BISPHOSPHONATES FOR OSTEOPOROSIS IN PEOPLE WITH CYSTIC FIBROSIS

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ABSTRACT

Background
Osteoporosis is a disorder of bone mineralization that can lead to reduced bone mineral density and an increased risk for fractures. It is found in about one third of adults with cystic fibrosis. Bisphosphonates have been shown to increase bone mineral density and decrease the risk of new fractures in post-menopausal women and in people receiving long-term oral corticosteroids.

Objectives
To assess the effects of bisphosphonates on the frequency of fractures, bone mineral density, quality of life, adverse events, study withdrawals, and survival in people with cystic fibrosis.

Search Strategy
We identified relevant trials from the Cochrane Cystic Fibrosis and Genetic Disorders Review Group register of controlled trials. This register comprises references identified from comprehensive electronic database searches, handsearching of relevant journals and of conference proceedings. Additional sources such as abstract books for osteoporosis conferences were handsearched by the authors.

Date of the most recent search of the Group's specialised register: April 2002.

Selection Criteria
Randomised controlled trials of at least six months duration that studied the use of bisphosphonates in adults with cystic fibrosis were considered for inclusion. Outcomes included one of the following: fractures, bone mineral density, quality of life, adverse events, study withdrawals, or survival.

Data collection and analysis
Information on study design, participants, interventions, and outcomes was abstracted from included studies. Two independent reviewers abstracted the information. Authors were contacted to obtain missing data.

Main Results
Two trials were identified in the trials search. Both trials with a total of 65 participants were included in this review. One study examined participants without lung transplant while the other study included only participants who had received a lung transplant. The intervention in both trials was pamidronate administered intravenously every three months.

In participants who had not received a lung transplant, bone mineral density at axial sites was increased after six months of treatment in the treatment group compared to the control group (lumbar spine weighted mean difference (WMD) [for % bone mineral density] was -5.80 (95% CI -8.69 to -2.91), hip WMD -3.00 (95% CI -5.40 to -0.60)). There was a small decrease in forearm bone mineral density in participants treated with pamidronate versus controls (distal forearm WMD 1.70 (95% CI -0.26 to 3.66)). Bone pain was the most common adverse event occurring in 11 out of 15 participants not using corticosteroids, relative risk (RR) 24.44 (95% CI 1.57 to 381.48). There was no significant difference in survival, RR 1.00 (95% CI 0.83 to 1.20), although this may be due to short follow-up and small sample size.

In participants who had received a lung transplant, the number of new fractures did not change with the use of pamidronate (non-vertebral RR 0.56 (95% CI 0.17 to 1.89), vertebral RR 3.38 (95% CI 0.39 to

29.29)). Bone mineral density at axial sites was increased after two years of treatment in the treatment group compared to the control group (lumbar spine WMD [for % change in bone mineral density] -6.20 (95% CI -8.12 to -4.28), femur WMD -7.90 (95% CI -10.02 to -5.78)).

Reviewers' conclusions

Intravenous pamidronate increases bone mineral density at axial sites in people with cystic fibrosis, although it can cause severe bone pain in participants not receiving corticosteroids. Additional studies in larger populations are needed to determine the effect on fracture rate and survival.

This review should be cited as:
Brenckmann C, Papaioannou A Bisphosphonates for osteoporosis in people with cystic fibrosis (Cochrane Review). In: *The Cochrane Library*, Issue 3, 2003. Oxford: Update Software.

BACKGROUND

Cystic fibrosis (CF) has been recognised as a unique disorder for approximately 60 years, and is the most common serious autosomal recessive genetic disorder in the Caucasian population. CF is estimated to occur in around one in 2,500 live births; around one in 25 individuals carry the defective gene (Yankaskas 1999). The major components of CF are lung disease and pancreatic insufficiency. In the past, only one third of individuals with CF lived to the age of 18 (Yankaskas 1999), although recent advances in medical science and technology have increased the life expectancy of people with CF into the third and fourth decades of life. Long-term sequelae of the disease, such as osteoporosis, liver disease, and diabetes mellitus, are now becoming apparent.

