Regional intra-arterial vs. systemic chemotherapy for advanced pancreatic cancer: a systematic review and meta-analysis of randomized controlled trials

CRD summary
The review concluded that regional intra-arterial chemotherapy was more effective and has fewer complications than systemic chemotherapy for treating advanced pancreatic cancer. These conclusions appeared reliable. However, relatively few trials were included, all were small and none were blinded. Therefore, the authors' recommendation for larger and more rigorous studies to confirm these findings is likely to be appropriate.

Authors' objectives
To compare the efficacy and safety of regional intra-arterial chemotherapy with systemic chemotherapy for advanced pancreatic cancer (stage III/IV).

Searching
PubMed, ISI, EMBASE, The Cochrane Library, Google, Chinese Scientific Journals Database (VIP) and China National Knowledge Infrastructure (CNKI) were searched up to 2010. Only published studies were included. Search terms were reported.

Study selection
Randomised controlled trials (RCTs) that compared regional intra-arterial chemotherapy with intravenous chemotherapy for advanced pancreatic cancer were eligible for inclusion. Major outcomes were: complete remission; partial remission; clinical benefit; pain-control; and complication rate. Outcomes definitions were reported.

Where reported, mean age ranged from 56 to 62 years; most patients were male. Rates of liver metastasis and types of chemotherapies varied between the trials and drug delivery routes varied between the intervention groups. Two-thirds of the studies were conducted in China.

The authors did not state how many reviewers selected the studies for inclusion.

Assessment of study quality
Two reviewers assessed study quality using the Cochrane risk of bias tool, which evaluated adequate randomisation methods, allocation concealment, blinding, incomplete outcome data, selective reporting, source of funding bias, baseline imbalance and early stoppage.

Data extraction
Two reviewers independently extracted study data, with discrepancies resolved by a third reviewer.

Methods of synthesis
Where appropriate, relative risks were pooled with a fixed-effect meta-analysis using the Mantel-Haenszel method. Heterogeneity was assessed with $I^2$ and Q.

Results of the review
Six RCTs (298 patients) were included. None of the studies were blinded, only one trial reported adequate randomisation methods. Methods of allocation concealment were unclear in all trials. There were no studies with incomplete outcome data, early stoppage bias, or baseline imbalances, and no funding bias was found.

Compared to systemic chemotherapy, patients receiving regional intra-arterial chemotherapy had significantly higher rates of partial remissions (RR 1.99; 95% CI 1.50 to 2.65). Greater clinical benefits (RR 2.34; 95% CI 1.84 to 2.97), lower total complication rates (RR 0.72, 95% CI 0.60, 0.87) and fewer haematological side effects (RR 0.76, 95% CI 0.63, 0.91) were found for intra-arterial treatment.
There was a trend favouring intra-arterial chemotherapy for complete remission rates, although the difference was not statistically significant (3.80; 95% CI 0.92 to 15.75). There was no statistically significant difference between the treatments in terms of gastrointestinal side effects. Median survival time with intra-arterial treatment (five to 21 months) was longer than for systemic chemotherapy (2.7 to 14 months). There was no evidence of significant heterogeneity between the trials.

**Authors’ conclusions**
Regional intra-arterial chemotherapy was more effective and has fewer complications than systemic chemotherapy for treating advanced pancreatic cancer.

**CRD commentary**
The review addressed a clear question and used clear but relatively broad inclusion criteria. Several bibliographic databases were searched, although unpublished studies were not included, therefore some studies may have been missed. At least two reviewers were involved at the data extraction and quality assessment stages of the review. It is unclear if similar steps were taken to minimise the risk of error and bias at the selection stage.

The studies were small and quality assessment showed they had limitations. Notably, none of the studies were blinded. Synthesis methods appeared appropriate. The results from the meta-analysis showed consistent and large effects for most of the key outcomes, and the conclusions reflected these findings. However, relatively few trials were included; all were small with several methodological limitations. Therefore, the authors’ recommendation for larger and more rigorous studies to confirm the review findings is probably appropriate.

**Implications of the review for practice and research**

**Practice:** The authors stated that regional intra-arterial chemotherapy was a good strategy for treatment of advanced pancreatic cancer and a good option for palliative or neoadjuvant therapy, especially in patients who did not respond to standardised therapy.

**Research:** The authors stated that larger and more rigorous studies were needed to confirm the review findings.

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.