

A Summary of a Cochrane Review of Bisphosphonates for Paget's Disease

The Cochrane Database of Systematic Reviews is a trusted resource for systematic reviews in health care. Our Specialist Paget's Nurse, Diana Wilkinson, summarises here a Cochrane Review for the use of Bisphosphonates as a treatment for Paget's Disease of Bone.

What is a Cochrane Review?

Cochrane is a non-profit organisation formed to facilitate evidence based choices about health interventions faced by health professionals, patients and policy makers. The name, Cochrane, came from a Scottish doctor, Archibald Cochrane (1909 – 1988), who challenged the medical care system. To make medicine more effective, he called for up-to-date, systematic reviews of all relevant randomised controlled trials concerning health care.

The work of Cochrane is recognised as representing an international gold standard for high quality, trusted information. Contributors from more than 120 countries work together to produce credible, accessible health information that is free from commercial sponsorship and other conflicts of interest. Many of the contributors are world leaders in their fields.

In the Cochrane Database of Systematic Reviews, each review addresses a clearly formulated question. A search is made for all the existing research that meets specific criteria. The evidence is gathered, appraised and summarised to help doctors, nurses, patients, carers, researchers and funders make informed decisions about health, including treatment.



Bisphosphonates for Paget's Disease

For people with Paget's disease, bisphosphonates are considered to be the treatment of choice. The Cochrane Review, 'Bisphosphonates for Paget's Disease of Bone in Adults' was published in December 2017 and written by a team of experts (see the reference on page 9), including Dr Luis Corral-Gudino and Professor Stuart Ralston, who are also involved in writing the new clinical Guideline for Paget's disease.

What are Bisphosphonates?

Paget's disease causes the normal bone renewal and repair (remodelling) process to become abnormal; bones become weak, enlarged and misshapen. Bisphosphonates are medications that slow down the bone remodelling process.

What Questions were Asked?

In considering bisphosphonates for Paget's disease, the authors wanted to discover whether bisphosphonate treatment is better or worse than dummy treatment (placebo) in relieving bone pain and whether treatment could prevent

complications. They also wanted to discover which bisphosphonates were best.

How was the Review Carried out?

Twenty studies of bisphosphonates, as treatment for Paget's disease in adults, were included in the review. These were Randomised Controlled Trials (RCTs) and involved 3168 people. Of the studies, ten (801 people) compared bisphosphonates with a placebo.

The studies were performed in the USA, Canada, the UK, Europe, Australia, New Zealand and Argentina. The participants in the studies had Paget's disease confirmed by x-ray or isotope bone scan. The studies included elderly people, slightly more men than women, and nearly all had blood results showing raised bone turnover.

Assessment and Quality of Evidence

Standard procedures expected by Cochrane were used. Two of the authors independently screened the search results, extracted data and assessed studies for risk of prejudice.

- Evidence was downgraded mainly due to limited data and concerns about study design.
- The quality of the evidence assessed regarding pain relief data provided moderate-quality evidence.
- The data on fractures was assessed as providing very low-quality evidence.
- Treatment discontinuation data provided moderate-quality evidence.

■ The data on side effects provided low-quality evidence.

Funding

Eleven studies were funded by drug manufacturers and four studies were funded by government agencies or charities. Funding sources were unclear in five of the studies.

What were the Findings of the Review?

- 1) All studies showed similar results.
- 2) Bisphosphonates for people with Paget's disease probably help to relieve bone pain.
- 3) It was found that of 100 adults with Paget's disease, 31 would experience complete pain relief, if they had treatment with bisphosphonates, compared with 9 people who did not have bisphosphonates.
- 4) For those with Paget's disease, pain relief was probably better with zoledronate than pamidronate or risedronate.
- 5) It was uncertain whether bisphosphonates can prevent bone fractures.
- 6) The effects on quality of life, the need for orthopaedic surgery and hearing loss prevention were not reported in studies that compared bisphosphonates with a placebo.

What about Side Effects?

The authors considered the side effects of bisphosphonates in people with Paget's disease. They found:

■ Side effects would be experienced in 64% of people who were given bisphosphonate treatment, compared with 48% of those who did not have bisphosphonates.

“For those with Paget’s disease, pain relief was probably better with zoledronate than pamidronate or risedronate”

■ Intravenous bisphosphonates can cause temporary fever or tiredness and those taking oral medications can experience mild gastrointestinal side effects.

■ Severe side effects causing treatment discontinuation were rare.

■ The number of people who stopped treatment due to side effects were the same for the bisphosphonate and placebo groups (4%).

Implications for Research

The data available for this review does not resolve the question of whether bisphosphonates could prevent long-term complications such as fractures, progression of deafness or the need for orthopaedic surgery. The authors recommend that appropriate research is,

therefore, needed in these areas and also to clarify the impact of bisphosphonates on the quality of life of people with Paget's disease. The authors also suggest that the role of bisphosphonates for people who do not have symptoms, and whose blood tests indicate that bone turnover is within the normal range, could also be investigated further.

Further Information

For further information or to discuss the review's findings please contact the Paget's Association's Nurse Helpline by telephone 0161 799 4646 or email helpline@paget.org.uk

The full Cochrane review can be found online: <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD004956.pub3/full>

Reference

Corral-Gudino L, Tan A. J. H., del Pino-Montes J, Ralston S.H. Bisphosphonates for Paget's disease of bone in adults. Cochrane Database of Systematic Reviews 2017, Issue 12. Art. No.: CD004956. DOI: 10.1002/14651858.CD004956.pub3.

Bisphosphonates for Paget's Disease

The following are the main bisphosphonates which are generally used to treat Paget's disease, here in the UK.

Intravenous Preparations

(Usually given in hospital as an outpatient)

■ **Zoledronate** (i.e. Aclasta): a single dose of 5mg, given into bloodstream, may be effective for many years (studies have shown it can be effective for up to 6 years and more).

■ **Pamidronate** (i.e. Aredia): several doses given into bloodstream, and repeated when necessary, dependant on symptoms. Doses can vary but commonly 30mg over 4 hours on 3 consecutive days initially. (Pamidronate has largely been superseded by zoledronate).

Oral Preparations

■ **Risedronate** (i.e. Actonel): 30mg daily for 2 months. If necessary, the course can be repeated after six months.