Hyperthermic intraperitoneal chemotherapy added to the treatment of ovarian cancer: a review of achieved results and complications

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CRD summary
This review concluded that hyperthermic intraperitoneal chemotherapy with surgical treatment for ovarian cancer seemed feasible; improved survival rates were reported at the cost of acceptable mortality rates. It was unclear which patients would benefit most from this treatment. The risk of bias in the review and the limited quality of the included studies should be considered when interpreting these conclusions.

Authors' objectives
To determine the efficacy of hyperthermic intraperitoneal chemotherapy in the management of patients with peritoneal carcinomatosis from ovarian cancer in terms of mortality, morbidity and survival.

Searching
PubMed, EMBASE, CINAHL and The Cochrane Library were searched (1998 to October 2008) for published studies in English with an abstract. Bibliographies of retrieved articles were handsearched for further studies.

Study selection
Studies of any design that investigated hyperthermic intraperitoneal chemotherapy with more than 10 patients with primary and recurrent ovarian cancer were eligible for inclusion. Eligible studies had to report mortality, morbidity or survival outcomes.

The included studies were of patients aged between 44 and 65 years old with primary advanced, persistent or recurrent ovarian cancer.

It appeared that two reviewers selected studies for inclusion and that disagreements were resolved by a third reviewer.

Assessment of study quality
The authors did not report that study quality was assessed.

Data extraction
Data were extracted for the outcomes of overall survival, progression-free survival, percentage of patients successfully cytoreduced and major morbidity and mortality.

The number of reviewers that extracted data was not reported.

Methods of synthesis
The studies were synthesised narratively and grouped by the outcomes of survival, mortality and major morbidity. The authors stated that meta-analysis was not appropriate due to the heterogeneity in patient populations and treatment regimens.

Results of the review
Sixteen studies were included in the review (546 patients, range 10 to 81). Eight studies were prospective (289 patients) and eight were retrospective (257 patients). The mean follow-up period ranged from 13.7 to 73 months.

Survival: Mean or median survival after surgery combined with hyperthermic intraperitoneal chemotherapy ranged from 19 to 76.1 months (12 studies). Five-year survival ranged from 15.0 to 63.4% (eight studies) and disease-free survival ranged from 10 to 57.1 months (14 studies). Mean and median survival was longer in patients who achieved optimal cytoreduction. There was no evidence of survival differences between patients with primary versus recurrent disease (five studies).

Mortality: Mortality rates up to 30 days after surgery ranged from 0.0 to 10.5% (14 studies). Postoperative mortality...
was reported for 14 out of 481 patients.

**Major morbidity:** Major morbidity rates after surgery combined with hyperthermic intraperitoneal chemotherapy ranged from 3.4 to 50.0%; 184 events were reported for 533 patients. Re-operation was needed in 0 to 16.6% of patients (21 times for 476 patients). Mean or median hospital stay ranged from eight to 25 days.

**Authors’ conclusions**
Adding hyperthermic intraperitoneal chemotherapy to the current treatment modalities for ovarian cancer seemed to be feasible. Improved survival rates were reported at the cost of acceptable mortality rates. However, there was a selection bias, so the morbidity should not be underestimated; it was unclear which patient would benefit most from this treatment.

**CRD commentary**
The research question was supported by well-defined inclusion criteria. Several relevant databases were searched, but searches were restricted to published studies in English, so publication and language bias could not be ruled out. It appeared that study selection was performed by two reviewers, which reduced the risk of reviewer error and bias. It was not clear whether similar steps were taken for data extraction.

Study quality did not appear to have been assessed. The design of the included studies was not well reported (such as whether there was a control group). So the reliability of the included studies could not be ascertained. A large proportion of the studies were reported to be retrospective studies inherently at risk of bias. Study sample sizes were small. The authors acknowledged that the included studies were prone to selection bias. Few details of the included interventions were provided in the review, but the authors stated that heterogeneity in patient populations and treatment precluded statistical pooling, so narrative synthesis appeared reasonable.

The authors’ conclusions are supported by the data presented, but the risk of bias in the review and the limited quality of the included studies should be borne in mind when interpreting this data.

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

**Practice:** The authors stated that it seemed reasonable to attempt to integrate heated intraperitoneal chemotherapy into the management of ovarian cancer.

**Research:** The authors stated that future studies should include the disease-free interval to sustain the extent of sensitivity for chemotherapy. Randomised controlled trials were needed to define whether hyperthermic intraperitoneal chemotherapy improved survival of patients with ovarian cancer and to find out which patients would benefit most; the authors reported that such a trial was being conducted.

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