Original Article

A RETROSPECTIVE STUDY OF CLINICAL PROFILE AND DRUG PRESCRIBING PATTERN IN OSTEOPOROSIS IN A TERTIARY CARE HOSPITAL

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ABSTRACT

Objective: To study the clinical profile and prescription pattern of drugs in the treatment of osteoporosis in a tertiary care centre in Karnataka, India.

Methods: This was a retrospective study carried out in a multi-speciality tertiary care hospital in Karnataka. Information was collected from case record forms of 100 patients of osteoporosis during a 12 mo tenure regarding various signs and symptoms they presented with and treatment provided.

Results: Majority of the subjects were females (90%). Low back ache was the most common presenting symptom. There was an increase in mean calcium (8.84±8.32 mg/dl) and phosphorus levels (2.45±1.83 mg/dl) as compared to baseline at the follow up visit. Vitamin D and calcium supplementation were the most commonly prescribed medications followed by analgesics, calcitonin and bisphosphonates. A total of 77 adverse reactions were reported, gastritis being the commonest one.

Conclusion: Vitamin D and Calcium supplements were more commonly prescribed than specific anti osteoporotic medications.

Keywords: Low back ache, Bisphosphonates, Vitamin D, Calcium, Prescribing trends.

INTRODUCTION

Osteoporosis is a major health problem, especially in elderly populations worldwide. It is commonly associated with fragility fractures at the hip, spine, and wrist. The World Health Organisation (WHO) ranks osteoporosis as a major global healthcare problem, second to cardiovascular diseases. WHO defines osteoporosis as a bone mineral density (BMD) of 2.5 standard deviations or more below the mean peak bone mass (average of young, healthy adults) as measured by dual-energy X-ray absorptiometry [1]. Although reliable epidemiological data is lacking in India, there were approximately 26 million osteoporosis patients in 2003 with the numbers projected to increase to about 36 million by 2013 [2]. In 2013, a total of about 50 million people in India were either osteoporotic (T-score lower than–2.5) or had low bone mass (T-score between –1.0 and –2.5) [3].

The pathogenesis of osteoporosis largely remains descriptive [4]. Imbalance between bone resorption and bone formation is the underlying mechanism by which osteoporosis occurs. Decrease in bone mass and an increase in fragility can occur because of failure to achieve optimal peak bone mass, bone loss caused by increased bone resorption, or inadequate replacement of lost bone as a result of decreased bone formation.

Osteoporosis is often called the "silent disease" because bone loss occurs without any overt symptoms for a long period. In many cases, the first "symptom" is a broken bone. Osteoporotic fractures are also known as fragility fractures as they occur in those situations where healthy people would not normally break a bone. Typical fragility fractures occur in the vertebral column, rib, hip and wrist.

Treatment of osteoporosis involves management of osteoporosis associated fractures, universal prevention measures, and medical treatment of the underlying disease. There is a range of anti-resorptive or anabolic options like bisphosphonates, calcitonin, teriparatide that are available for the prevention of osteoporotic fractures. Appropriate symptomatic treatment in the form of analgesics and muscle relaxants may also be initiated. All pharmacological management strategies for the prevention and treatment of osteoporosis also include recommendations for adequate calcium and vitamin D supplementation [5].

As human life span is gradually increasing, more and more elderly people are being treated for primary and secondary osteoporosis over increasing periods of time. In the absence of specific guidelines for the treatment of osteoporosis and with the availability of a wide variety of drugs in the market, treatment of individuals has become more of a trial and error practice. Most clinicians employ change in serum calcium and phosphorus levels as the means to monitor success/ failure of osteoporosis therapy.

Since there are no standard protocols, followed worldwide for the treatment of osteoporosis, more number of studies are required to find the most effective drugs for treating osteoporosis. In view of this, the present study was planned to investigate the clinical profile and prescribing patterns in patients of osteoporosis.

MATERIALS AND METHODS

This was a retrospective study carried out in a multi-speciality tertiary care hospital in Karnataka. It was carried out over a 12 mo period between January 2012 and December 2012.

Inclusion criteria

- Patients of either sex diagnosed with generalized osteoporosis.