Osteoporosis is a disorder of bone mineralization that decreases bone mineral density (BMD) and makes bones brittle and more susceptible to fracture. Osteopenia refers to a milder degree of bone demineralization. Bone density is currently measured using dual-energy x-ray absorptiometry (DEXA), which measures absolute bone density in gm/cm2 and compares it to a population mean. BMD is expressed as standard deviations from the population mean, either as a z-score (compared to age- and sex-matched data) or a t-score (compared to the healthy young adult mean for the participant's sex). The World Health Organization (WHO) classifies osteopenia as a t-score of between -1 and -2.5, and osteoporosis as a t-score of -2.5 or less (Kanis 1994). This definition is currently being revised since BMD is only one of the factors that determine the risk of fracture. It is osteoporotic fractures which account for the morbidity and mortality associated with osteoporosis (Cummings 1995).

Bisphosphonates (e.g. etidronate, alendronate, pamidronate) are currently considered the most efficacious pharmacological treatment available to treat postmenopausal and corticosteroid-induced osteoporosis. A two-year study of intermittent cyclical etidronate in 423 postmenopausal women demonstrated a significant increase in BMD at the spine and a decrease in new fractures (Watts 1990). In a study of 2027 women with at least one existing vertebral fracture (Black 1996) alendronate was shown to increase BMD at the spine and hip and to decrease fractures at the hip, wrist and spine after three years of treatment. Another study in 477 participants with glucocorticoid-induced osteoporosis found alendronate to be highly effective in increasing BMD at the spine and femoral neck, with a significant reduction in the number of incident fractures (Saag 1998). This evidence is particularly promising since corticosteroid use is associated with osteoporosis among people with CF.

Pamidronate in combination with calcium was studied over an 18 month period in an initial cohort of 35 postmenopausal women (mean age 64.5 years) with at least one atraumatic vertebral fracture due to osteoporosis. BMD increased after one year ($p<0.001$) in the lumbar spine although there were no changes in the femoral neck (Fromm 1991). A two year open study compared pamidronate with fluoride for the treatment of postmenopausal osteoporosis in 32 osteoporotic women (mean age 65 years). Pamidronate was administered intravenously every three months, and calcium and vitamin D were provided to both groups. Lumbar spine BMD increased significantly in both groups at 24 months, however, only increased in the femoral neck and radius in the pamidronate group (Thiebaud 1994). A three year randomized double-blind trial of 300 mg oral pamidronate daily compared with placebo was conducted in 105 participants with rheumatoid arthritis. After three years, lumbar spine and forearm BMD had increased significantly in the pamidronate-treated group while there were non-significant changes in the placebo-treated group. Changes

long-term treatment with oral bisphosphonates overcomes bone loss and increases bone mass when compared with placebo (Eggelmeijer 1996). Another one year study compared two regimens of intravenous pamidronate (a single infusion or once every three months) for the primary prevention of glucocorticoid-induced osteoporosis. The study population consisted of 32 participants who required long-term glucocorticoid therapy with at least 10 mg of prednisone daily. A highly significant difference was observed between both pamidronate regimens and the control group at the lumbar spine ($p<0.001$) and femoral neck ($p<0.01$). Both pamidronate regimens effectively achieved primary prevention of glucocorticoid-induced osteoporosis (Boutsen 2001).

A longitudinal study of 151 adult participants with CF aged 15 to 52 showed that 34% of participants had a z-score of -2 or less (DEXA)(Haworth 2001). Z-score definitions of osteopenia and osteoporosis vary between studies. A study in post-lung transplant participants with CF (Aris 1998) found around a two-fold increase in the risk of non-vertebral fractures for women aged 16 to 34 ($p=0.015$) and men aged 25 to 45 ($p=0.04$) compared with the general population. Vertebral compression and rib fractures were respectively 100- and 10-fold more common than predicted ($p < 0.001$). Incident new vertebral fractures are commonly defined as a 15% or greater reduction in anterior, posterior, or middle vertebral height. The etiology of osteoporosis in people with CF remains unknown, although chronic lung inflammation (Aris 2000a), vitamin D malabsorption, use of oral corticosteroids, and hypogonadism are thought to be associated. Although osteoporosis drugs are effective in other populations such as postmenopausal women, there is no standard clinical practice for the treatment of CF-related osteoporosis.

OBJECTIVES

To determine whether bisphosphonates cause the following changes in adults with CF:

(1) Decrease fractures (vertebral and non-vertebral).
(2) Improve BMD measured using DEXA or, if available, using other methods of bone density measurement such as single energy x-ray absorptiometry (SXA) and quantitative tomography (QCT).
(3) Increase quality of life.
(4) Increase adverse events, including bone pain and gastrointestinal adverse events.
(5) Change the number of withdrawals due to all causes and due to adverse events.
(6) Increase survival.

CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW

Types of studies

Randomised controlled trials. Published papers and abstracts will be included. Studies published in all languages were considered for inclusion.

Types of participants

Patients 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.

Types of intervention

All studies examining bisphosphonates for treating or preventing osteoporosis in people with CF were considered for inclusion. All doses and routes of administration were considered. Studies of a minimum of six months were included.

Types of outcome measures

(1) Fractures: number of participants and number of fractures at all sites, hip, spine, wrist
(2) Bone density as measured by dual-energy x-ray absorptiometry (DEXA): lumbar spine, total hip, femoral neck, total body; reported as percentage change from baseline. Data reported using other methods of bone density measurement such as single energy x-ray absorptiometry (SXA) and quantitative tomography (QCT) would be used if available but analysed separately
(3) Quality of life
(4) Adverse events such as bone pain and gastrointestinal adverse events (number of participants, number of adverse events)

(5) Total withdrawals and withdrawals due to adverse events
(6) Survival

SEARCH STRATEGY FOR IDENTIFICATION OF STUDIES

See: Cochrane Cystic Fibrosis and Genetic Disorders Group search strategy

Relevant trials were identified in the Cochrane CF and Genetic Disorders Review Group (CRG) register of controlled trials by the centre co-ordinator. This register was compiled by conducting computerised searches of MEDLINE from 1966 to present and EMBASE from 1974 to 1995 using the search strategy described in detail in module of the Cochrane CF and Genetic Disorders Group. The register of randomised, controlled trials is updated every three months. Unpublished work has been identified by searching through the abstract books of the three major CF conferences: the International CF conference, the European CF conference, and the North American CF conference.

The following terms were used in the search of the Group's trials register:
Osteroporosis
Pamidronate.

Other sources not covered by the CRG search strategy such as abstracts from a major osteoporosis conference (ASBMR-IBMS 2nd Joint Meeting 1998; ASBMR 21st Annual Meeting 1999) and references lists from retrieved articles were searched using the strategies described in the Cochrane Handbook, Section V, Appendix 2.

Date of the most recent search of the Group's specialised register: April 2002.

METHODS OF THE REVIEW

Two reviewers (CB, AP) independently reviewed the studies to assess which trials should be included. The two reviewers also independently assessed the quality of the studies using the system as described by Jadad (Jadad 1996). If there was disagreement about either whether a trial should be included, or the quality score it should receive, an independent reviewer from a third centre was asked to review the paper(s) in question. The reasons for excluding any trial were documented. Data were extracted independently by each reviewer for the outcome measures listed below. First authors of the included trials were contacted to verify their data and obtain unpublished data where necessary. Cochrane Review Manager version 4.1.1 was used to compile and analyse the data. The authors compared their data and resolved differences by referring to the original article. Any remaining differences were resolved by a third individual.

The relative risk was calculated for all binary outcome measures (adverse events, fractures, survival). The weighted mean difference between the treatment and control groups was calculated for the percent changes from baseline in BMD and laboratory values.

Separate analyses were conducted for participants who had received a lung transplant and for those who had not. At this stage, the number of people with CF who have received other organ transplants is small. Therefore, individuals with other organ transplants were included in the analysis of participants with a lung transplant, since they share a common risk factor for osteoporosis - long-term use of immunosuppressive agents which lower BMD.

DESCRIPTION OF STUDIES

Two clinical trials, both published in the English language, were identified by the trials search. Both trials met the inclusion criteria for this review (Aris 2000b; Haworth 2001). The trials were each published in two abstracts and in a journal article. Both studies had similar study designs, dose and duration of intervention, outcome measures, and study size. One study (Aris 2000b) was conducted in 34 post-transplant adult participants with CF while the second study (Haworth 2001) studied 31 non-transplanted adult participants with CF. Neither study reported sample size or power calculations. The difference in study population and

concomitant general health, activity levels and medications (prednisone, cyclosporin A, azathioprine in the transplant group) will contribute to heterogeneity in the results of this review.

Funding for one trial (Aris 2000b) was provided by grants from the CF Foundation and the Verne S. Caviness General Center for Clinical Research while Haworth and his colleagues received funding from the CF Trust in the UK (Haworth 2001).

Please refer to the Table of Included Studies for additional details.

METHODOLOGICAL QUALITY

One reviewer (AP) was blinded to the authors of the studies. The Jadad scale was applied to both studies (Jadad 1996).

