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FRACTURE RISK AND THE IMPACT OF SELECTIVE AND NON-SELECTIVE BETA BLOCKERS IN PRIMARY OSTEOPOROSIS AN OBSERVATIONAL STUDY

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ABSTRACT

Background: Bone fragility increases when bone mass decreases as a result of osteoporosis. Users of beta blockers had higher bone mineral density and a decreased risk of fractures, according to published studies.

Aim: The current study aimed to examine the impact of selective and non-selective beta-blockers on the risk of fracture in persons with osteoporotic Indians.

Methods: A total of 120 osteoporosis patients of both sexes were treated with cardio-selective beta-blockers (CSBB), non-selective beta-blockers (NSBB), and a control group. Each participant's bone turnover markers, bone mineral density, fracture risk, and T-scores were assessed, and conclusions were made.

Results: Following six months of testing, it was found that the three groups' mean T-scores differed significantly. The group receiving non-selective beta-blockers had significantly higher bone mineral density than the control group. There was statistically less chance of fracture in the CSBB and NSBB groups. In comparison to the control group, the NSBB and CSBB groups similarly showed lower bone turnover indices.

Conclusion: In summary, CSBB and NSBB can help individuals with osteoporosis achieve greater bone mineral density while reducing markers of bone turnover and fracture risk. NSBB showed a greater effect in reducing fracture risk at all three research locations. Furthermore, s-CTX showed a significant drop in bone turnover markers when compared to the CSBB group.

Keywords: bone turnover indicators, beta-blockers, bone fracture, and fracture risk

INTRODUCTION

A significant percentage of the global population suffers from osteoporosis, a bone disorder marked by a reduction in bone mineral density and an increase in the breakdown of bone structure. Osteoporosis is defined by WHO standards as the bone mineral density (BMD) T-score being 2.5 standard deviations or more below the peak bone mass. The elderly have both Type I osteoporosis (postmenopausal) and Type II osteoporosis (senile owing to age).

Fractures are among the most dangerous side effects of osteoporosis, as they raise the chance of death and inflict significant damage. In addition to causing an unbearable additional burden in the absence of the required resources and skilled personnel, osteoporosis and the fractures it causes also have a substantial financial impact. Research is focused on identifying the several risk factors for osteoporosis since it is critical. Osteoporosis is frequently associated with significant risk factors, such as low oestrogen levels, diabetes, gender, age, hypertension, history

of smoking, and usage of caffeinated drinks. Hereditary and environmental variables combine to cause age-related disorders such as osteoporosis and hypertension, with hypertension serving as a key risk factor for the latter.

Nonetheless, conflicting results on the connection between osteoporosis and hypertension may be found in the literature. Reports state that high blood pressure is detrimental to bone mineral density. A study with a predominantly female population found a link between high blood pressure and loss of femoral neck bone. The loss of calcium brought on by hypertension has also been connected to hip fractures. Additional research from the literature indicates that there is no link between high blood pressure and low bone density. Bone mineral density values were similar in patients with osteopenia and osteoporosis.3 One common treatment for hypertension is the use of beta-blockers, which are adrenergic receptor antagonists that decrease blood pressure by inhibiting cardiac adrenergic receptor channels and releasing renin from the kidney.

Recent research has also connected beta-blockers to modifications in bone metabolism and fracture healing. Adrenergic receptors have been found in osteoblast-like cells, which is an unusual finding. The production of osteoclasts depends on M-CSF (colony-stimulating factors), RANKL (receptor activator of nuclear factor kappa-B ligand), and osteoclastogenesis.4 Beta blocker users had lower fracture risk and 30% more bone mineral density across the torso, hips, and spine. According to a different research, beta blockers can target leptin and its signalling pathways in the hypothalamus to treat osteoporosis by stimulating a sympathetic positive tone.

