Bisphosphonates for the management of children/youth with cerebral palsy at risk of osteoporosis: A systematic review and meta-analysis using GRADE

Preliminary Findings

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Bisphosphonates may improve Bone Mineral Density (BMD) and reduce fracture rate among children and young people with CP and at risk of osteoporosis

Introduction

- **Cerebral palsy (CP)** is the most common motor disability in childhood, and can have various clinical impacts including low bone mineral density (BMD).[1]
- Although often asymptomatic, low BMD can result in painful fragility fractures.

Evidence for Bisphosphonate use[2]

'**Probably effective**' at improving BMD

'**Possibly effective**' at reducing fragility fractures

This review will establish the current level of evidence using the Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) approach for bisphosphonates for the treatment of low BMD in CP

Research Question

The systematic review will address the following question: among **children and young people with CP** and at risk of osteoporosis, what is the effect of **bisphosphonates**, compared to usual care, on **BMD and fracture rate**, at least one year following initiation of treatment?

Methods

Study Design: Systematic Review & Meta-analysis
Databases Searched: Ovid MEDLINE, CINAHL, AMED, Embase, Cochrane Reviews, ECM reviews, and clinical trial registries

Inclusion Criteria

- **Minimum 10 Participants**
- **Report BMD/BMC or fracture rate**
- **Randomized or non-randomized studies**
- **≤18 years old**

- The GRADE approach was used to evaluate the certainty of evidence
- Where applicable, meta-analyses were conducted, and forest plots were generated
- The threshold for meaningful clinical BMD improvement was an increase of 1 standard deviation of Z-scores[3,4]
- The threshold for meaningful clinical fracture rate improvement was a 15% decrease in fracture frequency[5]

Preliminary Results

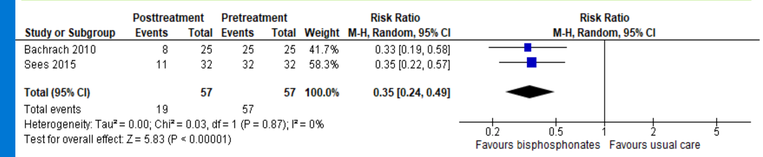
640 Studies Identified for Screening → 11 studies included from prior reviews → 3 new studies included

GRADE evidence certainty was **very low**, due to the limitations of an observational study design

Table 1. Random effects meta-analysis pre- and post-bisphosphonates, > 12 months following initiation of treatment

Region	Total Participants	Mean Difference (MD)	95% CI
Lumbar BMD	50	1.77	1.31-2.23
Femoral BMD	17	1.26	0.43-2.10

Figure 1. Forest plot of random effects meta-analysis for **Fracture rate** pre- and post-bisphosphonates, follow-up: 2 to 6.1 years



Conclusions

As the mean difference (MD) is greater than the clinical threshold, bisphosphonates, compared to usual care, may improve **lumbar and femoral BMD**, at least 12 months after initiation of treatment (GRADE very low certainty).

The 65% relative risk reduction in fracture rate exceeds the clinical threshold of 15%. Bisphosphonates, compared to usual care, may reduce **fracture rate** over a follow-up period greater than 2 years (GRADE very low certainty).

Relevance to Holland Bloorview Clients & Families

The evidence from this systematic review will inform an updated clinical practice guideline and care pathway, to help clients, families and clinicians choose a management option for low BMD in cerebral palsy.

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References

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