

Cochrane Database of Systematic Reviews

Glucocorticosteroids for infants with biliary atresia following Kasai portoenterostomy (Review)

Tyraskis A, Parsons C, Davenport M

Tyraskis A, Parsons C, Davenport M. Glucocorticosteroids for infants with biliary atresia following Kasai portoenterostomy. *Cochrane Database of Systematic Reviews* 2018, Issue 5. Art. No.: CD008735. DOI: 10.1002/14651858.CD008735.pub3.

www.cochranelibrary.com

Glucocorticosteroids for infants with biliary atresia following Kasai portoenterostomy (Review) Copyright © 2018 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd. [Intervention Review]

Glucocorticosteroids for infants with biliary atresia following Kasai portoenterostomy

Athanasios Tyraskis¹, Christopher Parsons², Mark Davenport¹

¹Department of Paediatric Surgery, King's College Hospital, London, UK. ²Specialist Neonatal and Paediatric Surgery, Great Ormond Street Hospital, London, UK

Contact: Mark Davenport, Department of Paediatric Surgery, King's College Hospital, London, UK. markdav2@ntlworld.com.

Editorial group: Cochrane Hepato-Biliary Group. **Publication status and date:** New, published in Issue 5, 2018.

Citation: Tyraskis A, Parsons C, Davenport M. Glucocorticosteroids for infants with biliary atresia following Kasai portoenterostomy. *Cochrane Database of Systematic Reviews* 2018, Issue 5. Art. No.: CD008735. DOI: 10.1002/14651858.CD008735.pub3.

Copyright © 2018 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

ABSTRACT

Background

Biliary atresia is a life-threatening disease characterised by progressive destruction of both intra- and extra-hepatic biliary ducts. The mainstay of treatment is Kasai portoenterostomy, as soon as the disease has been confirmed. Glucocorticosteroids are steroid hormones which act on the glucocorticoid receptor and have a range of metabolic and immunomodulatory effects. Glucocorticosteroids are used to improve the postoperative outcomes in infants who have undergone Kasai portoenterostomy.

Objectives

To assess the beneficial and harmful effects of glucocorticosteroid administration versus placebo or no intervention following Kasai portoenterostomy in infants with biliary atresia.

Search methods

We searched the Cochrane Hepato-Biliary Group Controlled Trials Register, Cochrane Central Register of Controlled Trials (CENTRAL) in the Cochrane Library, MEDLINE Ovid, Embase Ovid, Science Citation Index Expanded (Web of Science), and online trial registries (last search: 20 December 2017) for randomised controlled trials.

Selection criteria

We included randomised clinical trials which assessed glucocorticosteroids for infants who have undergone Kasai portoenterostomy. For harm, we also considered quasi-randomised studies, observational studies, and case-control studies that were identified amongst the search results.

Data collection and analysis

We used standard methodological procedures expected by Cochrane. We assessed the risk of bias for each trial according to prespecified domains. We analysed data using both random-effects and fixed-effect models. We performed the analyses using Review Manager 5.3 and Trial Sequental Analysis software. We considered a P value of 0.025 or less, two-tailed, as statistically significant. We planned to calculate risk ratios (RRs) for dichotomous outcomes, and the mean difference (MD) for continuous outcomes. For all association measures, we planned to use 95% confidence intervals (CIs) as well as Trial Sequential Analysis-adjusted CIs. We used Trial Sequential Analysis to control the risks of random errors; however, we were often unable to implement this beyond calculating the required information size as there were few trials and data. We assessed the certainty of the evidence using GRADE.

Main results

We found two randomised controlled trials fulfilling the inclusion criteria of our review. The trials provided data for meta-analysis. We judged the two trials as trials at low risk of bias. The two trials randomised a total of 213 infants to glucocorticosteroids versus placebo. In our Trial Sequential Analysis, the required information size (that is, the meta-analytic sample size) was not reached for any outcome. Trials were funded by charities, public organisations, and received support from private sector companies, none of which seemed to have an interest in the outcome of the respective trials. The effect of glucocorticosteroids after Kasai portoenterostomy on all-cause mortality is uncertain; the confidence interval is consistent with appreciable benefit and harm (RR 1.00; 95% CI 0.14 to 6.90; low-certainty evidence). The results showed little or no difference in adverse effects between the use of glucocorticosteroids or placebo after Kasai portoenterostomy, however this analysis was based on a single trial and we have low certainty in the result (RR 1.02; 95% CI 0.87 to 1.20;). Available data suggest that the proportions of infants who do not clear their jaundice at six months is similar between the two groups (RR 0.89; 95% CI 0.67 to 1.17; low-certainty evidence). All-cause mortality or liver transplantation did not differ at two years between the two groups (RR 1.00; 95% CI 0.72 to 1.39; low-certainty evidence). There were no data regarding health-related quality of life.

