Cochrane Database of Systematic Reviews - - Cochrane Review

Bisphosphonates for osteoporosis in people with cystic fibrosis

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Study design (if review, criteria of inclusion for studies)

Randomised controlled trials of at least six months duration studying bisphosphonates in people with CF.

List of included studies (9)

Aris 2000; Aris 2004; Boyle 2005; Chapman 2009; Haworth 2001; Haworth 2010; Papaioannou 2008

Participants

People of all ages and of both sexes with CF diagnosed clinically or by sweat and genetic testing, including all degrees of disease severity and bone density.

Interventions

Bisphosphonates

Outcome measures

Bone pain; Fever; Non-vertebral fractures; Percent change in BMD, distal radius, SXA (End of study); Percent change in BMD, distal radius, SXA (Time-points); Percent change in BMD, femur, DXA; Percent change in BMD, lumbar spine, DXA; Percent change in BMD, lumbar spine, DXA (End of study); Percent change in BMD, lumbar spine, DXA (Time-points); Percent change in BMD, total hip / femur, DXA (Time-points); Percent change in BMD, total hip/femur, DXA (End of study); Percent change in BMD, ultradistal radius, SXA; Survival; Total Fractures; Vertebral fractures; Withdrawals, due to adverse events; Withdrawals, total

Main results

Nine trials with a total of 385 participants (272 adults and 113 children (aged five to 18 years)). Trial durations ranged from six months to two years. Only two of the studies were considered to have a low risk of bias for all the domains. Bisphosphonates compared to control in people with cystic fibrosis who have not had a lung transplant Seven trials included only adult participants without lung transplants, one trial included both adults and children without lung transplantation (total of 238 adults and 113 children). Authors analysed adults (n = 238) and children (n = 113) separately. Adults Three trials assessed intravenous bisphosphonates (one assessed pamidronate and two assessed zoledronate) and five trials assessed oral bisphosphonates (one assessed risedronate and four assessed alendronate). Bisphosphonates were compared to either placebo or calcium (with or without additional vitamin D). Data showed no difference between treatment or control groups in new vertebral fractures at 12 months (odds ratio (OR) 0.22, 95% confidence interval (CI) 0.02 to 2.09; 5 trials, 142 participants; very lowâ€•certainty evidence) and two trials (44 participants) reported no vertebral fractures at 24 months. There was no difference in nonâ€•vertebral fractures at 12 months (OR 2.11, 95% CI 0.18 to 25.35; 4 trials, 95 participants; very lowâ€•certainty evidence) and again two trials (44 participants) reported no nonâ€•vertebral fractures at 24 months. There was no difference in total fractures between groups at 12 months (OR 0.57, 95% CI 0.13 to 2.50; 5 trials, 142 participants) and no fractures were reported in two trials (44 participants) at 24 months. At 12 months, bisphosphonates may increase bone mineral density at the lumbar spine (mean difference (MD) 6.31, 95% CI 5.39 to 7.22; 6 trials, 171 participants; lowâ€•certainty evidence) and at the hip or femur (MD 4.41, 95% 3.44 to 5.37; 5 trials, 155 participants; lowâ€•certainty evidence). There was no clear difference in quality of life scores at 12 months (1 trial, 47 participants; lowâ€•certainty evidence), but bisphosphonates probably led to more adverse events (bone pain) at 12 months (OR 8.49, 95% CI 3.20 to 22.56; 7 trials, 206 participants; moderateâ€•certainty evidence). Children The single trial in 113 children compared oral alendronate to placebo. All evidence: low certainty. At 12 months, no difference between treatment and placebo in new vertebral fractures (OR 0.32, 95% CI 0.03 to 3.13; 1 trial, 113 participants) and nonâ€•vertebral fractures (OR 0.19, 95% CI 0.01 to 4.04; 1 trial, 113 participants). There was also no difference in total fractures (OR 0.18, 95% CI 0.02 to 1.61; 1 trial, 113 participants). Bisphosphonates may increase bone mineral density at the lumbar spine at 12 months (MD 14.50, 95% CI 12.91 to 16.09). There was no difference in bone or muscle pain (MD 3.00, 95% CI 0.12 to 75.22), fever (MD 3.00, 95% CI 0.12 to 75.22) or gastrointestinal adverse events (OR 0.67, 95% CI 0.20 to 2.26). The trial did not measure bone mineral density at the hip/femur or report on quality of life. Bisphosphonates compared to control in people with cystic fibrosis who have had a lung transplant One trial of 34 adults who had undergone lung transplantation compared intravenous pamidronate to no bisphosphonate treatment. It did not report at 12 months and authors report the 24â€•month data (not assessed by GRADE). There was no difference in the number of fractures, either vertebral or nonâ€•vertebral. However, bone mineral density increased with treatment at the lumbar spine (MD 6.20, 95% CI 4.28 to 8.12) and femur (MD 7.90, 95% CI 5.78 to 10.02). No participants in either group reported either bone pain or fever. The trial did not measure quality of life.

Authors' conclusions

Oral and intravenous bisphosphonates may increase bone mineral density in people with cystic fibrosis, but there are insufficient data to determine whether treatment reduces fractures. Severe bone pain and fluâ€•like symptoms may occur with intravenous bisphosphonates. Before any firm conclusions can be drawn, trials in larger populations, including children, and of longer duration are needed to determine effects on fracture rate and survival. Additional trials are needed to determine if bone pain is more common or severe (or both) with the more potent zoledronate and if corticosteroids can ameliorate or prevent these adverse events. Future trials should also assess gastrointestinal adverse effects associated with oral bisphosphonates.

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See also

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Keywords

Adult; Bisphosphonates; Bone Density Conservation Agents; Bone Diseases; Osteoporosis; pharmacological_intervention; transplantation;