Does adjuvant steroid therapy post-Kasai portoenterostomy improve the outcome of biliary atresia? A systematic review and meta-analysis
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CRD summary
This review found steroids were ineffective in improving outcomes after intestinal surgery to allow bile duct drainage (Kasai portoenterostomy) in infants; further research was recommended. The conclusion on steroid ineffectiveness should be approached with caution due to review methodological issues. However, the authors' recommendation for further research appears appropriate given small size and limitations of the available included evidence.

Authors' objectives
To determine the efficacy of adjuvant postoperative steroid therapy on the outcome of Kasai portoenterostomy in patients with biliary atresia

Searching
MEDLINE, EMBASE and a Cochrane database (unspecified) were searched from January 1969 to June 2010 for studies in English. Search terms were reported. Reference lists of retrieved articles were searched for other relevant articles.

Study selection
Both randomised controlled trials (RCTs) and observational studies were eligible for inclusion in the review. Eligible studies needed to compare steroid therapy with standard therapy in infants who had undergone Kasai portoenterostomy surgery. Studies of any type of steroid used at any time after Kasai portoenterostomy were eligible. If different steroid doses or types were used within a study, the study was excluded. Risk ratios or odds ratios had to be present or calculable. Relevant outcomes were normalisation of serum bilirubin levels at six months after Kasai portoenterostomy and early liver transplantation (defined as within the first year after Kasai portoenterostomy).

In included studies, the mean age of infants at surgery was three months or younger. The procedure was performed by at least two surgeons in all studies except one. The use and duration of postoperative adjuvant therapies was not uniform across the included studies. Treatment protocols for steroids varied.

More than one reviewer appeared to be involved in study selection for the review.

Assessment of study quality
Methodology of non-randomised studies was assessed using the Newcastle-Ottowa scale. Studies with a low risk of bias were scored ‘A’ (7 to 9 points), with a moderate risk of bias ‘B’ (4 to 6 points) and with a high risk of bias ‘C’ (1 to 3 points). The Jadad score was used to assess RCTs.

Two authors were involved in the assessment of study quality, with discrepancies resolved by consensus.

Data extraction
The authors did not state how many reviewers were involved in the data extraction.

Methods of synthesis
Studies were combined using a random-effects model of meta-analysis to pool odds ratios and generate 95% confidence intervals. An odds ratio from a case-control study was assumed to approximate the risk ratio from a cohort study. Heterogeneity was assessed using $I^2$; analyses with $I^2$ higher than 50% (significant heterogeneity) were not statistically combined.

Sensitivity analyses were planned to investigate the effect of high dose steroids (10mg/kg) versus low/medium dose steroids on the outcomes of interest and to assess whether there was a dose-response effect.
**Results of the review**

Five studies were included in the review (233 participants) comprising one RCT and four observational studies (one cohort study and three case-control studies). Three of the observational studies were graded 'A' (low risk of bias). The included RCT scored 3 out of 5 on the Jadad scale as it did not describe randomisation and blinding procedures in detail.

There was no significant difference in the effect of steroids on normalising serum bilirubin levels at six months (OR 1.48, 95% CI 0.67 to 3.28; I²=50%; five studies). The effect of steroids on early liver transplantation was not statistically significant (OR 0.59, 0.21 to 1.72; I²=43%; three studies). It was not possible to calculate a dose-response effect.

There was an insufficient number of studies to appropriately assess publication bias.

**Authors' conclusions**

Although this review found that steroids were ineffective in improving outcomes of biliary atresia after Kasai portoenterostomy, limitations with the results interpretation were recognised; further research was recommended to fully address this issue.

**CRD commentary**

The review was based on defined inclusion criteria and was underpinned by a search of a small range of resources. It was possible that studies were missed as the review only considered articles published in English. Unpublished studies were not eligible for the review, so there was the possibility of publication bias which could not be fully assessed because of the low number of studies. It was unclear if more than one reviewer was involved in all processes of the review to minimise reviewer bias and error.

Study quality was assessed. Statistical pooling may not have been appropriate given the diverse study designs and varying steroid regimens.

The authors' conclusions on ineffectiveness should be approached with caution. However, given the size and limitations of the included evidence, the authors' recommendation for further research appears to be appropriate.

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

**Practice:** The authors stated that no concrete recommendations can be made on the use of steroids in the postoperative management of biliary atresia.

**Research:** The authors recommended a large, randomised double-blind trial using high-dose steroids to fully assess the effectiveness of steroids on the short-term and intermediate-term outcomes after post-Kasai portoenterostomy for patients with biliary atresia; such a trial should carefully address the confounding factors highlighted in this review.

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