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Original Research Article

A Prospective Trial to Compare the Efficacy of Bisphosphonate Therapy on Postmenopausal Osteoporotic Women with and Without Diabetes

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Abstract

Background: Type 2 diabetes and osteoporosis are postmenopausal issues among women. According to analysis, the diabetes is one of the major reasons of bone deterioration due to accumulation of advanced glycosylation. Therefore, more attention is required for treating the osteoporosis and prevents fractures in diabetic patients. For such patients, ibandronate 150 mg tablet is prescribed for once in month for increasing the bone mineral density. This is helpful for preventing the osteoporotic fractures. Moreover, osteoporotic is associated with the insulin secretion and sensitivity.

Aim: The study aims to conduct a prospective trial to compare the efficacy of bisphosphonate therapy on postmenopausal osteoporotic women with and without diabetes.

Method: The study was a multicenter prospective and open label design. The study was conducted from March 2020 to March 2022 at M.K.C.G. Medical College. The study protocol was reviewed by the ethical committee and managed according to standards and guidelines. The researcher has collected the consent form with all demographic information about the patients. For the analysis of the data collected for the study Shapiro-Wilk test was applied and normal distribution of variable was observed. The mean and standard deviation values were obtained through t-test.

Results: The diabetic groups are older and having higher body mass. Moreover, the BMD, TBS and T-scores were not significantly different in these groups. Here BMD was investigated for all patients and it was carried out that lumbar spine for both groups was 3.41% and 3.71%, femur neck was 1.30% and 1.18% as well as the total hip was 1.51% and 1.58% in non-diabetic group. Unlike the BMD, no significant difference was identified for TBS as before and after the treatment which was 0.20 and 0.80.

Conclusion: From the analysis, it has been carried out that bisphosphonate therapy is helpful for decreasing the bone turnover markers and increasing the BMD in postmenopausal women

both with and without diabetes. Oral ibandronate can be useful for offering the treatment to the patient and improving the health.

Keywords: Type 2 diabetes mellitus, Osteoporosis, Bisphosphonates

Background

There are various diseases having the direct or indirect impact on the health of the people. Type-3 diabetes mellitus (T2DM) is one of the most common causes of illness and influencing the physical and mental health of the people [1]. According to analysis, the diabetes is one of the major reasons of bone deterioration due to accumulation of advanced glycosylation [2]. However, the risk of fall increases is increasing the occurrence of hypoglycemic events and diabetic complications [3]. Therefore, more attention is required for treating the osteoporosis and prevent fractures in diabetic patients [4].

According to clinical studies, the postmenopausal women are having higher risk of fracture [5,6] . In addition to this, poor bone qualities, multiple comorbidities and use of various medications. As per the analysis, bisphosphonates is reducing osteocalcin level that is helpful for controlling the ostecoclast activities [7]. Apart from this, there were many concerns raised about bisphosphonates therapy that affect the glucose metabolism [8,9,10]. According to studies, the efficiency and safety of ibandronate among the T2DM patients is affecting the bone with high binding affinity. For such patients, ibandronate 150 mg tablet is prescribed for once in month for increasing the bone mineral density [11]. This is helpful for preventing the osteoporotic fractures. Moreover, osteoporotic is associated with the insulin secretation and sensitivity [12].

The co-occurrence of diabetes and osteocalcin is influencing the health of the patients and early treatment is recommended to the patients. The women after the menopause are facing the issues most as density of bone is weak [13]. This kind of situation is affecting the physical activities and increasing the risk of fracture and ibandronate.

Aim

The study aims to conduct a prospective trial to compare the efficacy of bisphosphonate therapy on postmenopausal osteoporotic women with and without diabetes

Method and Material

The study was a multicenter prospective clinical trial with an open label design. The study was conducted from March 2020 to March 2022 at M.K.C.G. Medical College. The study protocol was reviewed by the ethical committee and managed according to standards and guidelines. The researcher has collected the consent form with all demographic information about the patients.

Participants

For the study, the patients were selected who visited the hospital for other disease and following the instructions of the general physician. The selection criteria of the patients were age of at least 55 years and postmenopausal women. Moreover, the diagnosis of osteoporosis in lumbar spine, total hip or femoral neck among the women patients. The exclusion criteria of patient include treatment of osteoporosis within 3 years, underlying disease like heart failure, liver damage renal disease and use of the drugs that affect bone metabolism.

Intervention

For the intervention one tablet of 150 mg of ibandronate +24,000IU was offered to same date of every month a fixed amount of water is given to the patients before the investigation. Moreover, the vitamin D and calcium replacements were administrated for all subjects of drugs during the study.

Measurements

For measuring the effects of the disease patients have visited the clinic in every 6 months and followed the instruction of not having any kind of food and drink in morning. Moreover, the blood samples were collected. Apart from this, BMD was analyzed using different centers like dual-energy X-rays and Lunar Prodigy Advance.

Sample size

For the study, the percentage changes in lumbar spine BMD were compared between DB and non-DB patients. However, there was difference observed of 2 percent. Here, the SD was observed to be 4.5 considering the previous studies. Apart from this, study has involved the 120 patients considering the drop-out rate of 20%.

Statistical analysis

For the analysis of the data collected for the study Shapiro-Wilk test was applied and normal distribution of variable was observed. In addition to this, the mean and standard deviation values were obtained through t-test.

