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The effects of alendronate treatment in the diagnosis and management of proximal femur osteoporosis: A real-life scenario

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Abstract: Currently the increased focus is being given to reforming osteoporosis regimens. Optimizing the evaluation of pharmacological intervention occurs once a medicine has been approved. There is literature available on the use of alendronate in bone loss. The current study focuses on the efficacy assessment of alendronate on proximal femur bone density loss. Current work was carried out to analyze the data of the BMD. The study comprised of females who had received at least six months of Alendronate (70mg/week) for proximal femur osteoporosis. SPSS version-22 was used for analysis and a comparative change was regarded therapeutically significant. The reliability of the research was ensured by reporting cover-up and withdrawals. Among all the study participants who received Alendronate therapy the median height of females in centimeters (cms) was 155 (IQR =16) and the median weight was 55.5 Kilograms (Kgs) (IQR =15). The mean age of the population was 50.59±14.714. The study found the median T-score before therapy was -2.9 (IQR=0.7) and the median T-score after therapy was -2.51(IQR=1). The estimated difference of mean rank was statistically significant for pre- and post-therapy T-score (p=0.008). Hence, the results of this study indicate an improvement in BMD as a result of therapy. Alendronate at 70 mg per week is effective in reducing hip osteoporosis.

Keywords: Alendronate, bone mineral density, hip fractures, osteoporosis.

INTRODUCTION

Osteoporosis causes low bone density and its rates are higher over a fifty year's old population (Jung *et al.,* 2019). The most common osteoporosis fracture site is the hip (Dadra *et al.,* 2019). Significant differences among nations in the prevalence of osteoporosis exist. When the choice is made to start treatment with alendronate, the specification of the treatment method should be based on the minimal available purchasing cost. The lifestyle factors for bone density are poor BMI, low calcium intake, insufficient exposure to sunlight, and early menopause (Blackie, 2020). More than 8.9 million financial expenses are caused by osteoporosis worldwide every year and 1/3rd of all osteoporosis cases are occurring in Europe. Approximately 200,000 cases of osteoporosis are recorded annually in England and the National Health Service (NHS) has an estimated burden of around £ 1.73 billion. More than 1/3rd of adults and 1 in 5 men suffer from one or more osteoporosis fractures in their lifetime. Approximately 50% of patients with hip fractures can no longer live independently and 20% will die within 12 months of an osteoporosis fracture. In a population of Karachi city, the prevalence of osteoporosis is high among the adult population and it is associated with modifiable risk factors such as reduction of weight and increasing the physical activity etc. (Haris *et al.,* 2014).

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Over the next 50 years, fractures of osteoporosis are expected to increase with population growth if precautionary measures are not taken at present. Hospital stay in England has increased by 2.1% per year since 1999 due to hip fracture, while hospital bedding has doubled from 5.9% yearly. The treatment of osteoporosis switched to bisphosphonates in the early 1990's and Alendronate (70 mg once weekly orally) was documented for osteoporosis (Staford *et al.,* 2004). Implementation was approved for 70 mg/week in the BMD Bridging Research Study (Dennison, 2016). The disease is so serious that most patients die during the first 6 months (Kusen *et al.,* 2019) and 30 to 50 percent do not recover their normal pre-osteoporosis status (Kanis *et al.,* 2019). Osteoporosis management has increased clinical attention and new projects for effective screening and aggressive treatment to control the incidence of bone loss may indeed reduce the fracture rate among the population at higher risk (Melton *et al.,* 2005). There is no clear indication of a significant increase in the use of efficacious osteoporosis counseling in the countries.

