BISPHOSPHONATES FOR FRACTURE PREVENTION IN MALES – A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background
• The prevalence of osteoporosis and osteopenia is about 0.8 million and 11.8 million, respectively, in men older than 50 years.1
• About 13-22 percent of men develop at least one osteoporotic fracture during their lifetime.2
• The risk of hip fracture by age and bone mineral density (BMD) is similar in men and women; however, hip fracture poses a higher mortality risk in men.3
• In men with low BMD and at risk of fracture, less than 10% received treatment for osteoporosis.4

This supports the use of bisphosphonates in males at risk for fracture.

There is a lack of randomized controlled trials (RCTs) to confirm the efficacy of bisphosphonates for fracture prevention in males.

Objectives
• Objective of this systematic review and meta-analysis is to assess the efficacy of bisphosphonate therapy in the prevention of vertebral and non-vertebral fractures in males at risk for fracture receiving these agents compared to placebo.

Methods

Database Search
• MEDLINE/PubMed, The Cochrane Central Register of Controlled Trials in the Cochrane Library, Scopus, Clinicaltrials.gov, and EMBASE without language restriction

Selection Criteria
• Types of studies: RCTs with duration of at least one year
• Participants: Adult male participants at risk for fracture. RCTs that included both men and women that reported the number of males were also included.
• Intervention: Bisphosphonates at the FDA approved doses: Alendronate 70mg daily or 3mg weekly, Risedronate 35mg weekly, Ibandronate 2.5mg or 15mg once monthly or (3mg/weekly). Zoledronic acid 4 or 5mg/weekly (IV); Ibandronate 150mg IV weekly.
• Comparator: No treatment (placebo or calcium and/or vitamin D)

Outcomes: The number of fractures (clinical vertebral, morphometric vertebral, non-vertebral, hip, or any fracture) at the end of study duration

Data Extraction and Management
• Data Extraction: (1) study characteristics including (study design, publication year, study location, study duration, intervention, dosage, study quality, and funding source); (2) baseline patient characteristics (number of patients, age, male proportion, body mass index (BMI), T-score at lumbar spine, femoral neck, and total hip sites, were included for each study as calculated.
• Data were pooled using both fixed effects and random effects models.
• Statistical heterogeneity was assessed using a chi-squared test with significance set at a p-value of 0.10 and the I2 test with substantial significance set at a p-value of 0.05.
• Publication bias was examined using funnel plots and Egger’s test.
• Statistical heterogeneity was assessed using a chi-squared test with significance set at a p-value of 0.10 and the I2 test with substantial significance set at a p-value of 0.05.

Assessment of Study Quality: Potential sources of bias including
• Study design
• Comparator: No treatment (placebo or calcium and/or vitamin D)
• Participants: Adult male participants at risk for fracture. RCTs that included both men and women that reported the number of males were also included.
• Intervention: Bisphosphonates at the FDA approved doses: Alendronate 70mg daily or 3mg weekly, Risedronate 35mg weekly, Ibandronate 2.5mg or 15mg once monthly or (3mg/weekly). Zoledronic acid 4 or 5mg/weekly (IV); Ibandronate 150mg IV weekly.

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Results

• 40 studies were included in this meta-analysis; 19 of them reported fracture outcomes for males.
• Bisphosphonates had significant effects on reducing the risk of any fractures (Total population: RR=0.45, 95%CI=0.32-0.63; Male population: RR=0.40, 95%CI=0.22-0.73).
• There was very little evidence of heterogeneity (Total population: I2=0%, Male population: I2=11.9%-15.3%). No differences were found for fixed effects model and random effects model.
• A visual inspection of the funnel plots and the Egger’s tests (Total population: p=0.19; Male population: p=0.69) indicated no evidence of publication bias.
• Meta-regression showed that male proportion, age, BMI, BMD T-score at lumbar spine, femoral neck, and total hip sites, were unrelated to the effect size of bisphosphonates on fracture outcomes.

Conclusions
• Bisphosphonates significantly reduced the risk of any fracture and morphometric vertebral fractures, and the effect was consistent across studies with varying proportions of male patients.
• Bisphosphonates significantly reduce the risk of non-vertebral fracture risk at 12 months, which is earlier than currently believed.
• This supports the use of bisphosphonates in males at risk for fracture.

Limitations
• We only included articles published in peer-reviewed journals.
• The studies had very different patient populations and heterogeneity may be present even if studies were matched.
• There is a lack of consistent definitions for fracture outcomes in the included studies, particular non-vertebral fractures.
• Patient-level data are needed to confirm if treatment with bisphosphonates may be beneficial to men with osteopenia.

References