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## Musculoskeletal pain treated by bisphosphonate therapy

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### ABSTRACT

Osteoporosis is the disease in which bone mass decrease and dislocate the bone formation which decrease bone strength and increase the possibility of breakage. This provides the belief for their use in the treatment of diseases of high bone turnover, such as Paget's disease and hypercalcemia of malignancy. The antiresorptive action of bisphosphonate is also useful in the management of osteoporosis, in which the rate of bone resorption exceeds that of bone formation. Bisphosphonate increase the rate of bone resorbing and bone construction. It is efficient to increase the mass of spinal bone in women. 50% vertebral fracture is reducing by increasing the mass of spinal bone. The two basic transactions is applied in which first is not continuous giving of bisphosphonate, which is expected to reduce bone resorbing, the stage in which medicine is not giving bone development may continue at a standard time, causing normal calcium stability. The investigation and examine in the subject of medicine concerned with children start in 1997. In this regard review article on bisphosphonate recognized 24 prepare and produce text and software concerning to children of that time period. The major cause of this assess is to make a decision what fresh information has been acquired over the past seven years and to offer suggestions for the upcoming use of such drugs in children and what additional research needs to be undertaken. Now a day the information of osteoporosis in childhood has improved so have pressures to consider use of the pharmacological agents used to treat osteoporosis in adults. This assessment gives information about the given results on the usefulness and protection of bisphosphonate therapy for pediatric osteoporosis. By comparing the medical literature, bisphosphonate therapy has very opposing opinions. © 2010 Trade Science Inc. - INDIA

### INTRODUCTION

#### Musculoskeletal system

A musculoskeletal system is a functioning related to the locomotion. It provides quality to the body to move from one place to another with the aid of muscles and skeleton system. The musculoskeletal system gives shape, maintain, firmness, and mobility to the body.

#### Bisphosphonate

The first detail about bisphosphonate was issued in 19th century but earliest systematic examination held in 1960s for the lack of order of bone function. Its use

which is not related to medical is to make softer the land where the water is supplied by artificial mean for orange orchard.

A bisphosphonate group has similarity with pyrophosphate's structure and bisphosphonate stop the enzymes that consume in pyrophosphate (Figure 1).

#### Musculoskeletal pain

It produces the Effect upon the bones, muscles, ligaments, tendons, and nerves. It can be harsh or constant (long-lasting). Musculoskeletal pain can be limited to a small area, or prevalent. The common type of pain includes lower vertebrae, muscle pain and strain crack.

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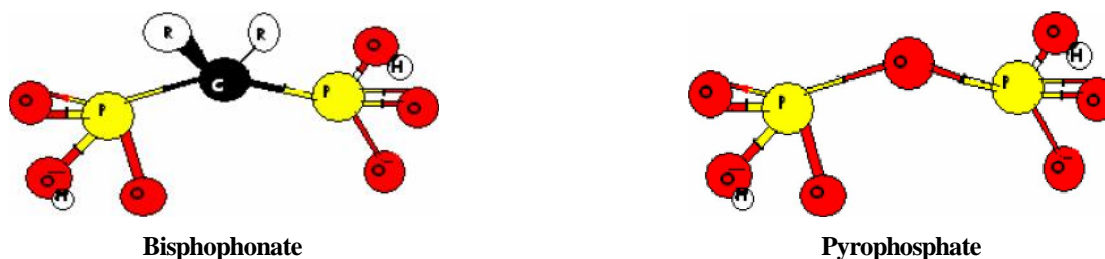


Figure 1 : Structures of bisphosphonate and pyrophosphate

### Symptoms

- 1 Restricted to a small area or widespread pain that can get worse with section
- 2 Painful or rigidity of the complete body
- 3 The response that your muscles have been done when it move forcefully or extra fatigue
- 4 Exhaustion
- 5 Arousing or sleep imperfectly
- 6 Jerk of muscle
- 7 The feeling of 'flaming' in your muscles

### Function of bisphosphonates

According to study of drugs bisphosphonate are a class of drugs. It is also called diphosphonates. It prevents the decrease of bone mass, used to cure the osteoporosis and interrelated diseases<sup>[1]</sup>. Bisphosphonate stop the activity of osteoclast.