Exclusion criteria

- Patients diagnosed with osteoporosis associated with malignancies.

- Patients with localised osteoporosis.

After obtaining clearance from the Institutional Ethics Committee (IEC), the hospital record files of 100 patients of osteoporosis satisfying the above inclusion criteria were analysed. The following details were collected

- Demography (age, gender)

- Clinical features at the time of presentation.

- Baseline investigations like serum calcium, phosphorus, Alkaline Phosphatase (ALP).

- Concomitant diseases if any.

- Drugs prescribed for treatment of osteoporosis.

- Concomitant medications, if any.

- Adverse effects that occurred in patients and measures taken to treat them. Causality assessment was done using WHO causality term assessment criteria.

- Serum calcium and phosphorus levels after 3 mo of treatment.

Data was further analysed using SPSS version 20. Analysis was done using descriptive statistics. Calcium and phosphorus levels were measured before and 3 mo after the start of therapy. Mean change in calcium and phosphorus levels was reported. Adverse drug reactions (ADRs), if any, were also reported.

RESULTS AND DISCUSSION

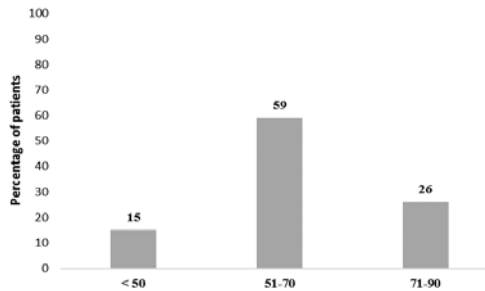Of the 100 study subjects, 90 were females.

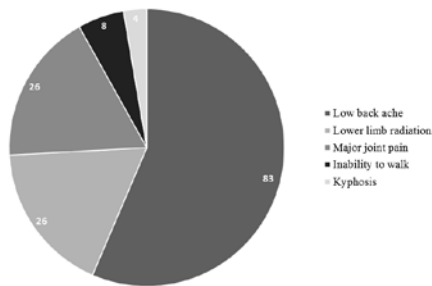
Fig. 1: Age groups in the study population

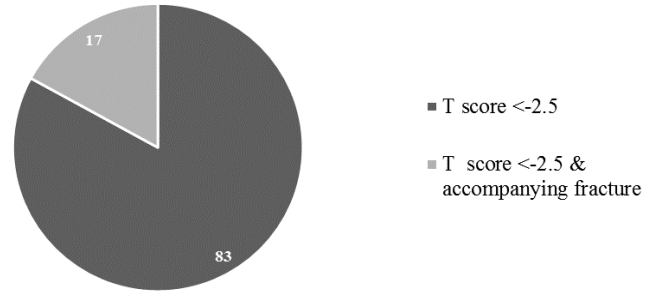Fig. 2: Clinical features in the study population

Fig. 3: T score values in study population

The most frequently prescribed dose range for vitamin D was 10-15 μg (63.92%) followed by 15-20 μg (27.84%) and 20-30 μg (8.24%). Calcium was most commonly prescribed in the dose range of 625-1000 mg (49.48%) followed by 200-500 mg (27.84%), 1200-1825 mg (10.31%) and 2000-2500 mg (12.37%). Paracetamol 650 mg daily was the most commonly prescribed oral analgesic (58.75%) followed by tramadol 75 mg (50%) and aceclofenac 200 mg (25%).

Tramadol plus paracetamol combination was the most commonly prescribed topical analgesic in 72.72% of the study subjects. The most commonly prescribed muscle relaxants was thiocolchicoside (62.96%) and tizanidine (37.04%).

Alendronate were the most commonly prescribed bisphosphonate (55.56%). It was either prescribed as once weekly or once daily dose. Ibandronic acid was the other commonly prescribed bisphosphonate given to 44.44% of the study population either as once daily or once monthly dosing. A total of 77 ADRs were reported in 53 out of the total 100 study subjects. This included gastritis (64.15%), sedation (22.64%), vomiting (20.75%), fatigue (20.75%), constipation (11.32%) and maculopapular rash (5.66%). None of the ADRs were serious or required discontinuation of the suspected drug. All the ADRs were classified as "possible" according to WHO causality term assessment criteria.

