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[Intervention Review]

Interventions for tophi in gout

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ABSTRACT

Background

Tophi develop in untreated or uncontrolled gout. Their presence can lead to severe and potentially fatal complications. To date there have been no systematic reviews focused on the management of tophi in gout.

Objectives

To assess the benefits and harms of non-surgical and surgical treatments for the management of tophi in gout.

Search methods

We searched three databases: the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE. We handsearched American College of Rheumatology (ACR) and European League against Rheumatism (EULAR) abstracts from 2010 to 2011, references from included studies and trial registries. We completed the most recent search on 20 May 2013.

Selection criteria

All published randomised controlled trials (RCTs) or controlled clinical trials with quasi-randomised methods of allocating participants to treatment examining interventions for tophi in gout in adults. Possible interventions included urate-lowering pharmacological treatment (e.g. benzbromarone, probenecid, allopurinol, febuxostat, pegloticase), surgical removal or other interventions such as haemodialysis.

Data collection and analysis

Two review authors extracted data from titles, abstracts and selected studies for detailed review, and extracted data and risk of bias independently. Major outcomes were number of participants with complete resolution of tophi, number of study participant withdrawals due to adverse events, joint pain reduction, function, quality of life, serum urate normalisation and total adverse events.

Main results

Only one study, at low risk of all biases, met the inclusion criteria. This was the pooled results from two RCTs (225 participants, 145 with tophi at baseline) randomised to one of three arms; pegloticase infusion every two weeks (biweekly), monthly pegloticase infusion (pegloticase infusion alternating with placebo infusion every two weeks) and placebo. Moderate-quality evidence from one study indicated that biweekly pegloticase 8 mg infusion reduced tophi in the subset of participants with tophi, but increased withdrawals due to adverse events in all participants, and monthly infusion appeared to result in less benefit.

Biweekly pegloticase treatment resulted in resolution of tophi in 21/52 participants compared with 2/27 who received placebo (risk ratio (RR) 5.45, 95% confidence intervals (CI) 1.38 to 21.54; number needed to treat for an additional beneficial outcome (NNTB) 3 (95% CI 2 to 6).

Eleven of 52 participants with monthly pegloticase treatment had complete resolution of one or more tophi compared with 2/27 who received placebo (RR 2.86, 95% CI 0.68 to 11.97).

Participant-reported pain relief of 30% or greater, function, quality of life, serum urate normalisation, were reported for all participants but not separately for those with tophi; therefore, we did not include the results.

Pegloticase administered biweekly resulted in more withdrawals due to adverse events compared with placebo (15/85 participants with pegloticase versus 1/43 participants with placebo; RR 7.59, 95% CI 1.04 to 55.55; number needed to treat for an additional harmful outcome (NNTH) 7, 95% CI 4 to 17). Pegloticase administered monthly also resulted in more withdrawals due to adverse events than placebo (16/84 participants with pegloticase versus 1/43 participants with placebo; RR 8.19, 95% CI 1.12 to 59.71; NNTH 6, 95% CI 4 to 14). Most withdrawals were due to infusion reactions.

Total adverse events were high in all treatment groups: 80/85 participants administered pegloticase biweekly reported an adverse event compared with 41/43 from the placebo group (RR 0.99, 95% CI 0.91 to 1.07); 84/84 participants administered pegloticase monthly reported an adverse event versus 41/43 in the placebo group (RR 1.05, 95% CI 0.98 to 1.14). As 80% of adverse events were due to flares of gout, probably unrelated to the drug treatment per se, this may explain the high rate of adverse events in the placebo group - who were essentially untreated.

Authors' conclusions

This study showed pegloticase is probably beneficial in the management of tophi in gout, in terms of resolution of tophi, but with a high risk of adverse infusion reactions. However, there is a need for more RCT data considering other interventions, including surgical removal of tophi.

PLAIN LANGUAGE SUMMARY

Interventions for tophi in gout

Background: what are tophi and what interventions are used?

Gout is caused by urate crystals forming either within or around joints. Inflammation can lead to pain, redness, warmth and swelling of the affected joints, making the area difficult to touch or move. Some of the reasons why people get gout include their genetic make-up, being overweight, ingesting certain medications (e.g. cyclosporine), impaired kidney function and lifestyle habits such as drinking excessive amounts of alcohol and sugar-sweetened drinks. Tophi are nodules that develop in people with poorly treated or uncontrolled chronic gout. Tophi can become infected, cause pain and lead to a decrease in function. Tophi can be treated with urate-lowering drugs (e.g. benzbromarone, probenecid, allopurinol, febuxostat, pegloticase), surgical removal or other interventions such as haemodialysis. Surgical interventions can be used where urgent removal is required, for example, for relief of nerve compression.

Study characteristics

This is a summary of a Cochrane review that shows interventions for the management of tophi. After searching for all relevant studies in May 2013, we found only one study (pooled results from two randomised controlled trials (clinical studies where people are randomly put into one of two or more treatment groups)) that randomised 225 people to pegloticase (every two weeks (biweekly) or monthly) or placebo, in the management of chronic gout; 145 participants had tophi and 131 contributed outcome data.

Key results: what happens to people with tophi who are treated with biweekly or monthly pegloticase versus placebo

Resolution of tophi

- 33 more people out of 100 had resolution of one or more tophi after six months' treatment with pegloticase biweekly compared with placebo (33% absolute improvement).

- 14 more people out of 100 had resolution of one or more tophi after six months' treatment with pegloticase monthly compared with placebo (14% absolute improvement).

- 40 people out of 100 in the biweekly pegloticase group had resolution of one or more tophi.

- 21 people out of 100 in the monthly pegloticase group had resolution of one or more tophi.

- 7 people out of 100 in the placebo group had resolution of one or more tophi.

Other outcomes were for all participants, and not separated out for those people with tophi. Therefore, we have not reported them in this review. However, we reported on withdrawal due to adverse events for the total population. Most withdrawals were due to adverse reactions to drug infusion.

Withdrawal due to adverse events

- 16 more people out of 100 withdrew from treatment with biweekly pegloticase compared with placebo (16% more withdrawals).

- 17 more people out of 100 withdrew from treatment with monthly pegloticase compared to placebo (17% more withdrawals).

- 18 people out of 100 withdrew from treatment with biweekly pegloticase due to adverse events.

- 19 people out of 100 withdrew from treatment with monthly pegloticase due to adverse events.

- 2 people out of 100 withdrew from treatment with placebo due to adverse events.

Quality of evidence

Moderate-quality evidence indicated that pegloticase biweekly or monthly probably resolves one or more tophi. However, this has to be weighed up against high withdrawal rates from treatment due to adverse events, mostly due to an increase in infusion reactions. Pain reduction, quality of life, serum urate normalisation and function were not reported separately in people with tophi. The evidence was downgraded due to imprecise results. Further research may change these results.

We do not know if other interventions, including surgery, are effective, as we found no randomised controlled trials that assessed other interventions.