### Diseases treated by bisphosphonate therapy

These are the diseases<sup>[2]</sup> which are treated by bisphosphonate therapy.

### Osteopathy

Diseases linked with the effects on the bone frame. There is a major concern by the use of this medicine in kids with osteogenesis imperfecta<sup>[3]</sup>. It comprises bisphosphonate that administer through vein and orally administer bisphosphonates.

### Hypercalcaemia

Hypercalcaemia is an increase calcium level in the blood. Bisphosphonates have been used in children with hypercalcaemia because of the several reason plus immobilization, leukaemia, hyperparathyroidism, subcutaneous fat necrosis<sup>[4]</sup>.

### Calcinosis

Circumstances linked to the soft tissue calcification. It connects to the plane of calcium phosphate crys-

tals and ends their development and coagulates with their ending.

### Features of bisphosphonate therapy

The department of Oncology<sup>[4]</sup> and Hematology in Italy reveals certain aspects of bisphosphonate therapy that for sixty years bisphosphonate has examined for the dealing of bone metastases and it shows the decrease in linked skeletal problems. I.V intake of bisphosphonate is usually secure and well endured with durable use, and the advance of more effective, second- and third-invention bisphosphonate is extremely enhanced the ease.

Bisphosphonate customarily use in bone problems and in breast cancer<sup>[5]</sup> but the advance type of bisphosphonate called Zoledronic acid expands the medical activities of all existing bisphosphonate. It directly effect on reducing the tumor<sup>[6]</sup> and increase the production of osteoblast<sup>[7]</sup>. One study showed that taking parathyroid hormone for one year and then a bisphosphonate for the following year could maintain or build bone density<sup>[8]</sup>. Parathyroid hormone enhances the bone power mainly by stimulating bone formation, whereas antiresorptive drugs reduce bone resorption<sup>[9]</sup>.

### Action of bisphosphonate

The presences of negative charge on two phosphate groups of the bisphosphonate nucleus give this compound increase the attraction for the exterior of bone.

### Inhibition of osteoclast

Bisphosphonate is not organic compound that aggregate to hydroxyapatite in bone and stop the bone breaking cell s and the absorbing of bone take place. They directly have an effect on bone dissolving cells amount and action. Bisphosphonates also work to re-

TABLE 1 : Orally intake bisphosphonate

Pharmaceutical companies	Name of medicine
Proctor & Gamble Pharmaceuticals	Risedronate sodium tablets (Actonel and Actonel + Ca, Proctor)
Merck & Company:-	Etidronate disodium tablets (Didronel) Alendronate sodium tablets (Fosamax and Fosamax + D)
Roche	Ibandronate sodium tablets (Boniva)

TABLE 2 : Injectable bisphosphonate

Novartis Pharmaceuticals Corp	Pamidronate disodium injection (Aredia) Zoledronic acid injection (Reclast and Zometa)
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pair the significant connection between bone damage and construction. Within these cells, they restrain the enzyme farnesyl pyrophosphate synthase<sup>[10]</sup>.

### Stimulation of osteoblast

Increase the manufacture of bone forming cells, which begin to reduce bone period, improved bone mass, and enhanced mineralization<sup>[11]</sup>. This increase in mineral thickness may supply to the greater force of bisphosphonate-treated bone.

### Bisphosphonate for osteoporosis

Orally administer bisphosphonates such as alendronate (Fosamax) in doses used for osteoporosis are not successful in myeloma.

### Efficacy of bisphosphonate

Bisphosphonates like pamidronate used as a given quantity and program are secure and useful. Fast blend can do a chemical swelling at the injection place along the route of the vein. Slower blend may evade this difficulty. Too fast an infusion can also cause low blood calcium. More powerful bisphosphonates could decrease expenditure by limitation the time necessary for administering through vein and by allow the development of other systemized statement that remove the need for administration through vein<sup>[12]</sup>, such as an area or an oral preparation.

In order of efficiency bisphosphonates therapy is the most flourishing treatment choice with a decrease in vertebral breakage of about 30-49%. Moreover Steroid persuade bone loss should be prohibited, and if corticosteroid-induced osteoporosis<sup>[13]</sup> is present it can be treated by bisphosphonate therapy.

