International collaborative systematic review of controlled clinical trials on pharmacologic treatments for acute pericarditis and its recurrences


CRD summary
The review concluded that a few small and/or low quality studies suggested a beneficial risk-benefit profile for colchicine, and a detrimental risk-benefit for steroids (particularly high-dose steroids) for the management of acute or recurrent pericarditis. The poor quality and small number of studies for each of the comparisons compromises the reliability of the pooled results.

Authors' objectives
To evaluate the benefits and safety of pharmacological treatments for acute or recurrent pericarditis.

Searching
PubMed, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL), Scopus, ClinicalTrials.gov, and BioMedCentral were searched to March 2010 for articles published in any language. Search terms were reported. Google Scholar was also searched. Three major conference proceedings were scanned from 2004 onwards. Reference lists of retrieved studies were searched.

Study selection
Controlled clinical trials of aspirin, colchicine, corticosteroids, non-steroidal anti-inflammatory drugs (NSAIDs), or statins for the management of acute idiopathic or recurrent pericarditis were eligible for inclusion. The comparator could be placebo or another pharmacological drug. Trials of specific forms of pericarditis that required targeted therapies (such as tuberculous, neoplastic, autoimmune or purulent pericarditis) were excluded.

The primary outcomes were rate of treatment failure and rate of pericarditis recurrence. Secondary outcomes included rehospitalisation and adverse events.

The included studies compared colchicine versus standard therapy, steroids versus standard therapy, high-dose steroid versus low-dose steroids, and statins versus standard therapy. Concurrent therapies included NSAIDs, steroids, aspirin and colchicine. Included patients had recurrent pericarditis or acute pericarditis. The mean age of patients ranged from 10 to 57 years; the proportion of men ranged from 35 to 62% (where reported). Included studies were conducted in Italy, Portugal and Finland.

Two authors independently performed study selection and disagreements were resolved by consensus.

Assessment of study quality
Two reviewers independently assessed study quality items including blinding, randomisation, completeness of outcome data, similarity of concurrent therapies, and allocation concealment. Disagreements were resolved by consensus. The overall quality of studies was classified as low or high risk of bias.

Data extraction
Two reviewers extracted data on treatment failure, pericarditis recurrences, rehospitalisation and adverse events, and used the data to calculate odds ratios (ORs) and 95% confidence intervals (CIs). Disagreements between reviewers were resolved by consensus. Study authors were contacted for missing data.

Methods of synthesis
A fixed-effects or random-effects meta-analysis was undertaken to obtain pooled odds ratios and 95% confidence intervals. Heterogeneity was assessed using $I^2$ and $X^2$. Studies were grouped according to intervention.

Publication bias was assessed using funnel plots, Egger's test and Peters' test.
Results of the review
Seven studies were included in the review (n=451 patients); three were randomised trials (n=259 patients) and four were comparative studies (n=192 patients). Sample size ranged from 15 to 120 patients. The quality of the included studies was variable, with four studies classified as high risk of bias, and three studies classified as low risk of bias. Length of follow-up ranged from 12 months to eight years.

Colchicine versus standard therapy (three studies): Compared with standard therapy, colchicine was associated with a statistically significant lower risk of treatment failure (OR 0.23, 95% CI 0.11 to 0.49; I²=0%; two studies) and recurrent pericarditis (OR 0.39, 95% CI 0.20 to 0.77; I²=23%; three studies). There was a non-significant trend towards more adverse events (OR 5.27, 95% CI 0.86 to 32.16; I²=0%; two studies). There was no statistically significant difference in rehospitalisation.

Steroids versus standard therapy (two studies): There was no statistically significant difference between steroids and standard therapy for recurrences, rehospitalisations and adverse events (one study).

Low-dose versus high-dose steroid (one study): Compared with high dose steroids, low dose steroids were associated with a statistically significantly lower risk of treatment failure/recurrence (OR 0.29, 95% CI 0.13 to 0.66), rehospitalisation (OR 0.19, 95% CI 0.06 to 0.63), and adverse events (OR 0.07, 95% CI 0.01 to 0.54).

Statins versus standard therapy (one study): There was no statistically significant difference between the statin and standard therapy groups for rehospitalisation and adverse events.

There was no evidence of publication bias with funnel plots, but Peters' test indicated significant publication bias (p=0.012).

Authors' conclusions
A few small and/or low quality studies suggested a beneficial risk-benefit profile for colchicine and a detrimental risk-benefit profile for steroids, particularly high-dose steroids.

CRD commentary
Inclusion criteria for the review were broadly defined. Several relevant data sources were searched, with no language restrictions, which minimised the risk of language bias. Publication bias was assessed and could not be ruled out; although the assessment publication bias with such a small number of studies may not be reliable. Attempts were made to reduce reviewer error and bias throughout the review process.

Study quality assessment (based on standard criteria) indicated the variable quality of the included data, which the authors acknowledged. It may not have been appropriate to pool the very small number of studies using a random-effects meta-analysis. Pooling studies with different study designs may not provide reliable results.

The poor quality and small number of studies for each of the comparisons compromises the reliability of the pooled results.

Implications of the review for practice and research
Practice: The authors stated that colchicine (0.5 to 1mg daily for three months) could be routinely used for patients with recurrent pericarditis, and selectively used in acute de nova pericarditis patients with a high risk of complications or recurrences. Steroids should be recommended for patients failing on colchicine or NSAID treatment.

Research: The authors stated that the ongoing research programme will provide further data on the role of colchicine. They also stated that a large-scale placebo-controlled trial was warranted to determine the role of steroids in acute pericarditis.

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