clin Chem Lab Med. 2001;39:414-417.
19. Wilper AP, Woolhandler S, Lasser KE, et al. A national study of chronic disease prevalence and access to care in uninsured US adults. Annals Int Med. 2008;149:170-176.
20. Sennerby U, Farahmand B, Ahlbom A, et al. Cardiovascular diseases and future risk of hip fracture in women. Osteop Int. 2007;18:1355-1362.
21. Keleş BY, Vural M, Onder B, et al. Evaluation of the effects of ß1-selective beta-blockers on bone mineral density and fracture risk in postmenopausal women. Turk J Med Sci. 2020;50:994-998.
22. Cherruau M, Facchinetti P, Baroukh B, et al. Chemical sympathectomy impairs bone resorption in rats: a role for the sympathetic system on bone metabolism. Bone. 1999;25:545-551.
23. Turker S, Karatosun V, Gunal I. β-Blockers increase bone mineral density. Clin Orthop Rel Res. 2006;443:73-74.
24. Levasseur R, Dargent Molina P, Sabatier JP, et al. Beta-blocker use, bone mineral density, and fracture risk in older women: results from the Epidemiologic osteoporosis prospective study. J Am Geriat Soc. 2005;53:550-552.
25. Yang S, Nguyen ND, Center JR, et al. Association between beta-blocker use and fracture risk: the Osteoporosis Epidemiology Study. Bone. 2011;48:451-455.
26. Wiens M, Etminan M, Gill S, et al. Effects of antihypertensive drug treatments on fracture outcomes: a meta-analysis of observational studies. J Inter Med. 2006;260:350-362.
27. Sharif PS, Abdollahi M. A systematic review on the relationship between use of statins and osteoporosis. Int J Pharmacol. 2011;7:180-188.

28. Apone S, Lee M, Eyre D. Osteoclasts generate cross-linked collagen N-telopeptides (NTx) but not free pyridinolines when cultured on human bone. Bone. 1997;21:129-136.
29. Park SG, Jeong SU, Lee JH, et al. The changes of CTX, DPD, osteocalcin, and bone mineral density during the postmenopausal period. Annals Rehab Med. 2018;42:441.

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