Our searches also yielded 19 observational studies, some of them containing limited information on harmful effects of glucocorticosteroid treatment. We presented the extracted information narratively. We identified one further ongoing trial with no currently available results.

Authors' conclusions

The two meta-analysed randomised clinical trials present insufficient evidence to determine the effects of using glucocorticosteroids versus placebo after Kasai portoenterostomy in infants with biliary atresia on any of the primary or secondary review outcomes. There is insufficient evidence to support glucocorticosteroid use in the postoperative management of infants with biliary atresia for long-term outcomes of all-cause mortality or liver transplantation. It is also unclear if glucocorticosteroids are able to reduce the numbers of infants who did not clear their jaundice by six months. Further randomised, placebo-controlled trials are required to be able to determine if glucocorticosteroids may be of benefit in the postoperative management of infants with biliary atresia treated with Kasai portoenterostomy. Such trials need to be conducted as multicentre trials.

PLAIN LANGUAGE SUMMARY

Glucocorticosteroids administered after Kasai surgical procedure for infants with blocked or damaged bile duct

Medications used postoperatively (immediately after surgery) for infants with blocked or damaged bile duct (that is, biliary atresia)

Review question

Do medications, called glucocorticosteroids (steroids), have beneficial or harmful effects in the health of infants with biliary atresia operated by the Kasai surgical procedure (that is, portoenterostomy)? We reviewed if there was any difference in death, need for a liver transplant, postoperative jaundice (yellowish or greenish pigmentation of the skin and whites of the eyes), and harmful effects.

Background

Biliary atresia is a rare condition that may occur once in 30,000 births. In biliary atresia, the common bile duct is blocked or damaged; as the bile cannot leave the liver, the liver becomes damaged. An operation called 'Kasai portoenterostomy' is used to replace the damaged bile ducts with a piece of the infant's intestine. This allows the bile to drain directly from the small bile ducts at the edge of the infant's liver, straight into the intestine. Medications called glucocorticosteroids have historically been used in the treatment of biliary atresia after surgery. Two benefits of glucocorticosteroids may be that they are anti-inflammatory, and they increase bile flow. Several studies have been carried out comparing infants taking glucocorticosteroids postoperatively to those who have been given a placebo (an inactive substance that can be made to resemble an active medication or therapy). These studies try to identify if there is any measurable difference in the clearance of jaundice, survival, and need for transplantation. To organise randomised clinical trials large enough to be able to detect differences is, however, challenging.

Study characteristics

We performed a search which included studies up to 20 December 2017. We identified two randomised clinical trials (where participants are divided by chance into the trial groups) which met the requirements for our review and followed-up the participants for at least two years. We identified 19 further observational studies from which we were able to report some findings on harms in a narrative form. The randomised trials included 107 infants who were given glucocorticosteroids and 104 who were given placebo. Trials were funded by charities, public organisations, and received support from private sector companies, all of which did not seem to have any interest in the outcome of the respective trials.

Funding

The included trials outlined their sources of funding, and the review authors deemed that there were no conflicts of interest. Review authors did not receive funding to carry out this review.

Key results

We did not find any differences between the groups of infants treated with glucocorticosteroids compared with placebo in terms of mortality, adverse events, ability to clear jaundice, or need for a liver transplant.

Glucocorticosteroids for infants with biliary atresia following Kasai portoenterostomy (Review) Copyright © 2018 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.



Quality of the evidence

We assessed the two trials as having low risk of bias (we had no concerns that their design and reporting may deviate from the truth), but they were at high risk of imprecision (inexact evaluations of outcomes). They used different categories for adverse events, and we were unable to combine the data from the trials. We could not include enough infants in our analyses (only two published trials) in order to detect small differences between the two intervention groups. The certainty of the evidence was low for mortality, adverse events, ability to clear jaundice, or need for a liver transplant outcomes. One further ongoing trial was identified, with no currently available results.

Future steps

We need further randomised clinical trials that compare glucocorticosteroids with placebo in order to find out if glucocorticosteroids are of benefit in the postoperative management of infants with biliary atresia. Such trials need to be conducted at different clinical centres.