Bone turnover markers and low bone mineral density are independent measurements of the risk of hip osteoporosis, and when both occur in one person, the risk is doubled. Bone turnover increased and bone mineral densities decreased are separate, phenomenal, hip osteoporosis risk indicators and, if both are probable, the risk is increased (Tarantino, *et al.,* 2017). Bone turnover decrease and the increase in hip BMD might be key to reducing the risk of

hip osteoporosis (Epstein, 2007). Alendronate has established anti-fracture efficacy in postmenopausal women against hip osteoporosis (Gul *et al.,* 2020); (Eastell *et al.,* 2019); (McClung *et al.,* 2001; Writing Group for the Women's Health Initiative Investigators, 2002; Reginster *et al.,* 2005). Alendronate efficacy has been reported, particularly for postmenopausal osteoporosis. The current study was designed to evaluate the efficacy of Alendronate in proximal femur osteoporosis.

MATERIALS AND METHODS

Design: Prospective drug-intervention study.
Setting: Outpatient clinic, Medical unit 6, JPMC, Karachi, Pakistan.
Participants: Alendronate (70 mg/week) was recommended to participants at random. Every month, all content was provided and participants were asked to take tablets until the study was completed.
Study duration: Jan 2016 to Dec 2016.
Sample size: A total of 350 people were screened with DEXA for osteoporosis out of which 20 were identified osteoporosis. Of the 20 participants, the research protocols were completed just by 10. Alendronate (70 mg/week) was measured according to a factorial schedule sample size. Only ten subjects followed the research protocol and six months of oral Alendronate (70 mg/week) so that they were properly taken into consideration. The AP L/S DEXA scan was performed at baseline and for the period consisting of 24 weeks. Six months after the last individual was reported, data were analyzed by SPSS 22 and relied on expectation to-treat.
Inclusion Criteria: Patients 50-96 years, postoperatively for at least three months, healthy with no known co-morbid disorders.
Exclusion Criteria: Previous fractures, patients who already had vitamin D / calcium supplements, pregnant women, smokers and those previously treated with a bisphosphonate.
A protocol for Tablet intake: After taking this tablet, the patient remains upright for thirty minutes, while the Alendronate is swallowed with a glass of plain water.

Ethical approval
This research was approved by the IRB (Institute Review Board), JPMC, Karachi, Pakistan.

STATISTICAL ANALYSIS

The data were statistically analyzed using SPSS version 22. The height and weight were reported using median and interquartile range (IQR). The pre and post therapy scores were compared by applying Wilcoxon signed-rank test p≤0. 05 was considered as statistically significant.

RESULTS

Among all the study participants who received Alendronate therapy the females had a median height in centimeters (cms) of 155 (IQR =16) and a median weight of 55.5 Kilograms (Kgs) (IQR =15) as shown in fig. 1. The mean age was 50. 59±14. 714.

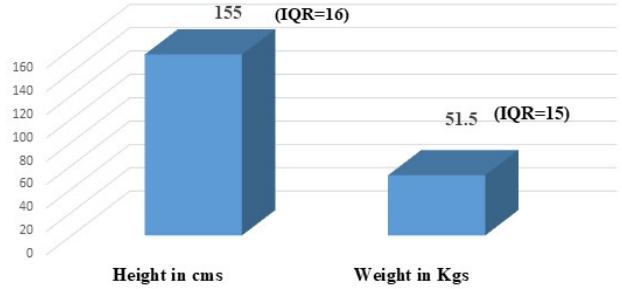

Fig. 1: Median Height and Weight of Study participant who received Alendronate therapy

The study found a median T-score before therapy of -2.9 (IQR=0.7) and the median T-score for after Alendronate therapy of -2.51 (IQR=1). Therefore, the estimated difference of mean rank was statistically significant for pre and post Alendronate therapy BMD T-score for the proximal femur (p=0.008) (table 1).

Table 1: Pre and post Alendronate therapy assessment of BMD scores of proximal femur bone density (n=10).

