Vitamin D and Calcium v/s Bisphosphonates in the Secondary Prevention of Osteoporosis and Prevention of Osteoporotic Fractures Following a Low Energy Fracture

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ABSTRACT

Introduction: Bones commonly involved in osteoporosis are the vertebra, forearm bones, and hip. Calcium, vitamin D and Bisphosphonates are used in the treatment of osteoporosis and prevention of a second fracture. Objective of the study was to study the effectiveness of bisphosphonates and Vitamin D and Calcium in osteoporosis and prevention of a second osteoporotic fracture.

Materials and Methods: Patients with osteoporotic/fragility fractures were included in the study. DEXA scan was performed at one month after discharge. Patients were divided into 3 groups, receiving Zoledronic acid, Calcium and Vitamin D, and no anti-osteoporotic prophylaxis. DEXA scan was repeated at 2 years and the three groups were compared. Patients were followed for a total of 5 years for the development of a second fragility fracture.

Results: Most of the patients with low energy fractures had osteoporosis. Patients receiving Zoledronic acid had a substantial increase in Bone Mineral Density as compared to those who received Vitamin D and calcium, or no prophylaxis. A total of 1 (2.6%) new low energy fracture (vertebral) occurred in patients receiving Zoledronic acid, 5 (13.5%) new low energy fractures (4 vertebral, 1 hip) occurred in patients receiving vitamin D and calcium and 7 (18.4%) new low energy fractures (5 vertebral, 1 hip, 1 wrist) occurred in patients receiving no prophylaxis.

Conclusion: Bisphosphonates are much better than vitamin D and calcium supplementation in increasing overall bone mineral density and preventing second fragility fracture in patients with osteoporosis.

Keywords: Calcium, Vitamin D, Bisphosphonates, Osteoporotic Fractures, Osteoporosis

INTRODUCTION

Osteoporosis is a systemic disease of the old age. It means increased demineralisation of the skeleton leading to decreased bone strength and an increased risk of fractures. It is the most common reason for a broken bone among elderly population. Osteoporosis may be primary (Age related loss of minerals from the skeleton), or secondary to endocrine, haematological, genetic, environmental or other factors. Primary osteoporosis is further classified into type 1 or post-menopausal and type 2 or senile osteoporosis.

Dual-energy X-ray absorptiometry (DEXA) is the most common method used to study Bone Mineral Density (BMD) or bone mass. It is used to identify people with osteopenia or osteoporosis. Since 1994, WHO has established the standard of diagnosis of diagnosing osteoporosis as a bone mass density of 2.5 standard deviations below that of a young adult, while it defines osteopenia is defined as a bone density of 1standard deviations below that of a young adult of same gender.[1] Measurements of bone mineral density can predict fracture risk, lower bone BMD higher are the chances of fracture even with minor traumas.[2]

Osteoporosis is often asymptomatic, but is just as dangerous and serious as hypertension, diabetes or dyslipidaemia. In USA in 2010, in 100 million population above 50 years of age, an estimated 10 million suffered from osteoporosis, while an additional 40 million suffered from osteopenia.[3]

Women are more commonly affected than men. This is because of the small bones in women, malnourishment in women that is common in developing countries as well as the deficiency of bone protective Estrogen in Post-menopausal women. Type 1 or postmenopausal osteoporosis occurs in 5% to 20% of women. The frequency of postmenopausal osteoporosis accounts for the overall female-male ratio of 2:1 to 3:1.[4]

The lifetime risk of suffering an osteoporotic fragility fracture for adult women is 1 in 3. For males, the risk is less, but remains substantial at 1 in 12[5] Following a fragility fracture, the risk of sustaining a subsequent fracture at least doubles, with a 30-40% increase during the three years following the fracture. A 10% loss of bone mass in the vertebrae can double the risk of vertebral fractures, and similarly, a 10% loss of bone mass in the hip can result in a 2.5 times greater risk of hip fracture.[6]

Osteoporotic patients usually sustain fractures following low energy traumas like fall. Bones that commonly break include the vertebra, forearm bones, and the hip.[7,8]