Treatment allocation in one study (Aris 2000b) was unblinded and in the second study (Haworth 2001) was not mentioned; thus both studies received a score of zero for allocation concealment on the Jadad scale. In one study, the authors reported that although the study was unblinded, the radiologist who interpreted the DEXA scans was unaware of the participant's treatment allocation (Aris 2000b). The authors also mentioned that the risk:benefit ratio of using sham injections was not sufficient to justify a double-blind design. No data on whether sham injections were used was reported in the other study (Haworth 2001).

One paper (Aris 2000b) stated that participants were stratified on the basis of gender and the severity of osteoporosis (study definition of osteoporosis was a spine z-score of -3.0; WHO guidelines (Kanis 1994) state that z-scores of -2.5 and below indicate osteoporosis) and then randomised in a "blocks of four" design. This study received a score of two on the Jadad randomisation criteria. The other paper (Haworth 2001) reported randomisation but did not report the methods and thus received a score of one.

Both studies reported complete follow-up and thus received a score of one.

Given the available published information on study design, one study received a score of three out of five (Aris 2000b) and the other a score of two out of five (Haworth 2001).

RESULTS

TRIAL OF PARTICIPANTS WHO HAVE NOT RECEIVED LUNG TRANSPLANT (Haworth 2001)

Fractures
No fractures were reported.

Percent Change in BMD
After six months, participants in the control group had lost BMD and participants receiving pamidronate had gained BMD at the lumbar spine (weighted mean difference (WMD) [for % change BMD] -5.80 (95% CI -8.69 to -2.91) and hip (WMD -3.00 (95% CI -5.40 to -0.60). Measurements of appendicular sites showed opposite trends: there was a non-significant decrease in BMD as measured by SXA of the distal forearm, WMD 1.70 (95% CI -0.26 to 3.66) and ultradistal forearm, WMD 2.70 (95% CI -0.19 to 5.59) in participants receiving pamidronate. Note that the BMD data used in this review are the final measurements taken in the study rather than an average of all measurements taken during the study.

Quality of Life
No quality of life measurements were reported.

Adverse Events
No participants in the control group experienced bone pain but 11 out of 15 participants in the treatment group experienced moderate to severe pain following the first dose of medication, relative risk (RR) 24.44 (95% CI 1.57 to 381.48). Nine participants reported severe bone pain. The pain was reported to be excruciating in seven participants rendering them bed bound and making sputum expectoration and

three of the four participants without bone pain in the treatment group did. Two of the nine participants also had febrile reactions and one developed phlebitis around the infusion site.

Withdrawals
There was no significant difference between treatment and control groups with respect to total withdrawals (2 out of 15 pamidronate, 1 out of 16 control), RR 2.13 (95% CI 0.22 to 21.17). One participant from each group died while the second participant in the pamidronate group withdrew in order to receive a double lung transplant. No participants withdrew due to adverse events.

Survival
Pamidronate did not significantly affect survival compared with the control group (1 out of 15 pamidronate, 1 out of 16 control), RR = 1.00 (95% CI 0.83 to 1.20).

TRIAL OF PARTICIPANTS WHO HAVE RECEIVED LUNG TRANSPLANT (Aris 2000b)

New Fractures
There was no statistically significant difference in the number of participants with new vertebral fractures for treated (3 out of 16) versus untreated (1 out of 18) participants, RR 3.38 (95% CI 0.39 to 29.29). There was also no statistically significant difference in the number of participants with new non-vertebral fractures in treated (3 out of 16) versus untreated (6 out of 18) participants, RR 0.56 (95% CI 0.17 to 1.89).

Percent Change in BMD
At the end of two years, the percentage change in BMD was significantly higher in the treatment group than in the control group at the lumbar spine, WMD [for % change in BMD] -6.20 (95% CI -8.12 to -4.28) and at the femur the WMD was -7.90 (95% CI -10.02 to -5.78).

Quality of Life
No quality of life measurements were reported.

Adverse Events
None of these participants, all of whom were receiving corticosteroids, experienced any bone pain. Participants were assessed 24 hours post-infusion for cellulitis, thrombophlebitis, or fever; no cases were detected. Twenty-four hours later, serum calcium, phosphorus, and magnesium and a complete blood count were analyzed. There were no significant differences compared with preinfusion data, with no episodes of hypocalcemia and three episodes of mild hypervitaminosis D that resolved spontaneously. The study in post-transplant participants found no significant difference in the degree of immunosuppression between the treatment and control groups.

Withdrawals
There were no withdrawals other than those due to death in either treatment arm.