Table 1: Distribution of calcium and phosphorus levels in study population

	Calcium levels			Phosphorus levels		
	Reduced	Normal	Increased	Reduced	Normal	Increased
Before treatment	25	74	1	2	80	18
After treatment	0	70	30	1	72	27

There was an increase in mean calcium and phosphorus levels as compared to baseline at the follow up visit (3 mo after initiation of therapy) as shown in table 2.

Table 2: Mean and percentage change in calcium and phosphorus levels

Parameter	At baseline visit*	At follow UP visit*	Percentage change in levels**
Calcium level	8.91±0.60	9.81±0.58	8.84±8.32
Phosphorus level	3.74±0.61	3.76±0.57	2.45±1.83

*All values expressed in mean±SD (mg/dl), ** All values in mean±SD

Table 3: Concomitant diseases and medications in the study population

Parameter	Males	Females	Total
Concomitant diseases			
Hypertension	6	34	40
Diabetes mellitus	5	18	23
Osteoarthritis	5	8	13
Rheumatoid arthritis	1	4	5
Concomitant medications			
Multivitamins	10	70	80
Proton pump inhibitors	10	64	74
Antihypertensives	6	36	42
Oral hypoglycaemic agents	5	19	24
Steroids	3	16	19
Pregabalin	8	10	18

Table 4: Prescription pattern of various drugs in osteoporosis

Drug class	Percentage of patients (%)
Vitamin D	
a. Tablet	97
b. Powder	34
c. Injection	1
Calcium salts	97
Analgesics	
a. Tablets	80
b. Topical	11
Calcitonin	45
Muscle relaxants	27
Bisphosphonates	19
Teriparatide	15

DISCUSSION

The present study assessed the clinical profile and various prescription patterns for 100 patients diagnosed with osteoporosis. Majority of the patients were in the 51-60 y age groups with the mean age of the study population being 62.42±13.11 y. This is in accordance with studies which have shown peak incidence of osteoporosis in India at the age of 50-60 y, as compared to 70-80 y in the West [6, 7]. The present study showed a female preponderance with male: female ratio being 1: 9. This data, although in unison with data available from studies in western populations, is in contradiction with studies done earlier in Indian populations which show a male predominance [8, 9]. The traditional belief that men are more commonly affected in India could be related to men seeking and getting better medical attention [10]. However, recent studies conducted in India show a reversal of the sex ratio in patients affected with osteoporosis with the numbers being a little tilted towards females [11].

Low backache, which could be a result of vertebral fractures or compression, was the most common presentation in the current study seen in 83% of the patients. Prevalence data from population based studies conducted worldwide indicate a substantial variation in overall prevalence ranging from 10% to 25% in women and from 10% to 27% in men [12-14].

The trend in calcium, phosphorus and serum ALP levels was similar to the results of another study done in South India measuring serum calcium, phosphorus and ALP levels in patients diagnosed with osteopenia and osteoporosis. Serum levels of calcium, phosphorus, and ALP are insensitive for diagnosing osteoporosis [15].

Hypertension was the most common comorbidity seen in a little over half the study population (52.63%). In an earlier report to study the association between hypertension and osteoporosis, women with hypertension were found to be affected more frequently by osteoporosis (33.2 vs. 23.3 %), and higher prevalence, of hypertension seen among women with osteoporosis (32.2 vs. 22.5 %) [16].

Knowledge about concomitant medications is important as certain drugs increase the risk of osteoporosis in the long run. Glucocorticoid-induced osteoporosis is the most common form of secondary osteoporosis. Glucocorticoids can increase apoptosis of osteoblasts thereby leading to bone loss. Glucocorticoids, which are taken on a long-term basis by an estimated 1% of the Indian adult population, especially the elderly, is a contributing factor to osteoporosis in India [17]. Out of the 24 subjects being prescribed oral hypoglycaemic agents, thiazolidinediones like pioglitazone was prescribed in 11 subjects (45.83%). This is of significance since these drugs are selective agonists of peroxisome proliferator-activated receptor-γ which in turn decrease osteo blastogenesis [18]. Proton pump inhibitors (PPIs) decrease intestinal calcium absorption thereby increasing bone resorption. PPIs decrease BMD at the lumbar spine and hip, and increase the risk of vertebral and non vertebral fragility fractures, depending on the drug dose and duration of therapy [19].