According to this theory, beta blockers that target leptin and its hypothalamic signalling pathway can be used to exacerbate osteoporosis.5. The available literature on the relationship between beta blockers and osteoporosis is lacking. Therefore, the goal of the current study was to evaluate how non-selective and selective beta-blockers, respectively, affected the risk of fracture in Indian participants who had primary osteoporosis.

MATERIALS AND METHODS

One hundred and twenty male and female participants with a verified diagnosis of primary osteoporosis participated in the current study. During the designated research period, the study population was drawn from the Institute's Department of Orthopaedics.

The inclusion criteria included male and female subjects, subjects 50 years of age or older, subjects with female osteoporosis, both hypertensive and normotensive subjects, subjects with a BMD T-score of 2.5 or higher, and subjects who were willing to participate in the study. Excluded from the study were subjects who declined to participate or provide consent, people taking drugs that raise the risk of osteoporosis (e.g., corticosteroids, antidepressants, anxiety medications), and people taking drugs that lower the risk (e.g., statins, nitrates, ACE inhibitors, and angiotensin receptor blockers). Each research participant provided written and verbal informed consent following a detailed description of the study's methodology.

After final inclusion, each topic's whole history was assembled, and an exam was given. The demographics comprised BMI, height, weight, gender, and age in addition to medical history. Associated risk factors, such as alcohol and tobacco use, were also assessed. The fracture index was utilised to determine the change (enhancement) in risk for each participant, and dual-energy x-ray absorptiometry was employed to determine an increase in T-scores and BMD. There were three different kinds of past fragility fractures that were found: hip, non-vertebral, and clinical vertebral.

The study also used ELISA to detect changes in urine NTX (urine cross-linked N-terminal telopeptides of type 1 collagen), urine DPD (urine-free deoxypyridinoline), and blood CTX (blood level of the C-telopeptide fragment of type 1 collagen). It was advised that all study participants take 500 mg of calcium supplements daily, 1 mcg of vitamin D3, and 70 mg of alendronate once a week in order to maintain bone density. The participants were divided into three groups at random. Group I's control subjects (n = 40) received normal osteoporosis medication and were released from the programme six months after it ended.

Group II (n=40) NSBB participants were given daily dosages of 10 mg propranolol to treat osteoporosis; dose increments were made contingent on the subjects' responses. The individuals' condition was assessed after six months to see if it had become better or worse. Patients in Group III who were part of the Cardio-selective - blocker Group (CSBB) (n = 40) were given the same treatment as the control group, plus an extra 5 mg of bisoprolol daily based on their response. The patients were monitored for six months following therapy to see if the disease rate for regression or development had changed.

Urine samples with creatinine adjustment were collected from each person after their first void in the morning, and venous blood samples were obtained for blood collection following an overnight fast. Among the laboratory

tests performed were liver function tests, 25-hydroxyvitamin D levels, thyroid function tests, and a blood chemistry panel. Initially, serum protein electrophoresis calcium/creatinine ratio, luteinizing hormone/follicle-stimulating hormone (LH/FSH), and testosterone were all measured in the laboratory. The length of time that subjects had used beta-blockers and bisphosphonates was assessed before they were enrolled in the study. Bone mineral density was measured using DXA (gold standard) in three regions: the left femur (neck and total), the forearm radius, and the spine L1-L4.

Additional biochemical study was conducted on urine DPD (human deoxypyridinoline), serum C-telopeptide, and urinary cross-linked N-terminal telopeptides of type 1 collagen (NTX). Using the ELISA, type 1 collagen (CTX) was broken up at a recall interval of six months. ELISA was also used to identify markers for bone turnover. Analytical ELISA was utilised to ascertain the CTX-1 quantities in human blood samples following the Chubb SS6 in 2012. NTX content in human urine samples was measured using urine NTX ELISA, which was based on Kanakis I7 in 2004 and Hamwi A8 in 2001. The collected data were statistically assessed using multivariate statistical techniques and logistic regression. To communicate the data, both tabular and descriptive approaches were employed.