Survival
Three participants died before the first BMD data could be collected at six months; these participants were excluded from further analysis and thus cannot be included as data in this review. The authors stated that the exclusion of these three participants did not significantly affect the subsequent analysis. No other participants died during the course of the study.

DISCUSSION

Based on data from two small studies, intravenous pamidronate increased axial BMD in people with cystic fibrosis. Participants who did not receive corticosteroids during the clinical trial were more likely to experience bone pain. There was no significant effect of treatment on fractures, withdrawals or survival. It was not possible to evaluate changes in quality of life since neither study measured this variable. It should be noted that BMD is only an intermediate outcome and that a more clinically important endpoint is the occurrence of new fractures.

These two studies provide valuable data on two different patient populations - people with CF who have received a transplant and those who have not. Although the duration of follow-up and the magnitude of effect

were different for the two studies, similar trends were seen for all treatment effects except bone pain, suggesting that the beneficial effects of intravenous pamidronate might be generalizable to a fairly broad population of people living with CF.

One trial (Aris 2000b) was not blinded while the Haworth study (Haworth 2001) did not state whether blinding was used. When participants are aware of the treatment they are receiving, they may be more or less likely to report adverse events. The judgment of individuals who collect and interpret patient data may be affected when the assessor is aware of the treatment a participant is receiving. Lack of blinding may result in biased results. No significant differences in the rate of vertebral and non-vertebral fractures (Aris 2000b) or survival (Aris 2000b; Haworth 2001) could be expected due to the small numbers of participants involved and the short duration of the studies.

The observed relationship between the use of oral glucocorticoid therapy and lack of bone pain may be explained by evidence that corticosteroids suppress the release of TNF-alpha (Steer 1997), an inflammatory cytokine known to increase bone resorption. Haworth and his colleagues suggest that bone pain may be avoided by prescribing a short course of oral corticosteroids before and at the time of pamidronate infusion (Haworth 2001).

REVIEWER'S CONCLUSIONS

Implications for practice

Based on two small studies, intravenous pamidronate causes a rapid increase in spine, hip, and femoral BMD and a statistically non-significant decrease in forearm BMD. Severe bone pain is common with the use of intravenous pamidronate in participants with CF not receiving oral corticosteroids. Currently, no other options for the treatment of CF-related osteoporosis have been reported in the public domain. No recommendation can be made concerning the use of bisphosphonates in participants with CF on the basis of this review.

Implications for research

This area of research would benefit from a large multicentre RCT of intravenous pamidronate or other bisphosphonates with separate analyses for participants with and without transplantation to measure the effectiveness of these therapies on outcomes important to people with CF, such as fractures. Data on bone pain and use of corticosteroids should also be recorded.

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POTENTIAL CONFLICT OF INTEREST

None known

TABLES

Characteristics of included studies

Study	Aris 2000b
Methods	Randomized controlled trial, parallel, two years, n=34 (16 treatment); stratified on basis of gender and severity of osteoporosis using spine z-score of -3.0, randomised in a "blocks of four" design
Participants	CF; 1 to 12 months post-lung transplantation; ambulatory; excluded if had primary graft failure or other post-operative morbidities that precluded long-term survival, renal insufficiency (serum creatinine > 3.0 mg/dl), or pregnancy; mean[SD] age 27.5[6.6] treatment, 29.1 [6.4] control; 16 female; consent obtained; groups similar in age, gender, baseline t-scores, renal function, hospitalization rates, immunosuppressant levels, change in lung function and body mass index over study period; 13 treatment and 12 controls had baseline t < -2.5 at minimum one site; all others 0 < t < -2.5 at minimum one site
Interventions	Intravenous pamidronate 30 mg every three months; all patients received 1 gm oral calcium and 800 IU vitamin D daily
Outcomes	new fractures (# fractures, long bone using clinical data, rib using posteroanterior chest radiographs, vertebral using lateral chest radiographs), BMD (spine, femur; 6, 12, 18, 24 months; Hologic QDR 1000/W), adverse events, compliance determined by patient interview, serum and urine biochemistry, kyphosis angles
Notes	44 patients eligibile, seven died before study, three died during first six months of study; final analysis included 34 patients
Allocation concealment	D
Study	**Haworth 2001**
Methods	Randomized controlled trial, parallel, six months, n=31 (15 treatment)
Participants	CF; no organ transplantation; mean[SD] age 26.1[5.8]; nine female; 70% of all eligible participants in a longitudinal study recruited after one year of follow-up; inclusion criteria of BMD z-score of < or=-2 at lumbar spine, proximal femur or distal forearm; three patients (two treatment) withdrew; consent obtained; groups similar with respect to age, gender, initial BMD, bone biochemistry, respiratory disease severity
Interventions	Intravenous pamidronate 30 mg every three months; all patients received 1 gm calcium; patients with pancreatic insufficiency received 900 IU vitamin D daily
Outcomes	BMD (lumbar spine, total hip, femur [DEXA]; distal radius, ultradistal radius [SXA and pQCT]), adverse events (bone pain); survival and withdrawals
Notes	
Allocation concealment	B