The prevention of osteoporotic fractures includes fall prevention, calcium and Vitamin D supplementation and lifestyle advice like exercising[9], stopping smoking and drinking etc,[10] as well as pharmacological therapy. Pharmacological treatment can be broadly divided according to their mode of action. These include anti-resorptive agents like the bi-

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sphosphonates (alendronate, risedronate, ibandronate and zoledronic acid), the Selective Estrogen Receptor Modulators (SERMs), antibodies like denosumab and bone forming agents like parathyroid hormone and teriparatide. Drugs like strontium ranelate appears to have both antiresorptive and anabolic activities.[11]

Calcium is an essential element in the human body. Calcium is not only important to bone health, but it is also essential for homeostatic functions. It is a vital component of bones. The primary functions of vitamin D are increasing intestinal calcium absorption, decreasing renal excretion and the stimulation of bone mineralisation. It is estimated that 90% of adults above 50 years of age do not get enough vitamin D from their diet.[12]

Calcium (1000 mg/day) and vitamin D (800 units/day) supplementations have been shown to reduce the incidence of osteoporotic fractures.[13,14]

Bisphosphonates are a class of drugs that prevent the loss of bone mass. They are the most common drugs used to treat osteoporosis.[15] Bisphosphonates inhibit the digestion of bone by encouraging osteoclasts to undergo apoptosis.[16] For zoledronic acid, an early effect (fractures reduced within 6–12 months of starting therapy) has been shown. A sustained effect has been shown through 5 years.[17] Administration of bisphosphonates results in changes in biochemical markers of bone turnover and in bone mineral density. Zoledronic acid increases spinal bone mineral density at 12 months to 5 percent above values found in patients receiving placebo.[18] Bisphosphonates have been shown to increase BMD and reduce fracture risk by between 30 and 60%.[6,19] We started this study to compare the usefulness of Calcium and vitamin D supplementation and the use of bisphosphonates in patients with an osteoporotic fragility fracture, in the prevention of second osteoporotic fracture and in secondary prevention of osteoporosis.

MATERIALS AND METHODS

A total of 113 patients aged over 50 years with a low energy fracture of Spine, Hip or Distal radius were included in the study.

Informed consent was obtained from each patient included in the study and The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a prior approval by the institution's human research committee.

Inclusion criteria

1. Age > 50 years
2. Any sex
3. Low energy trauma. (fall from standing height, sitting, no history of trauma, etc. were considered as low energy trauma, while road traffic accidents, fall from height etc. were considered high energy trauma)
4. Vertebral compression fracture, Hip fracture (intertrochanteric or neck of femur fracture) or Distal radius fracture.
5. 1st fragility fracture.

Exclusion criteria

1. Age < 50 years
2. High energy trauma
3. 2nd or more episode of fragility fracture.
4. Secondary causes of osteoporosis or fracture and/or significant medical history.

This was a randomised study. DEXA scan was performed at one month after discharge. After this, patients were matched for fracture type, BMD groups and sex and patients from each matched cluster were divided into 3 groups by toss of dice.

First group (38 patients) received annual Zoledronic acid 5 mg iv infusion, Second group (37 patients) received daily Calcium (1000mg) and Vitamin D (600 IU) supplements via oral route, And third group (38 patients) received no anti-osteoporotic prophylaxis. However they received diet modification, lifestyle modifications and anti-fall measures and so did the other two groups. The osteoporotic patients were given different treatments as the main objective of the study was finding the relation of these treatment modalities in prevention of second fracture in patients who had one fracture already. Although bisphosphonates are proven to increase bone mass, but whether this increase is translated into real life benefit like decrease in future fractures isn't well established in literature.

DEXA scan was repeated at 2 years and the three groups were compared with the first DEXA Scan and with each other. Patients were followed for a total of 5 years for the development of a second wrist, hip or spine fracture and this data was compared in the three groups.