The Turkey analysis, Pearson correlation, chi-square test, and post-hoc test were employed. Version 22.0 of SPSS, Armonk, NY: IBM Corp., 2013. The data were shown as mean, standard deviation, percentage, and numbers, with a significance threshold of 0.05%.

RESULTS

A total of 120 individuals were divided into three groups at random. Group I's control subjects (n = 40) were given conventional osteoporosis medication and released six months after the treatment plan was completed. For osteoporosis, members of Group II's non-selective beta-blocker group (n=40) were given daily doses of propranolol 10 mg. The patients' responses determined further dosage increases, which were given in a dose-dependent manner.

The patients' condition was rated as either declining or improving after six months. Group III had forty CSBB (Cardio-selective -blocker Group) participants who were given 5 mg of bisoprolol per day, contingent on the patient's reaction, in addition to receiving the same treatment as the control group. 30% (n=12) of the men and 70% (n=28) of the women were in Group I; 5% (n=2) of the men and 95% (n=38) of the women were in Group II; and 100% (n=20) of the women were in Group III. At a p-value of 0.01, the gender differences were statistically significant.

In group I, there were over 60% (n=24) normotensive patients and 40% (n=40) hypertension patients; in group II, there were an additional 65% (n=26) hypertensives, and in group III, there was an additional increase of 75% (n=30) hypertensives. At 0.14 for the p-value, it was not statistically significant. Group I had 20% (n=8) smokers, Group II contained 95% (n=38), and Group III contained 100% (n=40) non-smokers, with a p value of 0.09. 10% (n = 4) of participants in Group I, 20% (n = 8) of individuals in Group II, and 30% (n = 12) of subjects in Group III did not show any signs of fractures. One previous fracture was experienced by 40% (n = 16), 55% (n = 22), and 35% (n = 14) of the patients in Groups I, II, and III, respectively.

Two fractures were sustained by 50% (n = 20), 20% (n = 8), and 35% (n = 14) of individuals in groups I, II, and III, respectively. Out of Group II individuals, only 5% (n=2) had three previous fractures (Table 1). Groups I, II, and II study participants had baseline mean BMIs of 31.7 4.3, 32.6 6.4, and 33.3 6.3 kg/m2, respectively. With a p value of 0.75, this value was statistically non-significant. At a 0.05 significance level, Group I had the greatest mean height, followed by Group II, and Group III had the lowest mean height, with corresponding mean values of 161.26.5, 159.76.6, and 155.66.4 cm. The baseline mean weight of the three study groups was also comparable, with a p-value of 0.84.

. Groups I, II, and III had average ages of 60.3 6.2, 61.7 4.5, and 59.5 4.4 years, respectively, with a p-value of 0.35 (Table 2). The results of the study showed that at baseline and six months later, group I had a similar mean 5-year risk of vertebral fracture (p=0.16). With p=0.004 and 0.01 for Groups II and III, respectively, the risk was significantly higher before to therapy than six months following therapy. Group I's 5-year hip fracture risk was similar at baseline and six months later, with a p-value of 0.14. With p=0.005 and 0.01 for groups II and III, respectively, the hip fracture risk was significantly higher at the start of therapy than it was six months later.

Furthermore, there was a significant 6-month difference between the groups (p=0.06). Comparable results were noted for non-vertebral fracture risk in groups II and II, with significant decreases detected following a 6-month course of therapy (p=0.004 and 0.01, respectively). Baseline and six-month BMD for group I were similar

(p=0.94). Group II's BMP increased significantly from 0.8 to 0.9 at baseline to six months later, with a p-value of 0.001 for both groups.
There was a non-significant difference between the groups at baseline and after six months (p=0.66 and 0.07, respectively). The T scores of the three groups were similar at baseline (p=0.55), but significantly different after six months (p=0.001).