The National Institute of Health (NIH), USA recommends vitamin D 600 IU (15 μg) daily for men and women 19 to 70 y old and 800 IU (20 μg) daily for men and women 71 y and older. In the present study,

majority of the subjects (63.92%) were prescribed a daily dose ranging from 10-15 μg which was much less than the recommended dosage. Supplementation with vitamin D has been shown to improve musculoskeletal function and reduce the risk of falling in elderly women. Twenty-five trials that randomized women to vitamin D with or without calcium and measured bone density or fracture for at least one year revealed a 37% reduction in vertebral fractures [20].

The NIH recommends a Recommended Dietary Allowance (RDA) of 1000 mg/day for individuals 19-50 y of age and men 51-70 y and 1200 mg/day for women 51-70 y and all individuals>70 y of age for calcium. In the present study almost half the study population (49.48%) received calcium supplementation in the range of 625-1000 mg/day and 27.84% of the population received 200-500 mg/day. Thus most of the subjects received an inadequate dose of calcium every day. 22% of the patients received calcium supplementation>1200 mg/day. A meta-analysis of 29 studies, with over 63,000 individuals analysed, concluded that best effect in patients suffering with osteoporosis was seen with minimum doses of 1200 mg of calcium and 800 units of vitamin D daily [21]. Bisphosphonates were prescribed in only 18% of the patients in the present study. There has been a decline in the prescription rate of bisphosphonates due to the development of adverse reactions like gastritis and availability of better anti osteoporotic drugs [22]. 45% of the patients in the present study were prescribed calcitonin in the form of nasal spray. In a meta-analysis comprising of fourteen double-blind, placebo-controlled trials that evaluated the analgesic efficacy of calcitonin for osteoporosis-related vertebral fracture pain, thirteen studies demonstrated statistically significant improvement in pain or function in calcitonin-treated patients [23].

Serum calcium levels had increased from 8.91±0.60 mg/dl at baseline to 9.81±0.58 mg/dl with a percentage increase of 8.84 % from baseline to follow up. As compared to 25 subjects, with calcium levels below normal at baseline visit, none of the subjects had a similar serum calcium level at follow up visit. This is attributed to the calcium and vitamin D supplementation along with other drugs like teriparatide.

Although adverse drug reactions, as reported, as reported in the case files of the study subjects were noted down, these could not pin point a particular anti-osteoporotic medication as the cause of the ADR. Gastrointestinal side effects including gastritis, vomiting and constipation constituted the major spectrum of ADRs. This could be attributed to bis phosphonate therapy as shown by a study conducted by van den Bergh JPW *et al.* [24]. However, no literature reports are available regarding the adverse event profile of the various drugs used in osteoporosis.

There were a few limitations in the present study. One of them is the non-availability of T-score values at follow up visit. T-score data would have helped in monitoring the efficacy of anti osteoporotic drugs better. Since data from only one follow up visit was available, the long term effects of anti osteoporotic medications could not be determined.

CONCLUSION

Osteoporosis, though one of the most common diseases affecting both elderly men and women, is also one of the most neglected diseases. Lack of overt symptoms in the initial stages of the disease,

unavailability of cheaper diagnostic tools to aid in early diagnosis and lack of consensus among physicians, on a common treatment regime, makes the situation grim. In the present study, calcium and vitamin D supplementation, albeit given to almost all the patients, the dose was much lesser than the RDA fixed for these nutrients. However, increase in serum calcium and phosphorus levels was seen in all the study subjects. Use of specific anti resorptive drugs like bisphosphonates and teriparatide was limited. These factors might have long term implications in the treatment of osteoporosis and thus need to be addressed.

CONFLICT OF INTERESTS

Declared None

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