RESULTS

A total of 113 patients aged over 50 years with a low energy fracture of Spine, Hip or Distal Radius were included in the study. 65 patients (57.5%) had vertebral compression fracture, 26 patients (23%) had hip fractures while 22 (19.5%) had distal radius fracture. Out of the 65 vertebral fractures 16 occurred in men and 49 (75%) occurred in women. Out of the 26 hip fractures 10 occurred in men while 16 (62%) occurred in women, and out of the 22 distal radius fractures 6 occurred in men while 16 (72%) occurred in women.

In total 32 fractures (28.3%) occurred in men while 81 fractures (71.7%) occurred in women. DEXA scan was performed at one month after discharge and found that; Out of 65 patients with vertebral fractures 52 (80%) had osteoporosis, 9 (14%) had osteopenia, while 4 (6%) had normal bone mineral density (BMD). Out of 26 patients with hip fractures 16 (61.5%) had osteoporosis, 4 (15.5%) had osteopenia, while 6 (23%) had normal bone mineral density, Out of 22 patients with Distal radius fractures 9 (41%) had osteoporosis, 5 (23%) had Osteopenia, while 8 (36%) had normal bone mineral density. In total 77 patients (68%) had osteoporosis, 18 (16%) had osteopenia, while 18 (16%) had normal BMD. Patients were matched for fracture type and sex and were divided into 3 groups. First group (38 patients) received annual Zoledronic acid infusion, Second group (37 patients) received daily Calcium and Vitamin D supplements, And

third group (38 patients) received no anti-osteoporotic pharmacological prophylaxis.

We repeated DEXA scan at 2 years and found that patients receiving Zoledronic acid had a 5.1% increase in BMD at spine as compared to patients receiving Vitamin D and Calcium who had a 0.8% increase in BMD as compared to patients receiving no prophylaxis who had a 0.2% increase in BMD. Patients receiving Zoledronic acid had a 3.2% increase in BMD at Hip as compared to patients receiving Vitamin D and Calcium who had a 0.4% increase in BMD as compared to patients receiving no prophylaxis who had a 0.3% Decrease in BMD. Patients receiving Zoledronic acid had a 1.8% increase in BMD at Distal radius as compared to patients receiving Vitamin D and Calcium who had a 0.6% increase in BMD as compared to patients receiving no prophylaxis who had a 0.3% increase in BMD.

Patients were followed for 5 years for the development of a second fracture. 1 new vertebral fracture occurred in the group receiving zoledronic acid (2.6% incidence), 4 new vertebral fractures occurred in the group receiving Vitamin D and calcium (10.8% incidence) and 5 new vertebral fractures occurred in the group receiving no prophylaxis (13% incidence).

No new hip fracture occurred in the group receiving zoledronic acid (0% incidence), 1 new Hip fracture occurred in the group receiving Vitamin D and calcium (2.7% incidence) and 1 New hip fracture occurred in the group receiving no prophylaxis (2.7% incidence). No new wrist fracture occurred in the group receiving zoledronic acid (0% incidence), no New wrist fracture occurred in the group receiving Vitamin D and calcium (0% incidence) and 1 new wrist fracture occurred in the group receiving no prophylaxis (2.7% incidence). A total of 1 (2.6%) new low energy fracture occurred in patients receiving zoledronic acid, 5 (13.5%) new low energy fractures occurred in patients receiving Vitamin D and calcium and 7 (18.4%) new low energy fractures occurred in patients receiving no prophylaxis.

DISCUSSION

Osteoporotic/fragility fractures are the most common fractures in elderly population. In our study 57.5% had vertebral compression fracture, 23% had hip fractures while 19.5% had distal radius fracture. Similar statistics are also seen in other countries like the Unites States having 47% vertebral fractures, 17% hip fractures and 17% distal radius fractures.[20]

Various authors have recommended screening in women older than 65 years, in post-menopausal women, in people with risk factors for osteoporosis or patients with secondary causes that may lead to osteoporosis but there is no specific guideline for screening for osteoporosis, and the risk to benefit ratio of screening for osteoporosis is still being evaluated.[21,22]

Osteoporosis is often asymptomatic, but is just as dangerous and serious as hypertension, diabetes or dyslipidaemia. The lifetime risk of suffering an osteoporotic fragility fracture for adult women is 1 in 3. Following a low energy osteoporotic fracture, the risk of sustaining a second osteoporotic fracture at least doubles, with 30–40% increase in fractures in the first 3 years following the fracture.[6] Unfortunately in both developed as well as developing countries orthopedicians and doctors in general aren't approaching osteoporosis with the seriousness that it deserves.