With a p-value of 0.14, the mean T scores for group I were comparable. Ratings for Groups II and III were significantly higher six months after therapy compared to baseline, with p0.001 for both (Table 3). When assessing the markers for bone turnover, urine DPD was similar for all three groups at baseline (p=0.23) and higher for Group I after six months, followed by Groups III and II (p0.001). Urine DPD significantly dropped in all three groups at six months, with p0.0001 for each group.
The three groups' baseline urine NTX levels were similar (p=0.96), with group I having significantly higher levels than groups II and III (p0.001).

When NTX was compared to the baseline at six months, it significantly dropped in all three groups, with p0.0001 for each group. Serum CTX was significantly higher in group I at baseline (p-value = 0.03), and after six months, it was similar in all three groups (p-value = 0.06). For all three groups, the decline at six months from the baseline was statistically significant, with p0.001 for each group (Table 4).
Discussion Three groups of 120 individuals were randomly assigned to the current investigation. Group I's control subjects (n = 40) received normal osteoporosis medication and were released from the programme six months after it ended.

At the end of the six-month period, the NSBB (Non-selective Beta-Blocker Group) participants in DGroup II (n=40) were assessed for improvement or decline. Patients in Group III who were part of the Cardio-selective -blocker Group (CSBB) (n = 40) were given the same treatment as the control group, plus an extra 5 mg of bisoprolol daily based on their response.
The results of the study showed that at baseline and six months later, group I had a similar mean 5-year risk of vertebral fracture (p=0.16). With p=0.004 and 0.01 for Groups II and III, respectively, the risk was significantly higher before to therapy than six months following therapy. Group I's 5-year hip fracture risk was similar at baseline and six months later, with a p-value of 0.14.

Groups II and III had a significantly higher hip fracture risk at baseline compared to six months after therapy (p=0.005 and 0.01, respectively). Furthermore, a significant 6-month difference between groups was observed by p=0.06. Similar results were seen for non-vertebral fracture risk, showing a significant reduction in groups II and II following a 6-month course of therapy (p=0.004 and 0.01, respectively). These findings were consistent with the studies conducted in 2011 by Salari Sharif P et al9 and Yang S et al10, in which the authors discovered that after a 6-month course of medication, individuals with osteoporosis had a decreased risk of fracture for all vertebral, non-vertebral, and hip fractures.
At baseline and six months later, BMD was seen to be comparable (p=0.94).

Group II's BMD increased significantly from 0.8 to 0.9 between baseline and six months, with a p-value of 0.001 for both groups. The difference between the groups at baseline and six months later was not statistically significant (p=0.66 and 0.07, respectively). The T scores of the three groups showed no significant difference after six months (p=0.001), although they were equal at baseline (p=0.55). The mean T scores for group I were comparable, as shown by the p=0.14 value. After six months of therapy, Groups II and III's scores were significantly higher than baseline (p 0.001 for each).

These results supported studies by Park SG et al. (2018) and Cosman F et al. (2014), which discovered that those receiving osteoporosis treatment had significantly greater bone mineral density (BMD) and tissue tension (T) ratings than those who did not get it.
In terms of the markers for bone turnover, urine DPD was equal for all three groups at baseline (p=0.23) and higher for Group I after 6 months compared to Groups III and II (p0.001). Urine DPD significantly dropped in all three groups at six months, with p0.0001 for each group. The three groups' baseline urine NTX levels were similar (p=0.96), with group I having significantly higher levels than groups II and III (p0.001).
When NTX was compared to the baseline at six months, it significantly dropped in all three groups, with p0.0001 for each group. These bone turnover indicator results were comparable to those obtained from urine analysis in

studies by Javed F et al. (2012) and Rossini M et al. (2016), which also published comparable results for bone turnover markers.

The results of the study showed that at baseline (p=0.03), serum CTX was significantly higher in group I and was similar in all three groups after six months (p=0.06). All three groups showed statistically significant decreases at six months following the baseline, with p0.001 for each group.

