Adenosine improves post-procedural coronary flow but not clinical outcomes in patients with acute coronary syndrome: a meta-analysis of randomized trials


CRD summary
The review concluded that adjunctive adenosine improved post-procedural coronary flow but without consistent advantages on clinical outcomes in patients with acute coronary symptoms. This was a reasonably well-conducted review but low event rates and uncertain trial quality make the reliability of the authors’ conclusions unclear.

Authors’ objectives
To determine the efficacy of adjunctive adenosine therapy on angiographic and clinical outcomes in patients with acute coronary syndromes undergoing percutaneous coronary intervention or thrombolysis.

Searching
MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL) databases and Google Scholar were searched from January 1993 to August 2011 without language restrictions; search terms were reported. Proceedings from relevant scientific sessions and references of retrieved studies were searched for additional articles.

Study selection
Eligible studies were randomised controlled trials (RCTs) that compared adenosine with placebo in patients with acute coronary syndromes undergoing percutaneous coronary intervention or thrombolysis. Trials had to report clinical outcomes. Trials of elective percutaneous coronary intervention, trials in a bypass surgery setting and trials that compared use of a compound similar to adenosine but with different chemical properties were excluded.

The primary outcome was all-cause mortality. Secondary outcomes included incidence of no-reflow (defined as thrombolysis in myocardial infarction zero flow), infarction, heart failure symptoms (New York Heart Association class III/IV) and ST-resolution (defined as post-procedural resolution ≥50%).

Most trials investigated patients with ST-elevation myocardial infarction; one trial included a mixed patient population. Intracoronary adenosine was administered during percutaneous coronary intervention in most trials; intravenous adenosine was given after thrombolysis in three trials. Doses varied (up to 70 μg/kg/min). Where reported, ischaemic time before treatment ranged from 106 to 270 minutes. Follow-up ranged from one to 12 months (median six).

It was not clear how many reviewers were involved in study selection.

Assessment of study quality
Two reviewers assessed the methodological quality of the included trials according to allocation sequence and concealment, blinding (patient and investigator) and completeness of data.

Data extraction
Data were extracted to allow the calculation of odds ratios (OR) and 95% confidence intervals (CI) for all outcomes of interest.

It was not clear how many reviewers extracted data.

Methods of synthesis
Summary odds ratios with 95% CI were calculated using a fixed-effect model (no statistical heterogeneity) or a random-effects model (significant or moderate statistical heterogeneity). Heterogeneity was assessed using Cochran’s Q test and I². Sensitivity analyses investigated removal of individual trials one at a time, removal of individual trials according to increasing dose of intracoronary adenosine and trials of patients with ST-elevated myocardial infarction. Subgroup analyses investigated treatments (percutaneous coronary intervention versus thrombolysis), follow-up (up to six months versus more than six months) and numbers of participants (101 or less versus more than 101). Publication bias was
examined using a funnel plot and Egger’s test of asymmetry

Results of the review
Ten RCTs (3,821 patients) were included in the review.

Mortality: No statistically significant between-group difference was found (OR 0.87, 95% CI 0.69 to 1.09; I²=0%; nine RCTs, 3,793 patients).

Secondary outcomes: No statistically significant between-group differences were found for re-infarction, heart failure and ST-resolution. A significant reduction in favour of adenosine was found for post-procedural no-flow (OR 0.23, 95% CI 0.08 to 0.70; I²=28%; five RCTs, 865 patients).

Sensitivity and subgroup analyses did not alter the main findings. No publication bias was found.

Authors’ conclusions
Adjunctive adenosine improved post-procedural coronary flow but did not improve survival or reduce rates of myocardial infarction and heart failure symptoms in patients with acute coronary symptoms treated with percutaneous coronary intervention or thrombolysis.

CRD commentary
The review question was supported by clear inclusion and exclusion criteria. Several relevant sources were searched for published and unpublished trials. There were no language restrictions. No publication bias was found but this was difficult to reliably assess for so few trials. Appropriate steps were taken to minimise risks error and bias in the assessment of trial quality; it was unclear whether similar steps were taken during study selection and data extraction. Trial quality was assessed using appropriate criteria but results were not reported. Where low rates of clinical events were observed the Peto odds ratio may have been a better choice in the synthesis. Attempts were made to assess the robustness of the results attained in the planned sensitivity and subgroup analyses but the effect of concomitant adjunctive therapies could not be evaluated due to lack of data.

This was a reasonably well-conducted review but low event rates and uncertain trial quality make the reliability of the authors conclusions unclear.

Implications of the review for practice and research
Practice: The authors stated that short-term treatment with adjunctive adenosine was not effective in achieving significant lasting improvements in clinical outcomes.

Research: The authors stated a need for further RCTs to look at different treatment strategies to improve coronary flow and clinical outcomes in patients with acute coronary symptoms.

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