Meta-analysis of intraperitoneal chemotherapy for gastric cancer
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CRD summary
This review concluded that intraperitoneal chemotherapy in patients undergoing curative resection for gastric cancer may be beneficial compared with gastrectomy. The authors’ conclusions follow from the evidence identified. However, given the limited search and language restrictions applied, some relevant studies might not have been included in the review.

Authors’ objectives
To assess the efficacy and safety of intraperitoneal chemotherapy (IPT) in patients undergoing curative resection for gastric cancer.

Searching
MEDLINE and EMBASE (both from 1980 to 2003), Cancerlit (from 1983 to 2003) and the Chinese Biomedical Database (from 1990 to 2003) were searched. The reference lists of identified trials and review articles were also checked. Only studies reported in Chinese or English were considered for inclusion in the review.

Study selection
Study designs of evaluations included in the review
Only randomised controlled trials (RCTs) were eligible for inclusion in the review. The studies could be single-blind, double-blind or without blinding.

Specific interventions included in the review
Studies assessing the effects of IPT, with or without carbon particles (CH) or intraperitoneal hyperthermic perfusion (IHCP), compared with gastrectomy alone were eligible for inclusion. Studies using oral or intravenous chemotherapy, chemoimmunotherapy, or radiotherapy were excluded from the review. The studies included in the review assessed a variety of chemotherapy regimens.

Participants included in the review
The studies had to involve patients who had undergone potential curative surgery for locally advanced gastric cancer to be eligible for inclusion. The studies that were included in the review were set in Austria, China, Korea and Japan.

Outcomes assessed in the review
No specific inclusion criteria relating to the outcomes were given. The outcomes included in the review were death and the side-effects of chemotherapy.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection. However, the authors stated that there was good agreement between the two reviewers with regards to the eligibility of studies.

Assessment of study quality
The quality of the included studies was assessed using the 5-point Jadad scale plus consideration of allocation concealment. Two reviewers independently assessed the validity of the included studies. Any disagreements were resolved through discussion.

Data extraction
The authors stated that two reviewers independently assessed the outcome data using a pre-designed strategy; no further details were provided. The data appeared to have been extracted in an intention-to-treat format. Survival and mortality data were extracted.

**Methods of synthesis**

How were the studies combined?
A pooled odds ratio (OR), along with 95% confidence interval (CI), was calculated using a fixed-effect model. Publication bias was assessed using Rosenthal's fail-safe N.

How were differences between studies investigated?
The chi-squared test was used to investigate whether statistical heterogeneity was present between the studies included in the meta-analysis. A sensitivity analysis, which explored the effects of excluding trials with a low Jadad score, was also performed. Subgroup analyses were also executed; these investigated the effect of follow-up time (less than 60 months versus more than 60 months), chemotherapy group (IPT without CH and IHCP versus IPT with CH versus IHCP alone) and setting (Asia versus non-Asia).

**Results of the review**
Eleven RCTs (n=1,161) were included.

Three of the included RCTs were deemed to be of high quality: one trial was double-blind with a sample size calculation and two trials used intention-to-treat analyses. According to the authors, the calculated fail-safe N of 104 indicated that no important publication bias was present.

The pooled analysis showed that there were fewer deaths with IPT than surgery alone (OR 0.51, 95% CI: 0.40, 0.65). No statistically significant heterogeneity was identified and the exclusion of trials with low Jadad scores did not affect the results of the meta-analysis. The subgroup analysis of chemotherapy group suggested that there were fewer deaths with IHCP (7 RCTs) and IPT with CH (2 RCTs) than with IPT (2 RCTs) compared with surgery; the ORs were 0.48 (95% CI: 0.35, 0.67), 0.52 (95% CI: 0.29, 0.94) and 0.57 (95% CI: 0.35, 0.92), respectively. The subgroup analysis of setting suggested that trials based in Asian countries (9 RCTs) had fewer deaths than those from non-Asian countries (2 RCTs), ORs of 0.49 (95% CI: 0.38, 0.64) and 0.67 (95% CI: 0.32, 1.41), respectively. The subgroup analysis of length of follow-up suggested that the benefit of IPT compared with surgery was more significant in trials with a follow-up of less than 60 months (6 RCTs) than in those with a follow-up of more than 60 months (5 RCTs), ORs 0.40 (95% CI: 0.27, 0.59) and 0.60 (95% CI: 0.44, 0.82), respectively.

Five of the 11 included RCTs reported mild complications, three reported no significant differences between the IPT group and surgery group, and two reported complications in the chemotherapy group. One RCT, which was conducted in Austria, was terminated early due to serious adverse events and death in the chemotherapy group.

**Authors' conclusions**
IPT after curative resection for locally advanced gastric cancer may be beneficial to patients.

**CRD commentary**
The review question was relatively clear in terms of the interventions, study designs and participants eligible for inclusion in the review. Some relevant sources were searched. However, unpublished literature was not sought and language restrictions were applied, which could lead to language bias; there was no evidence of publication bias according to the fail-safe N calculated. It appears that appropriate methods might have been employed in determining the eligibility of studies, assessing their quality, and extracting the data, which reduces the possibility of reviewer bias and error. Established criteria were used to assess the quality of the included studies. These suggested that the included studies were generally of poor quality, although sensitivity analyses suggested that the lower quality studies were not affecting the results of the meta-analysis.
Limited details of the included studies were provided. This made it difficult to assess whether the meta-analysis was appropriate, although the directions of the treatment effects appeared consistent and no statistical heterogeneity was identified. The authors’ conclusions follow from the evidence identified but, given the limited search and language restrictions applied, pertinent studies might have been omitted from the review.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice.

Research: The authors stated that in order to form definitive conclusions about the use of IPT, more multicentre, randomised, double-blind trials with rigorous study designs are needed. The authors also advised future researchers to describe the toxicity of medicine by World Health Organization standards.

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