These results were comparable to those of Akkawi I15 in 2018 and Zhnag M et al16 in 2010, when authors reported a substantial decrease in serum CTX following therapy for osteoporosis, which was also observed in the present study's results.

Conclusion

Taking into account its limitations, the current study comes to the conclusion that CSBB and NSBB can aid in increasing bone mineral density while lowering indicators of bone turnover and fracture risk in individuals with osteoporosis. At each of the three study sites, NSBB had a more noticeable impact on lowering fracture risk. Additionally, s-CTX demonstrated a substantial decrease in bone turnover indicators as compared to the CSBB group. This study had certain drawbacks, including a smaller population when shirt monitoring and regional bias were taken into account.

REFERENCES

1. Sennerby U, Farahmand B, Ahlbom A, Ljunghall S, and Michaëlsson K. Cardiovascular diseases and future risk of hip fracture in women. Osteoporosis International. 2007;18:1355-62.
2. Wilper AP, Woolhandler S, Lasser KE, McCormick D, Bor DH and Himmelstein DU. A national study of chronic disease prevalence and access to care in uninsured US adults. Annals of internal medicine. 2008;149:170-6.
3. Singh AP, Jain M. Singh S, Rangari P. Management of proximal humerus fracture - a case-control prospective study. IJMSDR. 2018;2:4:172-94.
4. Murarka k, Agrawal R, Rangari P, Murarka A. Hemiarthroplasty of intracapsular femoral neck fracture with Austin Moore prosthesis. IJMSDR. 2019;3:263-70.
5. Rajshekhar S, Rajasekhar M, Baghel VS, Rangari P. Long pfn nailing in comminuted high subtrochanteric fractures of the femur in elderly patients- a hospital-based clinical trial. IJMSDR. 2019;3:33-9.
6. Chubb SP. Measurement of C-terminal telopeptide of type I collagen (CTX) in serum. Clinical biochemistry. 2012;45:928-35.
7. Kanakis I, Nikolaou M, Pectasides D, Kiamouris C, and Karamanos N. Determination and biological relevance of serum cross-linked type I collagen N-telopeptide and bone-specific alkaline phosphatase in breast metastatic cancer. Journal of pharmaceutical and biomedical analysis. 2004;34:827-32.
8. Hamwi A, Ganem A-H, Grebe C, et al. Markers of bone turnover in postmenopausal women receiving hormone replacement therapy. Clinical Chemistry and Laboratory Medicine (CCLM). 2001;39:414-7.
9. Salari Sharif P, Abdollahi M and Larijani B. Current, new and future treatments of osteoporosis. Rheumatology international. 2011;31:289-300.
10. Yang S, Nguyen ND, Center JR, Eisman JA, and Nguyen TV. Association between beta-blocker use and fracture risk: the Dubbo Osteoporosis Epidemiology Study. Bone. 2011;48:451-5.
11. Park SG, Jeong SU, Lee JH, et al. The changes in CTX, DPD, osteocalcin, and bone mineral density during the postmenopausal period. Annals of rehabilitation medicine. 2018;42:441.
12. Cosman F, de Beur SJ, LeBoff M, et al. Clinician's guide to prevention and treatment of osteoporosis. Osteoporosis international. 2014;25:2359-81.
13. Rossini M, Adami S, Bertoldo F, et al. Guidelines for the diagnosis, prevention, and management of osteoporosis. Reumatismo. 2016;68:1-39.
14. Javed F, Khan SA, Ayers EW, et al. Association of hypertension and bone mineral density in an elderly African American female population. Journal of the National Medical Association. 2012;104:172-8.

15. Akkawi I and Zmerly H. Osteoporosis: current concepts. Joints. 2018;6:122-7.

16. Zhang M, Li Y and Liu Y. Study on the influencing factors for bone mineral density among 24831 people in Changchun. Chin J Osteoporos. 2010;16:125-7.

