Octreotide for advanced hepatocellular carcinoma: a meta-analysis of randomized controlled trials

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CRD summary
The review found that it was unclear from the evidence available whether octreotide was effective for treating patients with advanced hepatocellular carcinoma. The review was well conducted in most respects and the authors’ conclusions appear reliable.

Authors’ objectives
To evaluate the effectiveness of octreotide in advanced hepatocellular carcinoma patients.

Searching
The Cochrane Central Register of Controlled Trials (CENTRAL), PubMed, EMBASE, Chinese Biomedical Database, Chinese Journals Full-text Database and Chinese Scientific Journals Database were searched to June 2008. Search terms were reported. Search start dates varied across sources but spanned 1966 to 1994. The search was not restricted by publication status or language.

Study selection
Randomised controlled trials (RCTs) of octreotide used alone for untreated and inoperable hepatocellular carcinoma (diagnosed using criteria specified in the review) were eligible for inclusion. Control groups were required to receive placebo or best supportive care. The review primary outcomes were median, six-month and 12-month survival; secondary outcomes were alpha-fetoprotein levels, quality of life and side effects.

Participants in the included trials were predominantly male; their mean age was 65 to 69 years (where specified) and their age ranged from 24 to 87 years (where specified). Participants differed widely with regard to prognostic factors such as: tumour stage and spread; liver function; aetiology of disease; and disease severity score.

Two reviewers independently selected studies for inclusion, with disagreements resolved by a third reviewer.

Assessment of study quality
Validity assessment was conducted in accordance with Cochrane Collaboration methods. Items assessed included randomisation, allocation concealment, blinding, length of follow-up, losses to follow-up and number of drop-outs.

Two reviewers independently conducted the assessment.

Data extraction
For each trial, risk ratios (RRs) were extracted or calculated for dichotomous variables and mean differences for continuous variables, with 95% confidence intervals (CIs).

Two reviewers independently extracted the data. Authors were contacted for more information as required.

Methods of synthesis
Trials were combined to calculate pooled risk ratios or weighted mean differences (WMDs) and 95% confidence intervals. Both fixed-effect and random-effects models were used: if both models yielded similar results, the fixed-effect results were reported. Heterogeneity was assessed using the \( \chi^2 \) statistic and quantified using the I\(^2\) statistic. If there was significant heterogeneity (p less than 0.05), a random-effects model was reported.

Results of the review
Six RCTs were included in the review (n=350 patients, range 13 to 119). Five RCTs described adequate randomisation methods, none described adequate allocation concealment, only one trial was double blinded, and only one trial described losses to follow-up. Follow-up ranged widely across trial groups, from 0.37 months (minimum) to 32.5 months (median), where reported.

Four RCTs reported median survival time; two trials reported a statistically significant benefit in the octreotide group (p<0.05 and p=0.002). Two trials reported no statistically significant difference between the groups.

Six month survival rate was significantly higher in the octreotide group, using a fixed-effect model (RR 1.30, 95% CI 1.02 to 1.66; three RCTs; χ²=0.09; I²=58.8%), but there was no statistically significant difference between the groups when a random-effects model was used.

There was no statistically significant difference between the groups in 12-month survival rate (three RCTs).

Four RCTs reported alpha-fetoprotein level. Three RCTs found a benefit from octreotide. One RCT found no statistically significant difference between the groups.

Five RCTs reported quality of life. Four RCTs reported strong improvement in the octreotide group, while the fifth RCT (which was double-blinded) reported no statistically significant difference between the groups.

Five RCTs reported side effects and found that octreotide was well tolerated by most participants.

Authors' conclusions
It was unclear from the evidence available whether octreotide was effective for treating patients with advanced hepatocellular carcinoma.

CRD commentary
The objectives and inclusion criteria of the review were clear and relevant sources were searched for studies, without restriction by language or publication status. Publication bias was not formally assessed. Steps were taken to minimise bias by having more than one reviewer independently select studies, assess validity and extract the data.

Appropriate statistical techniques were used to combine the trials and assess heterogeneity. The authors highlighted the small amount of evidence available, the limited quality of the included trials and the differences in participant characteristics that could account for the inconsistency in the review findings.

The review was well conducted in most respects and the authors' conclusions appear reliable.

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

Research: The authors stated that future studies should ensure sufficient power, stratify participants (e.g. by clinical characteristics), blind participants and all study personnel, ensure adequate allocation concealment, and consider excluding participants with end-stage disease. Outcomes, including costs, should be reported in line with the CONSORT (Consolidated Standards of Reporting Trials) statement. Topics for future studies could include use of somatostatin analogues in combination with other therapies for early disease, use of short-acting versus long-acting octreotide, and the prognostic value of somatostatin receptors.

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Not stated.

Bibliographic details
Record Status
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.