## Protection and acceptability of long-run bisphosphonate therapy

Postmenopausal osteoporosis is an unrelieved therapeutic situation that needs long-run treatment<sup>[14]</sup>. The recently manufacture bisphosphonate does not act on bone mineralization, which cause the weakness in bone or lessen bone feature<sup>[15]</sup>. The bisphosphonate diminish formation of a new bone but do not damage minute fracture repairing. The bisphosphonate has negligible nonskeletal poisonous because they attach to bone and not adherent to other tissues. Bisphosphonate are released through glomerular filtration, intravenous administration of large dosages of pamidronate to patients with severe chronic renal failure or patients on dialysis. As bisphosphonate therapy is used in the treatment of severe kidney failure.

Bisphosphonate also has some gastrointestinal side effects<sup>[16]</sup>. Oral bisphosphonate stimulate severe esophagitis in some patients, may result in gastritis and cause diarrhea. Those patients suffering from esophageal disease should restrain from oral bisphosphonate.

### Clinical uses

- 1 Orally administer bisphosphonate in the cure of osteoporosis<sup>[17]</sup>
- 2 The apply of bisphosphonate in the curing of osteoporosis
- 3 Bisphosphonate cures the bone disorder
- 4 Bisphosphonate (bisphosphonate) affect in youth Osteoporosis<sup>[18]</sup>
- 5 Aseptic necrosis of the upper and lower jaw in patients having highly develop cancer cure with Bisphosphonate Therapy<sup>[19]</sup>
- 6 Bisphosphonate in the treatment of throbbing secondary malignant tumor of bone<sup>[6]</sup>
- 7 Bisphosphonate are used for the treatment of other bone diseases such as Paget disease

### Side effects

The more severe side effects related to bisphosphonate in adults such as uveitis, thrombocytopenia, or esophageal or oral ulcerations are rare in newborn. Harsh respiratory pain has happened with create of pamidronate therapy in newborn with a previous time of rash airway disease. In teenager girls, there is panic for possible critical effects on reproduction

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health. The half-life of teenagers and pamidronate is expected in and this agent can be free from bone years after destruction of therapy.

Severe reactions in relation to the direction of oral therapy have been seen with both alendronate and risedronate. GIT upset has been reported with all orally administered bisphosphonate.

The slower healing was noted mostly in children with OI<sup>[20]</sup> who had received bisphosphonates for three or more years.

Bisphosphonate has generally been well accepted in pediatric patients. A severe-phase reaction including fever, malaise, nausea, diarrhea, and muscle or bone pain occurs in the majority children with the beginning of intravenous or oral agents.

Hypocalcaemia, hypophosphatemia, and hypomagnesemia<sup>[21]</sup> have been experimental so to decrease the danger of this deficit, enough vitamin D stores and taking the calcium must be make definite before and all over bisphosphonate treatment ; using a lower early dose of the more strong bisphosphonate, zoledronic acid<sup>[22,23]</sup>, may also be supportive.

Long-term effects are not known. The already stomachache or abdominal pain, which may cause distasteful by orally administer bisphosphonates. It causes kidney problems, heartburn, or esophagitis. It should not be taken by pregnant women<sup>[24]</sup>.

## CONCLUSION

In large scale, bisphosphonates reduce the danger of fractures of the vertebrae, hip, and other bones<sup>[25]</sup>. Bisphosphonate can guard against fast bone loss after leaving HRT. But oral bisphosphonates are not so good it cause many problems. Studies show that bisphosphonates increase bone thickness and density. Bisphosphonate therapy is careful part of schedule medical care in many tertiary pediatric centers for children with reasonable to severe OI<sup>[26]</sup>. Bisphosphonate use in the oral syndrome of osteonecrosis of the jaw (ONJ), where necrotic bone is exposed ONJ is frequently associated with pain and super infection. ONJ patients with cancer receiving bisphosphonate therapy almost 1%-10.

For osteoporosis linked<sup>[27]</sup> with persistent illness, bisphosphonate treatment is suggested only in the set-

ting of clinical trial or as concerned therapy for children with reduction in bone mass/density related with low-trauma extremity fracture and symptomatic vertebral compression.

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