Results

Table 1: Basic details of group

	Non-Diabetic patients (*n* = 55)	**Diabetic patients (*n* = 49)**	**P value**
Age, years (median (IQR))	64 (62–72)	72 (66–78)	< 0.001
Age at menopause	50(49–54)	53 (47–53)	0.423
Menopause duration	17 (13–22)	24 (13–27)	0.037
BMI, kg/m^2 (mean (SD))	21.4 (3.8)	26.4 (3.7)	< 0.001
Fasting glucose, mg/dL (median, (IQR))	94 (95–107)	128 (118–148)	< 0.001
HbA1c, % (median, (IQR))	6.9 (6.1–.6.4)	7.7 (7.0–7.4)	< 0.001
Bone mineral density, g/cm^2 (mean (SD))			
Lumbar	0.787 (0.079)	0.814 (0.710)	0.098
Femoral neck	0.678 (0.112)	0.643 (0.097)	0.663
Total hip	0.769 (0.083)	0.778 (0.111)	0.607
Bone mineral density, T score (mean (SD))			
Lumbar	−2.29 (0.72)	−2.44 (0.79)	0.180
Femoral neck	−2.12 (0.67)	−2.93 (0.79)	0.544
Total hip	−1.54 (0.73)	−1.71 (0.89)	0.085
Trabecular bone score [a] (mean (SD))	1.278 (0.052)	1.298 (0.071)	0.294
Previous fracture – number (%)	7 (11.9)	12 (24.5)	0.071
Serum β-CTX, ng/liter (median (IQR))	0.378 (0.270–0.583)	0.370 (0.215–0.513)	0.421
Serum P1NP, ng/liter (median	51.1 (32.7–62.9)	47.4 (27.7–61.6)	0.346

(IQR))			
25-Hydroxivitamin D, ng/mL (mean (SD))	24.57 (13.69)	30.36 (14.16)	0.192

For the study, 120 patients enrolled and 104 have completed the study. According to analysis, the diabetic groups is older and having higher body mass. Moreover, the BMD, TBS and T-scores were not significantly different in these groups. Here BMD was investigated for all patients and it was carried out that lumbar spine for both groups was 3.41% and 3.71%, femur neck was 1.30% and 1.18% as well as the total hip was 1.51% and 1.58% in non-diabetic group. Unlike the BMD, no significant difference was identified for TBS as before and after the treatment which was 0.20 and 0.80.

Table 2: Safety assessment

	Non-Diabetic patients(n=63)	**Diabetic(n=57)**
Number of patients	6(8.9%)	6 (11.5%)
Fever	0	1
Myalgia	3	2
Dyspepsia	2	2
Weight loss	1	1

The table 2 has provided the information related to the safety of the patients and total 12 out of 120 patients were identified with adverse events. However, 1 patient from non-diabetic group had fever and withdrawn from the investigation. Moreover, 3 patients from non-diabetic group have myalgia and 2 from the diabetic group. Apart from this, 2 patients from each group had dyspepsia and 1 from each group weight loss.

Table 3: Changes in glucose metabolism

Clinical variables	**Pre-treatment Median (Interquartile range)**	**Post-treatment Median (Interquartile range)**	**P**
Fasting glucose, mg/dL (median, (IQR))	126 (112–142)	132 (116–146)	0.463
HbA1c, % (median, (IQR))	5.4 (5.03–6.70)	7.50 (8.03–7.07)	0.425

Table 3 has provided information related to the glucose metabolism before and after treatment and it was identified that both groups were significantly different in this study.

Discussion

According to analysis, the diabetes is one of the major reasons of bone deterioration due to accumulation of advanced glycosylation. However, the risk of fall increases with events and diabetic complications. Therefore, more attention is required for treating the osteoporosis and prevents diabetic patients from fractures. In addition to this, poor bone qualities, multiple comorbidities and use of various medications. As per the analysis, bisphosphonates is reducing osteocalcin level that is helpful for controlling the ostecoclast activities. Apart from this, there were many concerns raised about bisphosphonates therapy that affect the glucose metabolism.

According to outcome of the current study, the diabetic groups is older and having higher body mass. Moreover, the BMD, TBS and T-scores were not statistically correlated in these groups. Here BMD was

investigated for all patients and it was carried out that lumbar spine for both groups was 3.41% and 3.71%, femur neck was 1.30% and 1.18% as well as the total hip was 1.51% and 1.58% in non-diabetic group. Unlike the BMD, no significant difference was identified for TBS as before and after the treatment which was 0.20 and 0.80. Moreover, to the glucose metabolism before and after treatment and it was identified that both groups were significantly different in this study.

The study of Black and Rosen (2016) [14] has suggested that bisphosphonate treatment is useful for the patients for minimizing the level of osteocalcin secretion. It will also help in managing the level of glucose metabolism. Apart from this, the outcomes of the study were not able to provide the information related to the affect of bisphosphonate on DB patients related to glucose metabolism [15]. Moreover, the study has also identified that the altered osteocalcin is having minor impact on glucose metabolism and affecting the health of the patients. [16]

Conclusion

From the analysis, it has been carried out that bisphosphonate therapy is helpful for decreasing the bone turnover markers and increasing the BMD in postmenopausal women both with and without diabetes. Oral ibandronate can be useful for offering the treatment to the patient and improving the health.

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