BISPHOSPHONATE USE FOR CONTROL OF CHRONIC SEVERE BONE PAIN IN CHILDREN WITH MALIGNANCY ASSOCIATED BONE INVOLVEMENT

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Background: Bone involvement occurs commonly in pediatric malignancies, due to infiltration, metastasis or avascular necrosis. Pain is frequently chronic, debilitating, requires narcotic analgesia and can result in immobilization in bed or wheelchair.

Intravenous bisphosphonates whilst primarily acting as osteoclast inhibitors also result in rapid and often complete pain relief in primary bone fragility disorders. When administered to children with malignant conditions affecting bone, significant improvement in pain, associated morbidity mobilization has been seen.

Objective and hypotheses:

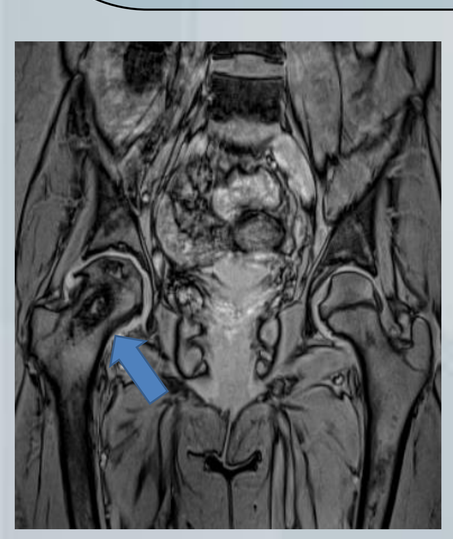
To describe results of use of zoledronic acid for management of bone pain in children with various malignant conditions.

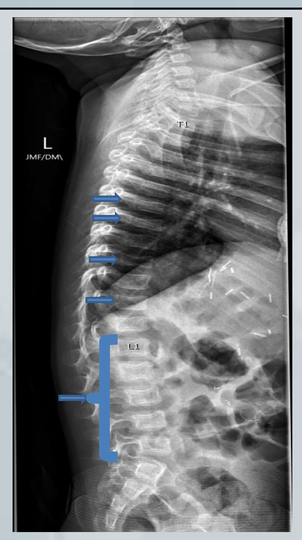
Patients and Methods:

We describe 11 children with chronic bone pain due to acute lymphoblastic leukaemia (ALL)[4], acute myeloblastic leukaemia[3] , metastatic neuroblastoma, rhabdomyosarcoma, hepatoblastoma or rhabdomyosarcoma[4]

Bone involvement:

Glucocorticoid induced avascular necrosis (AVN) related to chemotherapy for haematological malignancies[6] widespread bony metastases from solid tumours[4] multiple vertebral fractures related to ALL[1] but continuing long after remission.





A. B. C.

A. MRI image of Pt 3 showing AVN of right hip. B. Lateral Xray spine image of Pt 8 showing multiple vertebral compression fractures. C. Bone scan image of Pt 9 showing diffuse bony uptake in lumbar vertebrae, pelvis, upper femora

Interventions

intravenous zoledronic acid 0.04mg/kg 4 monthly for 12-24 months

Results:

Complete resolution of pain occurred in all after 1-2 infusions of zoledronic acid. No further analgesia was required. Mobility was restored in all and schooling resumed where appropriate. As previously reported, once bony collapse occurred in AVN, restoration of normal joints was impossible. Hip replacement was needed later in one. Two children died due to progression of their malignancy later.

Table 1: Patient details

Patient no.	Primary diagnosis	Treatment history leading to bone involvement	Bony involvement	Duration of treatment (years)	Outcome
1.	ALL	Corticosteroids as part of chemotherapy	AVN ankle	2	Weaned off analgesia. Has not needed joint replacement
2.	AML	Corticosteroids as part of chemotherapy/ 3 BMT's	AVN hip and Knee/ Multiple vertebral collapse fractures	3	Weaned off analgesia .Has not needed joint replacement.
3.	ALL	Corticosteroids as part of chemotherapy	AVN hip and knee	2	Weaned off analgesia. Needed hip joint replacement.
4.	AML	Corticosteroids as part of chemotherapy/ BMT/ Lung transplant for BO	AVN hips and knees	2	Analgesia weaned. Needed hip replacement
5.	ALL	Corticosteroids as part of chemotherapy	AVN ankle	1.5	Has not needed joint replacement
6. Ben	ALL	Corticosteroids as part of chemotherapy/ BMT	AVN ? site		
7.	APML	Corticosteroids as part of chemotherapy	Vertebral compression fractures	2	Weaned off all analgesics
8.	Hepatoblastoma	Corticosteroids following liver transplant	Vertebral compression fractures	1*	Weaned off all analgesics
9.	Hepatic Rhabdomyosarcoma	EpSSG and UK CCLG Chemo protocol + EBRT	Widespread bone metastasis- pelvis, spine, femur	2	Weaned off all analgesics/ Had extensive disease leading to demise
10.	Neuroblastoma		Widespread bone metastasis- pelvis, spine	2	Weaned off all analgesics
11.	Neuroblastoma		Bony metastasis	2	Weaned off all analgesics/ had disease relapse leading to demise

BMT- Bone marrow transplant, BO- Bronchilotis obliterans, EBRT- Extrenal beam radiotherapy

Conclusion:

Intravenous zoledronic acid administered in the setting of severe chronic bone pain associated with bony metastases, AVN or vertebral collapse in children and adolescents with malignancy results in sustained remission of bone pain, improved mobility and cessation of need for narcotic and other analgesia. This class of drug should be considered for management of malignancy related bone pain in children and adolescents.

1.August KJ, Dalton A, Katzenstein HM, George B, Olson TA, Wasilewski-Masker K, et al. The use of zoledronic acid in pediatric cancer patients. Pediatric blood & cancer. 2011;56(4):610-4.

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Bone & Mineral Metabolism

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