BMD: bone mineral density
CF: cystic fibrosis
DEXA: dual-energy x-ray absorptiometry
pQCT: peripheral quantitative computed
SD: standard deviation
SXA:single energy x-ray absorptiometry

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** Indicates the major publication for the study*

GRAPHS

To view a graph or table, click on the outcome title of the summary table below.

To view graphs using MetaView, click on the "Show metaview" link at the top of the graph.

Without lung transplantation				
Outcome title	No. of studies	No. of participants	Statistical method	Effect size
Percent change in BMD, Lumbar spine, DEXA, 6 months	1	28	Weighted Mean Difference (Fixed) 95% CI	-5.80 [-8.69, -2.91]
Percent change in BMD, Total hip, DEXA, 6 months	1	28	Weighted Mean Difference (Fixed) 95% CI	-3.00 [-5.40, -0.60]
Percent change in BMD, Distal radius, SXA, 6 months	1	28	Weighted Mean Difference (Fixed) 95% CI	1.70 [-0.26, 3.66]
Percent change in BMD, Ultradistal radius, SXA, 6 months	1	28	Weighted Mean Difference (Fixed) 95% CI	2.70 [-0.19, 5.59]
Bone pain (# patients), 6 months	1	31	Relative Risk (Fixed) 95% CI	24.44 [1.57, 381.48]
Withdrawals, total (# patients), 6 months	1	31	Relative Risk (Fixed) 95% CI	2.13 [0.21, 21.17]
Withdrawals, due to adverse events (# patients), 6 months	1	31	Relative Risk (Fixed) 95% CI	Not estimable
Survival (# patients), 6 months	1	31	Relative Risk (Fixed) 95% CI	1.00 [0.83, 1.20]
With lung transplantation				
Outcome title	No. of	No. of	Statistical method	Effect size

	studies	participants		
Vertebral fractures (# patients), 24 months	1	34	Relative Risk (Fixed) 95% CI	3.38 [0.39, 29.29]
Non-vertebral fractures (# patients), 24 months	1	34	Relative Risk (Fixed) 95% CI	0.56 [0.17, 1.89]
Percent change in BMD, Lumbar spine, DEXA, 24 months	1	34	Weighted Mean Difference (Fixed) 95% CI	-6.20 [-8.12, -4.28]
Percent change in BMD, Femur, DEXA, 24 months	1	34	Weighted Mean Difference (Fixed) 95% CI	-7.90 [-10.02, -5.78]
Bone pain (# patients), 24 months	1	34	Relative Risk (Fixed) 95% CI	Not estimable
Withdrawals, due to adverse events (# patients), 24 months	1	34	Relative Risk (Fixed) 95% CI	Not estimable
Survival (# patients), 24 months	1	34	Relative Risk (Fixed) 95% CI	Not estimable

COVER SHEET

Title	**Bisphosphonates for osteoporosis in people with cystic fibrosis**
Reviewer(s)	**Brenckmann C, Papaioannou A**
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SYNOPSIS

Bisphosphonates are effective in increasing bone density in people with cystic fibrosis but more research is needed

Cystic fibrosis (CF) is a serious genetic disorder that affects cells in the exocrine glands (sweat glands and others). Osteoporosis is a disorder of the bones that can lead to reduced bone density and brittleness and is a common problem for people with CF. Bisphosphonates are drugs that increase bone density, and they are used to treat osteoporosis caused by menopause or the use of corticosteroid drugs. The review of trials found using bisphosphonates such as pamidronate for osteoporosis is promising for people with CF. However, these drugs cause severe bone pain in people not using corticosteroids. More research is needed.

Index Terms

Medical Subject Headings (MeSH)
Bone Density [drug effects]; Cystic Fibrosis [complications]; Diphosphonates [therapeutic use]; Fractures [prevention & control]; Lung Transplantation ; Osteoporosis [drug therapy]; Randomized Controlled Trials
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