Efficacy of adjuvant chemotherapy using oral fluorinated pyrimidines for curatively resected gastric cancer: a meta-analysis of centrally randomized controlled clinical trials in Japan

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CRD summary
This review assessed the efficacy of oral fluorinated pyrimidines (o-FP) for long-term maintenance therapy in Japan for curatively resected gastric cancer. The authors concluded that adjuvant chemotherapy using o-FP for long-term maintenance therapy appears to be effective. Given the poor reporting of the review process and the lack of quality assessment, these results should be treated with caution.

Authors' objectives
To assess the efficacy of oral fluorinated pyrimidines (o-FP) for long-term maintenance therapy in Japan for curatively resected gastric cancer.

Searching
MEDLINE, PubMed and The Cochrane Library were searched between 1980 and March 2005. Search terms were reported. Additional studies were sought through review articles and reference lists of selected articles.

Study selection
Randomised controlled trials (RCTs) with central randomisation comparing adjuvant chemotherapy for curatively resected gastric cancer with surgery alone, mainly targeting o-FP for adjuvant chemotherapy, were eligible for inclusion. Studies were undertaken in Japan.

The included studies assessed both oral and intravenous chemotherapy regimens at different dose and frequency. The regimens comprised mitomycin C (MMC), 5-fluorouracil (5-FU), cytarabine (ara-C) and uracil and ftoraful (UFT). These regimes were compared with surgery alone. The duration of the chemotherapy regimens ranged from 14 days to 18 months. The duration of follow-up was between five to nine years. The proportion of males ranged from 62-76%. The primary outcome was survival.

The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
For each study hazard ratios (HRs) for survival were extracted. The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction.

Methods of synthesis
Pooled HRs for survival were calculated using the DerSimonian and Laird random-effects model. Statistical heterogeneity was assessed using the Q statistic.

Results of the review
Four RCTs (n=1,330) were included in the meta-analysis.

The estimated HR was 0.73 (95% CI: 0.60, 0.89, p=0.002) indicating a significant effect of o-FPs for chemotherapy on overall survival. There was no significant heterogeneity between studies.

Recalculation of the estimated HR adjusted for the experiment-wise type I error rate of 5% gave a value of 0.72 (95% CI: 0.57, 0.91, p=0.005), indicating a significant effect of o-FPs for chemotherapy on overall survival. There was no
significant heterogeneity between studies.

Authors’ conclusions
In Japan, for gastric cancer patients following curative resection, adjuvant chemotherapy using o-FP for long-term maintenance therapy appears to be effective compared to surgery alone.

CRD commentary
The review addressed a clear question and undertook an adequate search for published studies. There was no specific search undertaken for unpublished literature, thus publication bias may have been present. Reporting on the review process was limited. It is unclear how many of the authors were involved in study selection and data extraction. No assessment of the methodological quality of the included studies was undertaken. The methods used for synthesising the studies were appropriate and sources of heterogeneity were explored. Given the uncertain quality of the included studies, and the lack of reporting of the review process, the reliability of the results of the review may be compromised. It is questionable whether these findings are generalisable to gastric cancer patients outside of Japan.

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

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