Antibiotic prophylaxis in transarterial therapy of hepatocellular carcinoma: a meta-analysis

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CRD summary
Routine use of antibiotic prophylaxis against postoperative infections in patients undergoing transarterial therapy for hepatocellular carcinoma may not have been necessary. The cautious conclusions reflected the evidence presented. However, their reliability was unclear given the limited size and poor quality of the evidence base. The authors’ recommendation for larger prospective trials appears appropriate.

Authors’ objectives
To compare the effect of prophylactic antibiotic treatment versus no prophylactic antibiotic treatment on infectious complications following transarterial procedure for hepatocellular carcinoma.

Searching
MEDLINE, EMBASE, The Cochrane Library and Chinese biomedicine literature database were searched. Search terms were reported. Reference lists of retrieved articles were checked for additional studies. There were no language restrictions.

Study selection
Studies that compared the effect of any antibiotic or combined antibiotics with no prophylactic antibiotic or placebo were eligible. Participants had to undergo transarterial procedure for hepatocellular carcinoma. Randomised and non-randomised studies were included if they had a control group.

The primary outcome of interest was any proven systemic infection such as bacteraemia, septicaemia and sepsis, hepatic abscess and other clinical indications of infection. Secondary outcomes included suspected infection or clinical signs of infection (such as fever, elevated white blood cell count or C-reactive protein level) and duration of hospital stay.

Where reported, patients’ mean/median age was approximately 60 years old. Where reported, most participants were male and had either hepatitis B or C; most had multiple tumour lesions. Where reported, most patients had a Child-Pugh score of A, and mean white blood cells count ranged from 4.8 to 7.3 \( \times 10^9/L \).

Two of the studies used transarterial chemoembolisation, one used transarterial embolisation and one study used one of the two procedures or Yttrium-90. Intravenous cephalosporin alone or combined with metronidazole antibiotics were the most often used before transarterial therapy. Other treatments included ciprofloxacin as initial or maintenance therapy. Regimens varied among the studies. Depending on the antibiotics used, treatment lasted from half an hour to 10 days. Diagnosis of bacterial infection (biological fluid cultures) and hepatic abscesses (using computed tomography) were described in one study each. All treatments were compared to no treatment. Studies were conducted between 1992 and 2007 in Germany, Spain, the USA and China.

Two reviewers independently selected the studies. Disagreements were resolved by discussion.

Assessment of study quality
The quality of randomised controlled trials (RCTs) was evaluated using the Cochrane risk of bias tool which covered: methods of randomisation; allocation concealment; blinding; and intention-to-treat analysis.

Two reviewers independently assessed study quality.

Data extraction
Data on primary and secondary outcomes were extracted to calculate risk ratios (RRs) and 95% confidence intervals (CIs) for dichotomous data, and mean differences (MDs) and 95% confidence intervals for continuous data.

Data were extracted and cross-checked by two reviewers.
Methods of synthesis
A meta-analysis was performed when there was no evidence of considerable heterogeneity. A fixed-effect model was used unless there was significant statistical heterogeneity, in which case a random-effects model was employed. Heterogeneity was assessed using the $X^2$ and $I^2$ statistics. A sensitivity analysis was performed to examine potential risk of bias.

Results of the review
Four studies (three RCTs and one retrospective observational study) were included (224 patients included; 210 patients analysed). Follow-up ranged from one month after discharge to a median of 28 months. All included studies were of poor quality.

Only one study reported cases of hyperpyrexia and acute symptoms of toxicity after transarterial chemoembolisation (one in the prophylactic antibiotic group and one in control). Pooled analyses showed no significant differences between the two groups in rates of patients developing fever (four studies), changes in peripheral white blood cell count or serum C-reactive protein levels (three studies) and length of hospital stay (four studies). Where measured, no evidence of heterogeneity was found ($I^2=0\%$). One study reported on hepatic abscess with no incident reported.

Authors' conclusions
Routine use of antibiotic prophylaxis against postoperative infections in patients undergoing transarterial therapy for hepatocellular carcinoma may not be necessary.

CRD commentary
The review question and inclusion criteria were clear. Several bibliographic sources were searched. Appropriate steps were taken to minimise the risk of error and bias during the study selection, data extraction and quality assessment processes.

The results of the quality assessment were reported and indicated that studies were of poor quality. Methods of measurement of the primary outcome were only reported in one study, which made the reliability of the main findings unclear. Few studies and patients were included in the review, and studies may not have been sufficiently powered to detect a significant difference between the intervention and control groups. Pooling of RCTs and observational studies may not have been appropriate, but results of the observational study were largely consistent with the RCTs.

The cautious conclusions reflected the evidence presented. However, their reliability was unclear given the limited size and quality of the evidence base. The authors' recommendation for future large prospective trials seems appropriate.

Implications of the review for practice and research
Practice: The authors stated that a more judicious use of antibiotics was recommended for patients at increased risk of infection, notably those with concurrent biliary tract disease or a history of biliary reconstruction surgery.

Research: The authors stated that large scale prospective trials that assessed the effects of antibiotic use in patients undergoing transarterial therapy for hepatocellular carcinoma were needed. A sample of 1000 patients might be required to investigate outcomes such as bacteraemia and liver abscess. Further studies should specify the criteria for the diagnosis of bacterial infections. Bacterial infection outcomes should be based on the results of bacterial cultures. The link between postoperative infection and variables such as advanced age and previous gastrectomy should be investigated. The impact of different transarterial therapy modalities on postoperative infections required further research.

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