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[Intervention Review]

Colchicine for prevention of cardiovascular events

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ABSTRACT

Background

Colchicine is an anti-inflammatory drug that is used for a wide range of inflammatory diseases. Cardiovascular disease also has an inflammatory component but the effects of colchicine on cardiovascular outcomes remain unclear. Previous safety analyses were restricted to specific patient populations.

Objectives

To evaluate potential cardiovascular benefits and harms of a continuous long-term treatment with colchicine in any population, and specifically in people with high cardiovascular risk.

Search methods

We searched the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, ClinicalTrials.gov, WHO International Clinical Trials Registry, citations of key papers, and study references in January 2015. We also contacted investigators to gain unpublished data.

Selection criteria

Randomised controlled trials (parallel-group or cluster design or first phases of cross-over studies) comparing colchicine over at least six months versus any control in any adult population.

Data collection and analysis

Primary outcomes were all-cause mortality, myocardial infarction, and adverse events. Secondary outcomes were cardiovascular mortality, stroke, heart failure, non-scheduled hospitalisations, and non-scheduled cardiovascular interventions. We conducted predefined subgroup analyses, in particular for participants with high cardiovascular risk.

Main results

We included 39 randomised parallel-group trials with 4992 participants. Colchicine had no effect on all-cause mortality (RR 0.94, 95% CI 0.82 to 1.09; participants = 4174; studies = 30; $I^2 = 27\%$; moderate quality of evidence). There is uncertainty surrounding the effect of



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colchicine in reducing cardiovascular mortality (RR 0.34, 95% CI 0.09 to 1.21, $l^2 = 9\%$; participants = 1132; studies = 7; moderate quality of evidence). Colchicine reduced the risk for total myocardial infarction (RR 0.20, 95% CI 0.07 to 0.57; participants = 652; studies = 2; moderate quality of evidence). There was no effect on total adverse events (RR 1.52, 95% CI 0.93 to 2.46; participants = 1313; studies = 11; $l^2 = 45\%$; very low quality of evidence) but gastrointestinal intolerance was increased (RR 1.83, 95% CI 1.03 to 3.26; participants = 1258; studies = 11; $l^2 = 74\%$; low quality of evidence). Colchicine showed no effect on heart failure (RR 0.62, 95% CI 0.10 to 3.88; participants = 462; studies = 3; $l^2 = 45\%$; low quality of evidence) and no effect on stroke (RR 0.38, 95% CI 0.09 to 1.70; participants = 874; studies = 3; $l^2 = 45\%$; low quality of evidence). Reporting of serious adverse events was inconsistent; no event occurred over 824 patient-years (4 trials). Effects on other outcomes were very uncertain. Summary effects of RCTs specifically focusing on participants with high cardiovascular risk were similar (4 trials; 1230 participants).

Authors' conclusions

There is much uncertainty surrounding the benefits and harms of colchicine treatment. Colchicine may have substantial benefits in reducing myocardial infarction in selected high-risk populations but uncertainty about the size of the effect on survival and other cardiovascular outcomes is high, especially in the general population from which most of the studies in our review were drawn. Colchicine is associated with gastrointestinal side effects based on low-quality evidence. More evidence from large-scale randomised trials is needed.

PLAIN LANGUAGE SUMMARY

Effects and safety of long-term use of colchicine on heart disease

Background

Colchicine is a very old, inexpensive treatment. It has strong effects against inflammation and is widely used in inflammatory diseases like gout. There are many studies on colchicine in inflammatory diseases. Inflammation is also an important component for the development of heart attacks or strokes. Some recent studies have shown that colchicine may have positive effects on heart disease.

Review question

We aimed to review all available studies evaluating longer-term use of colchicine. We wanted to describe the benefits and harms for people with or without established coronary heart disease. We looked at all studies that lasted at least six months, that included adults, and that compared health effects of colchicine use with the use of any other treatment. We took a closer look at people with previous heart issues.

Key results

We included 39 trials with 4992 participants in our analyses. Four trials included 1230 participants in total with heart disease. Colchicine treatment had no effect on death from any cause. There is uncertainty around the effect of colchicine on cardiovascular (heart-related) death. Results showed that cardiovascular death may be reduced, but this was not clear because some of our analyses showed a reduced risk while others did not. The risk for myocardial infarctions (heart attacks) was reduced, but this finding was based on only two studies and a total of 22 events. Colchicine did not clearly increase the risk of total harms but colchicine increased the risk for gastrointestinal intolerance, which was typically described as mild and short-lived. We found no clear effects on strokes, heart failure, emergency hospitalisations or unplanned invasive cardiac treatments.

Four of the 39 studies reported that they systematically looked for serious side effects linked to use of colchicine. Serious side effects can be life-threatening or require hospitalisation. No participant in these four studies was reported to have such a serious side effect. This means that possible serious side effects seem to be relatively rare: for example, the results indicate that among 800 people who are treated for one year, none would suffer a serious side effect. However, we have some concerns about the certainty of this result, because the reporting of serious harms in the studies was not ideal; for example, because the definitions of serious adverse events differed between studies, and it was not always clear what would be considered a serious adverse event. We found no difference in effects of colchicine in people at high cardiovascular risk.

The evidence is current to January 2015.

Conclusions

Overall, we found that further research would probably change our assessment of the benefits and harms of colchicine. Our findings should therefore be interpreted with caution. However, new treatments in heart diseases are urgently needed. Although there is much uncertainty around the benefits and harms of colchicine treatment, it may be associated with cardiovascular benefits, especially on myocardial infarction. We therefore think that large high-quality clinical trials should be conducted to further investigate colchicine in heart disease.