BMD Scores	Median score (IQR)	p-value
Pre-Therapy BMD scores	-2.9 (0.7)	0.008
Post Therapy BMD Scores	-2.5 (01)	

DISCUSSION

Bone is indeed a dynamic living part of the human body. Throughout our entire life, bone tissue cells are formed and older cells are also replaced with new cells. The rate of older bone falling-out is higher than the rate of bone regeneration when someone has osteoporosis. Bones lack the minerals like calcium if this happens. Bone weakening causes damage compared to a slight knock or fall. It makes the bones brittle. Alendronate has a place in the drug class called bisphosphonate. The efficacy of drugs at a decreased fracture rate and the reliability of safety of treatment outcomes in RCTs are a choice of solutions to manage osteoporosis. A meta-analysis of Papapoulos *et al.* (2005) has shown that Alendronate plays an important role in the management of osteoporosis. A total of 6,804 ladies of 6 RCTs was examined with a BMD T score equal to or below -2.5 in age groups 39-91 years. Studies have shown that 29 of 10,000 people are at risk of hip fracture and are in the Alendronate group. With reliable results of RCTs, the overall risk reduction rate was 55%. Declines in the frequency of treatment of Alendronate hip

fractures are apparent from all previous assessments. The adequacy of Alendronate in postmenopausal women with osteoporosis has been indicated in a report published by the WHO Scientific Group (WHO Logical Gathering, 2003). However, the RCTs did not show any significant events in the Alendronate group (Tu *et al.,* 2018); (Black *et al.,* 1996); (Cummings *et al.,* 1998). Ten years of Alendronate safety has been confirmed (Bone *et al.,* 2004) also, a decrease in bone turnover remained stable over the 10-year duration of Alendronate. Further use of Alendronate has been significantly associated with increases in the lumbar spine and hip BMD. However, safety information and guidelines on vertebral and non-vertebral fractures are also very valuable. Therefore, Alendronate may be a choice for postmenopausal osteoporosis patients. The risk of hip fractures in the fracture intervention study mentioned a significant decrease in bone-specific alkaline phosphatase. 1-year improvement in alkaline phosphatases in postmenopausal women treated with Alendronate has been reported with a 39% decrease in hip fractures (Bauer *et al.,* 2004). A literature study reported that Alendronate treated women had a 30 percent reduced bone-specific alkaline phosphatase and 74 percent lower risk of hip fracture (Bauer *et al.,* 2004). Alendronate is effective in decreasing the risk of hip fracture over a range of ages. The adequacy of patients with a BMD T score of -2.5 is all the more evident compared to patients with a BMD T femoral neck score of –2.0 (Hochberg *et al.,* 2002; Hochberg *et al.,* 2005). Retrospective studies confirm that the coherence and persistence of an expanded population of current Alendronate patients to analyze osteoporosis in the authentic, practical terms are poor and lacking (Rabenda *et al.,* 2008). A large number of females are in line with bisphosphonate care and approximately 40 percent of females have been treated for 12 months without any variation in treatment (Rabenda *et al.,* 2008). Consistency and compliance in patients receiving Alendronate have become a difficult task. Alendronate has the recommended dosing regimen per week and is proportional to the daily dosage routine (Kendler *et al.,* 2004; Rossini *et al.,* 2006). Alendronate has the same safety and sensitivity profiles for osteoporosis, daily, and once a week (Schnitzer *et al.,* 2000; Rizzoli *et al.,* 2002; Simon *et al.,* 2002). Compliance with bisphosphonate therapy is associated with the risk of fracture. As a recovery strategy, hip fracture occurs critically. A literature study has indicated that women who are advised Alendronate every week are 16.4% less likely to experience the harmful effects of hip fractures than on a daily basis (Rabenda *et al.,* 2008). Once a week, Alendronate regimen increases patient adherence to the medication. There are certain limitations to this research. The small sample size and time of the study were key drawbacks.

CONCLUSION

From the study it was concluded that 70 mg alendronate weekly is correlated with a significantly higher hip BMD in Pakistani local population. This therapy also improved the patient compliance and decreased the rates of adverse effects, for example, fragility fractures. Early and low frequency doses may reduce medical costs as well.

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