Effect of Intravenous Bisphosphonate Therapy among Boys with Duchenne Muscular Dystrophy and Vertebral Fractures due to Osteoporosis

INTRODUCTION
- Boys with Duchenne Muscular Dystrophy (DMD) can have quality of life-limiting back pain caused by vertebral fractures due to osteoporosis. (Prevalent vertebral fracture rate reported as 32%)
- IV bisphosphonate (BP) therapy can increase bone mass and density, but more importantly improve bone pain, stabilize vertebral fractures, and reshape fractured vertebral bodies in pediatric patients.
- Only one previous report of BP use in DMD using PO alendronate (0.08 mg/kg/day) for 2 years in 16 boys with no change in spine bone mineral density (BMD) after 2 years of treatment.
- The impact of BP therapy on clinically relevant factors beyond BMD, such as vertebral fractures and back pain, has not been documented.

AIM
- To evaluate safety and efficacy of IV BP therapy in the treatment of painful vertebral fractures among boys with DMD

METHODS
- 12 month, retrospective, observational study involving boys with DMD treated for spinal osteoporosis in the Pediatric Bone Health Clinic at CHEO from 2003 to 2009
- Spinal osteoporosis was diagnosed in the presence of two clinical criteria:
  (i) Vertebral Fracture, defined as a 20% loss in height of vertebral body at any time point, or a minimum loss in height of at least 1 vertebral body compared to a prior film
  (ii) Back Pain localized to the site of fracture on palpation
- Treatment was either IV pamidronate (0 mg/kg/year) divided into 3 doses, q 4 months or IV zoledronic acid (0.1 mg/kg/year) divided into 2 doses, q 6 months
- Primary outcomes:
  (i) Back pain: Improved, stable or worse compared to pre-treatment
  (ii) Change in 6-point quantitative vertebral morphometry: Measurement of anterior, middle and posterior heights (AH, MH, PH) to calculate AP, MP and PP ratios. The worst of the 3 ratios ≥ 0.85 (a 15% loss in height) was determined for T4-L4 and categorized as per the Genant scoring system at baseline and 12 months
- A statistically significant change in height ratio from baseline to 12 months was based on the Least Significant Change (LSC), calculated as the Precision error X 3.65 to give 95% confidence
- Existing fracture improved if change exceeded LSC, stabilized if change did not exceed LSC and deteriorated if the change in height loss was ≥ 15% and change exceeded LSC at 12 months
- Secondary outcomes:
  (i) New fractures, defined as a change in height loss ≥ 15% at 12 months in a previously normal vertebral body and changed LSC
  (ii) Change in lumbar spine BMD
  (iii) Clinical side effects

RESULTS: BASELINE

- Site and Severity of the 27 Vertebral Fractures at Baseline

- Examples of Vertebral Fracture Severity

RESULTS: 12 MONTHS

- Evolution of vertebral fractures based on statistically significant changes

- Example of a re-shaping vertebral body

SUMMARY
- In boys with spinal osteoporosis and DMD, IV BP therapy administered over 12 months was associated with improvements not only in spine BMD, but also in the more clinically relevant back pain and vertebral morphology
- Therapy was generally well-tolerated

CONCLUSIONS
- This pilot study supports the use of IV BP therapy on compassionate grounds for boys with DMD and symptomatic vertebral fractures
- Provides background data for the development of larger BP trials in this population
- Contributes to the development of methodology for quantifying vertebral changes in growing patients undergoing osteoporosis therapy

REFERENCES