Antioxidant therapy in the management of acute, chronic and post-ERCP pancreatitis: a systematic review
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CRD summary
The review concluded that there was insufficient data to support use of antioxidant therapy in management of acute or chronic pancreatitis and prevention of pancreatitis. The conclusions were supported by the data, but should be interpreted with some caution due to the possibility of missed studies, lack of details regarding generalisability and unclear quality.

Authors' objectives
To determine whether antioxidants improved the outcome of patients with pancreatitis.

Searching
PubMed, Scopus, The Cochrane Library and EBM reviews databases and Google Scholar were searched to February 2009. Search terms were reported. Reference lists of key papers were screened. The review was restricted to studies in English.

Study selection
Clinical trials that assessed use of antioxidants in management of acute or chronic pancreatitis or prevention of pancreatitis were eligible for inclusion.

The included studies assessed one or more of the following at various doses and administered orally or intravenously: glutamine, curcumin, vitamin C, vitamin E, glutathione precursors, allopurinol, selenium, methionine, beta-carotene, alpha-tocopherol, N-acetylcysteine, S-adenosyl methionine (SAMe) and dimethyl sulphoxide. Control interventions included placebo, delayed treatment, standard total parenteral nutrition and lower-dose antioxidant. A broad variety of outcomes was assessed and included pain, use of analgesia, hospitalisation, infection, operation, mortality, morbidity, organ dysfunction, quality of life, physical and social functioning, health perception, cure rate, cost, prevention of pancreatitis, severity of pancreatitis and adverse events.

The authors did not state how studies were selected for inclusion.

Assessment of study quality
Studies were assessed for methodological quality using the Jadad scale to assign a score out of five depending on whether they fulfilled items on randomisation, randomisation description, double blinding, blinding description and reporting of withdrawals. Studies were considered to be of high quality if they scored 3 or more points.

The authors did not state how many reviewers performed quality assessment.

Data extraction
Data were extracted as 2x2 tables. These were used to calculate relative risks (RR) and 95% confidence intervals.

The authors did not state how many reviewers performed data extraction.

Methods of synthesis
Where appropriate, relative risks were pooled using the Mantel-Haenszel fixed-effect model or DerSimonian and Laird random-effects model where there was substantial heterogeneity. Heterogeneity was assessed statistically using the Q statistic and graphically using L’Abbé plots. Publication bias was assessed using funnel plots.
Results of the review
The authors stated that 22 RCTs were included, but only 21 were listed in the tables (n=3,234): 14 RCTs assessed management (n=714) and seven assessed prevention (n=2,520). Nineteen studies scored 3 on the Jadad scale and three scored 2 or less. No details of exact criteria fulfilled were reported.

Results varied across studies. None of the antioxidants showed consistent beneficial effects across multiple outcomes. Studies that assessed prevention found that antioxidant therapy failed to prevent pancreatitis in almost all trials. The only antioxidant for which there were sufficient data to perform a meta-analysis was allopurinol for the prevention of pancreatitis. These studies found no difference between allopurinol and placebo for the prevention of pancreatitis (RR 0.86, 95% CI 0.42 to 1.77; four RCTs). There was strong evidence of heterogeneity (p=0.0062).

Authors' conclusions
The present data did not support a benefit of antioxidant therapy alone or in combination with conventional therapy in management of acute or chronic pancreatitis and prevention of pancreatitis.

CRD commentary
The review objective was clearly stated, although it only considered patients with pancreatitis rather than the prevention of pancreatitis. Inclusion criteria were clearly defined. The literature search was adequate for published studies, but the restriction to English-language studies and lack of a search for unpublished data meant that relevant studies may have been missed. Publication bias was assessed, but this was only possible for the four studies that assessed use of allopurinol for prevention of pancreatitis; analysis based on such a small number of studies is unlikely to be reliable. The review process methods were unclear and the possibility of errors and bias could not be ruled out. Study details were summarised in tables. There was a discrepancy between the number of studies reported and the number listed in the tables. There were very few details on participants of the included studies and so the generalisability of the included studies was unclear. Study quality was formally assessed, but important criteria such as allocation concealment were not considered and the results were presented only as summary quality scores, which made the results difficult to interpret. The mostly narrative synthesis was appropriate given the differences between studies. The statistical pooling was appropriate where conducted.

The authors' conclusions were supported by the data, but should be interpreted with some caution due to the possibility of missed studies, lack of details regarding generalisability and unclear quality.

Implications of the review for practice and research
Practice: The authors stated that there was insufficient evidence to support use of antioxidants alone or in combination with conventional therapy in management or prevention of pancreatitis.

Research: The authors stated that further double blind, randomised, placebo-controlled clinical trials with large sample sizes needed to be conducted.

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