Introduction

Bisphosphonates are a class of drugs capable to work against the osteoclast-mediated bone loss. In link with treatments for malignancy, it has several potential roles like treating hypercalcaemia, as adjunctive therapy to anti-neoplastic treatments such as in multiple myeloma, breast cancers and prostate cancers. Its anti-osteoclastic effects make it an attractive agent against bone mineral density loss in osteoporosis which may occur as a result of treatment against malignancies.

Pharmacology of Bisphosphonates

Bisphosphonates are chemically stable derivatives of inorganic pyrophosphate (PPi), which is a naturally occurring by-product of many body's synthetic reactions (Fig. 1). PPi can inhibit calcification by binding to hydroxyapatite crystals. In addition to the property as like PPi, bisphosphonates is also capable of suppressing bone resorption through the inhibition of hydroxyapatite breakdown.

The potency of bisphosphonates is mainly governed by the structural moiety (in the R2 position) attaching to the central carbon. The presence of nitrogen or amino group (Fig.1C) can increase the antiresorptive potency of bisphosphonate by a factor of 10 to 10,000 relative to the early non–nitrogen-containing bisphosphonate (Fig. 1B)\(^1\).

Fig 1.
Bisphosphonate structures and relative potencies in osteoclast inhibition
(adapted from Matthew T. Drake, Bart L. Clarke, Sundeep Khosla

Treatment for hypercalcaemia of malignancies

Hypercalcaemia is always thought to be an oncological emergency. It happens in around 10-20% of cancer patients along their course of diseases. Hypercalcaemia most commonly occurs in malignant diseases like lung cancer, breast cancer, renal cell carcinoma, head-and-neck cancer, and multiple myeloma, which is thought to be mediated by cellular release of cytokines, parathyroid hormone-related protein, and prostaglandins. The typical symptoms include nausea, cramps, bone pain and even mental changes. If untreated, hypercalcaemia can lead to dehydration and is potentially life threatening. Except in situation of extreme hypercalcaemia requiring calcitonin, patients with hypercalcaemia are usually manageable by hydration and intravenous bisphosphonates. The usual time to reach normalized calcium level is around 4-7 days after bisphosphonate administration.

Bisphosphonates are effective against hypercalcaemia because of its potent inhibition...