There is no screening protocol for vitamin D levels and osteoporosis in general population, high risk population or even those with fractures suggestive of osteoporosis. Orthopedicians and family physicians are more interested in fixing the fractures with very little attention paid to treating the underlying cause. Patients with osteoporotic fractures are rarely advised DEXA, vitamin D and Calcium supplements are prescribed for very brief durations; Bisphosphonates are used in occasional patients, there is no concept of lifestyle modification for treatment of osteoporosis and the follow-up of osteoporosis is much less than adequate. Various studies like NICE have highlighted the inadequate bone health services even in the developed countries and have advocated secondary prevention of osteoporotic fractures and have promoted the pharmacological management of osteoporosis.[23]

In our study most of the low energy fractures occurred in women accounting for 71.7% of fractures. 68% of the patients with low energy fractures had osteoporosis, 16% had osteopenia, while 16% had normal BMD. In our study we found that vertebral compression fracture were the most common fragility fractures followed by hip and distal radius fracture. Patients receiving Zoledronic acid for 2 years had a substantial increase in BMD at spine, hip and distal radius as compared to those who received Vitamin D and calcium, and patients who received vitamin D and Calcium for 2 years had more increase in BMD than those who received no anti-osteoporotic prophylaxis but this difference wasn't that substantial. Similar results have also been seen in previous studies, indicating that administration of bisphosphonates increases bone mass as compared to a placebo.[24] Patients were followed for 5 years for the development of a second fracture. A total of 1 (2.6%) new low energy fracture (vertebral) occurred in patients receiving zoledronic acid, 5 (13.5%) new low energy fractures (4 vertebral, 1 hip) occurred in patients receiving Vitamin D and calcium and 7 (18.4%) new low energy fractures (5 vertebral, 1 hip, 1 wrist) occurred in patients receiving no prophylaxis.

Previous studies have also found that bisphosphonates are associated with decrease in risk of osteoporotic fractures.[24-26] We conclude that bisphosphonates are much better than Vitamin D and calcium supplementation in increasing overall bone mineral density in patients with osteoporosis.

Vitamin D and calcium supplementation seem to increase bone mineral density and prevent second fractures as compared to no prophylaxis but this difference isn't as large as that between bisphosphonates and no prophylaxis.

Over the past decades, the seriousness of osteoporosis is slowly being recognised all over the world. Various organisations like the British orthopaedic association recommend that orthopaedic surgeons should not only treat the fractures but should also treat the cause of the fracture, and should also initiate appropriate assessment and treatment for the

prevention of further fractures.[5] There is a great need to educate the general population and health care providers about osteoporosis.

We recommend the use of bisphosphonates as well as calcium and vitamin D supplementation in patients with known osteoporosis or a fracture suggestive of osteoporosis. In our institute we treat all low energy fractures of hip, spine or wrist as osteoporosis. Vitamin D and calcium are started immediately on discharge on a once daily oral dosage. Bisphosphonates are started after a month of fracture treatment. In our institute we prefer the use of zolidronic acid over other bisphosphonates. We have found it to be safe and easy to administer. Patients are more comfortable with annual administration of this drug rather than daily or monthly use of other bisphosphonates. Patient compliance is high with this drug and the overall results are also good.

We also discuss and encourage DEXA test to female patients attending our clinic who are above 60 years and to male patients who are above 70 years of age. However this test is purely voluntary. If this test is done, we put the patients with osteopenia on Vitamin D and Calcium supplementation and encourage them to take healthy diet and exercise regularly and to stop smoking. In patients with osteoporosis, we also start annual Zoledronic acid.

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