TABLES

S. No	Characteristics	Group I		Group II		Group III		p-value
		%	n=40	%	n=40	%	n=40	
1.	Gender							
a)		30	12	5	2	0	0	**0.01**
b)	Males	70	28	95	38	100	20	
2.								
a)	Females	60	24	35	14	25	10	0.14
b)		40	16	65	26	75	30	
3.	the heart rate							
4.		80	32	95	38	100	40	0.09
5.	Normotensive	20	8	5	2	0	0	
6.								
a)	Hypertensive	10	4	20	8	30	12	5.67
b)		40	16	55	22	35	14	
c)	smoking history	50	20	20	8	35	14	
d)		0	0	5	2	0	0	

Table 1: Demographics and clinical data in 3 groups of study subjects

S. No	Parameters	Group I	Group II	Group III	p-value
1.	**BMI (kg/m2)**	31.7±4.3	32.6±6.4	33.3±6.3	0.75
2.	**Height (cm)**	161.2±6.5	159.7±6.6	155.6±6.4	**0.05**
3.	**Weight (kg)**	82.6±9.5	84.2±17.7	81.4±17.6	0.84
4.	**Age (years)**	60.3±6.2	61.7±4.5	59.5±4.4	0.35

Table 2: Demographics data at baseline in 3 groups of study subjects

S. No	Parameters	Group I	Group II	Group III	p-value
1.	**5-year vertebral fracture risk**				
a)	Before	8.5±2.3	8.3±2.2	7.7±2.2	0.53
b)	After	9.3±2.3	7.0±2.2	7.2±2.3	**0.008**
c)	p-value	0.16	**0.004**	**0.01**	
2.	**5-year hip fracture risk**				
a)	Before	5.6±2.6	5.3±2.5	4.7±2.5	0.54
b)	After	6.5±2.6	4.3±2.3	3.7±2.4	**0.006**
c)	p-value	0.14	**0.005**	**0.01**	
3.	**5-year non-vertebral fracture risk**				
a)	Before	22.6±3.7	22.6±3.5	21.1±3.5	0.54
b)	After	24.2±3.7	20.3±3.4	19.9±3.6	**0.007**
c)	p-value	0.18	**0.004**	**0.01**	
4.	**BMD (g/cm2)**				
a)	Before	0.8±0.3	0.8±0.3	0.8±0.3	0.66
b)	After	0.8±0.3	0.9±-0.3	0.9±-0.3	0.07
c)	p-value	0.94	**<0.001**	**<0.001**	
5.	**T-score**				
a)	Before	-3.5±0.3	-3.3±0.7	-3.6±1.2	0.55
b)	After	-3.7±0.4	-2.5±0.6	-2.7±0.9	**0.001**
c)	p-value	0.14	**<0.001**	**<0.001**	

Table 3: 5-year fracture risk, BMD, and T-scores in 3 study groups at baseline and 6 months

S. No	Parameters	Group I	Group II	Group III	p-value
1.	**Urine DPD (nmol/L)**				
a)	Before	27.6±6.5	23.3±6.2	26.3±7.2	0.23

b)	After	20.2±6.6	13.3±2.7	14.7±3.9	**<0.001**
c)	p-value	**<0.001**	**<0.001**	**<0.001**	
2.	**Urine NTX (nmol/L)**				
a)	Before	64.7±3.7	64.8±6.7	64.7±7.6	0.96
b)	After	57.4±3.3	34.7±5.7	33.4±3.5	**<0.001**
c)	p-value	**<0.001**	**<0.001**	**<0.001**	
3.	**Serum CTX (ng/ml)**				
a)	Before	86.2±25.7	44.7±42.8	63.5±43.3	**0.03**
b)	After	71.4±24.7	38.3±36.8	52.5±37.7	0.06
c)	p-value	**<0.001**	**<0.001**	**<0.001**	

Table 4: Intergroup comparison of bone turnover markers at baseline and 6 months following therapy