Morphine-augmented hepatobiliary scintigraphy: a meta-analysis

Authors' objectives
To compare the sensitivity and specificity of morphine-augmented hepatobiliary scintigraphy (MA-HBS) with that of conventional hepatobiliary scintigraphy (C-HBS), in the diagnosis of acute cholecystitis.

Searching
MEDLINE was searched from 1966 to 1993 for English language articles with MeSH 'Cholecystitis' or 'Radionuclide imaging'. The bibliographies of retrieved articles were examined, and local experts in the field of nuclear medicine were contacted.

Study selection
Study designs of evaluations included in the review
Articles not reporting original data (e.g. reviews, editorials, news articles, letters, case reports) were excluded. Studies where the total number of patients could not be determined, was less than 20, or did not equal the sum of the patients in subgroups mentioned were excluded.

Specific interventions included in the review
Only studies of the diagnostic accuracy of MA-HBS and/or C-HBS were eligible for inclusion in the review. For MA-HBS a positive test had to be defined as non-visualisation of the gallbladder 20-30 min after morphine administration. For MA-HBS studies morphine augmentation had to be generally commenced 60 min after the start of the study if there was non-visualisation of the gallbladder.

Studies were excluded if the criteria for positive and negative test results were not described or if outdated radiopharmaceuticals were used (e.g. 131I Rose Bengal).

Reference standard test against which the new test was compared
Included studies had to confirm diagnosis using an acceptable 'gold' standard - surgery with confirmation by pathology, autopsy, or clinical follow-up with establishment of an alternative diagnosis.

Participants included in the review
The included studies were of patients with suspected acute cholecystitis (may have included some patients with severe illness) who had fasted for at least two hours before the study.

Studies were excluded if they were of atypical patients (e.g. jaundiced patients only or pregnant patients only). Studies that selected patients after surgery had established the diagnosis were also excluded.

In addition, articles that focused exclusively on the following populations were excluded: patients with liver dysfunction; patients with chronic cholecystitis; patients with late development of symptoms of acute cholecystitis after another illness; patients who used total parenteral nutrition; patients fasting longer than 24 hrs without cholecystokinin pre-treatment.

In C-HBS studies, data from patients whose gallbladders were visualised within 60 min, and who were therefore not candidates for MA-HBS, were excluded.

Outcomes assessed in the review
Studies were excluded if sensitivity and specificity could not be calculated from the data presented. Studies where information on acute cholecystitis could not be differentiated from other diagnoses involving the biliary tract were also excluded.
How were decisions on the relevance of primary studies made?
Non-physician research staff reviewed candidate titles. Two independent readers reviewed the remaining studies using pre-determined exclusion criteria relating to patient selection, diagnostic method, gold standard and study design. Reviewers were asked not to consider the authors, institution and publication source.

Assessment of study quality
The authors do not report a method for assessing validity.

Data extraction
Two independent readers extracted the data necessary to calculate the sensitivity and specificity of MA-HBS and/or C-HBS.

Methods of synthesis
How were the studies combined?
The estimates of sensitivity and specificity across studies were combined in a meta-analysis using cluster sampling; the estimated variance of the combined proportion incorporates the between- and within-study estimate variation.

How were differences between studies investigated?
The Pearson chi-squared test was used to determine whether the study results were sufficiently homogeneous to allow them to be combined.

Results of the review
A total of 9 studies were included: 4 on C-HBS involving 214 patients and 5 on MA-HBS involving 166 patients.

The specificity of MA-HBS (0.84, 95% confidence interval, CI: 0.75, 0.94) was significantly greater than that of C-HBS (0.68, 95% CI: 0.61, 0.75) (p=0.008). The sensitivities of the two techniques were similar.

Authors' conclusions
The results of most MA-HBS studies cannot be compared with the results of C-HBS studies because articles describing C-HBS often include non-candidates for MA-HBS. However, when appropriate controls are instituted, the results of this meta-analysis suggest that MA-HBS is more specific than C-HBS in the diagnosis of acute cholecystitis.

CRD commentary
This was a generally adequate systematic review. The research question was clearly stated and well defined in terms of inclusion and exclusion criteria, and the review methodology was generally well reported and robust. The search strategy was limited to a single bibliographic database (MEDLINE) and English language articles, and as such is unlikely to have retrieved all relevant studies. In addition, no assessment of the impact of publication bias was reported.

No information was given on the characteristics (including study quality) of individual studies included in the meta-analysis. It is therefore difficult to assess the extent to which the results of the review may have been prejudiced by methodological flaws in the primary studies. The methods used to pool individual study findings were appropriate and well described. However, estimates of diagnostic accuracy were obtained for the two tests from different studies, and comparisons between them are therefore of dubious value.

In summary, although the reported sensitivities and specificities of MA-HBS and C-HBS follow readily from the findings of the review, the authors' conclusions that the specificity of MA-HBS was superior to that of C-HBS and that the two techniques have similar specificities are not valid, being based upon indirect comparisons.
Implications of the review for practice and research
The authors did not state any implications for practice or further research.

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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.