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Original research

Postoperative steroids after Kasai portoenterostomy for biliary atresia: A meta-analysis

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HIGHLIGHTS

- Ten studies, with 1229 patients, were included in this systematic review.
- Steroids may not improve jaundice-free or cholangitis rates over non-steroid.
- The quality of available evidence is limited to make a definitive conclusion.

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ABSTRACT

Aim: The aim of this systematic review and meta-analysis was to determine if adjunct steroids affect jaundice-free, cholangitis, and survival rates after Kasai portoenterostomy. **Methods**: The literature was searched using the following terms: biliary atresia, portoenterostomy, steroids, glucocorticoids, dexamethasone, prednisolone, and hydrocortisone. The primary outcome was the jaundice-free rate. Secondary outcomes were cholangitis and survival rates. **Results**: Ten studies were included in the systematic review and 8 in the meta-analyses. Steroid treatment regimens were inconsistent between studies. The pooled odds ratio (OR) for the jaundice-free rate did not significantly favor steroid over non-steroid treatment (1.95; 95% confidence interval [CI]: 0.91–4.11; $P = 0.087$), nor did the pooled OR for the cholangitis rate (0.75; 95% CI: 0.48–1.17; $P = 0.202$). Overall survival ranged from 58 to 95% in the steroid group and from 36 to 96% in the control group. Native liver survival ranged from 30 to 56% in the steroid group and from 31 to 48% in the control group. The survival data were not suitable for meta-analysis. **Conclusions**: Although these results imply that adjunct steroids after Kasai portoenterostomy for BA may not improve jaundice-free or cholangitis rates, the quality of available evidence is limited and therefore not definitive. Additional high quality studies are needed.

1. Introduction

Biliary atresia (BA) is rare neonatal condition that has been reported to occur in 1 in every 10,000 to 19,000 live births [1–4]. Interestingly, BA may be more common among East Asian populations, with one Taiwanese study reporting an incidence of approximately 1.8 in every 10,000 live births [5]. Pathologically, BA is a progressive obliterative cholangiopathy that may affect both the intra- and extrahepatic branches of the biliary tree [1,2]. The major symptoms are cholestasis, fibrosis, and cirrhosis. If left untreated, BA ultimately leads to portal hypertension, liver failure, and death by two years of age [1,2].

There are two treatments currently available for BA; Kasai portoenterostomy and liver transplantation [1,6]. Of these, Kasai portoenterostomy is the first line treatment, the goal of which is to facilitate bile flow, clear jaundice, and normalize bilirubin levels [1,6,7]. Despite being effective in a relatively large proportion of cases [1], Kasai portoenterostomy is not a curative procedure, and BA ultimately progresses (at variable rates) necessitating the need for liver transplantation [2]. Indeed BA is the most common reason for liver transplantation in children [1]. As the availability of donor livers is always limited, optimizing the success Kasai portoenterostomy is of paramount importance to improve overall rates of survival among patients with BA.

Various adjuvant therapies have been given to patients after Kasai portoenterostomy in an attempt to prevent complications and therefore improve rates of procedural success [1,2]. Of note, in addition to exerting anti-inflammatory and immunomodulatory effects, corticosteroids have been purported to improve bile salt-

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dependent bile flow [1,2,7]. As such, various reports have described adjunct treatment with steroids after Kasai portoenterostomy. The results from these studies, however, have been inconclusive, as discussed in several review articles [1,2,7]. Further, the findings of a systematic review and meta-analysis published in 2011 suggest that adjuvant steroids do not facilitate the normalization of bilirubin levels six months after Kasai portoenterostomy or delay the need for liver transplantation [8]. This meta-analysis, however, did not examine other key factors related to successful treatment, including jaundice-free or cholangitis rates.

To gain further information on the efficacy of adjunct steroids after Kasai portoenterostomy for BA, we conducted a systematic review and meta-analysis of the available literature. The specific aim of our study was to determine if adjunct steroids affect jaundice-free, cholangitis, and survival rates.

2. Materials and methods

2.1. Search strategy

PubMed and The Cochrane Central Register of Controlled Trials were searched using combinations of the following key terms: biliary atresia, portoenterostomy, steroids, glucocorticoids, dexamethasone, prednisolone, hydrocortisone. The literature search was performed on 30 April 2013.

2.2. Selection of studies

2.2.1. Inclusion criteria

Studies were considered for inclusion in the systematic review and meta-analysis if they: were comparative studies; involved patients with BA who underwent Kasai portoenterostomy and received adjuvant steroid therapy; involved patients who had not received liver transplantation; and reported on the effectiveness of adjuvant steroid therapy.

2.2.2. Exclusion criteria

Studies were excluded from the systematic review and meta-analysis if they: were single-arm studies; involved patients who did not receive adjunct steroid therapy; or were reported as letter, comment, editorial, or case report format articles.

2.3. Data extraction

Data were extracted from eligible studies by two independent reviewers. A third reviewer was consulted to resolve any disagreements between reviewers. Information/data extracted included first author and year of publication, study design, treatment groups, number of patients, age and sex distribution of patients, and postoperative jaundice-free, cholangitis, and survival rates.

2.4. Outcomes

The primary outcome of interest was the jaundice-free rate after treatment. The secondary outcomes were the cholangitis and survival rates after treatment.

2.5. Quality assessment

The Newcastle-Ottawa scale was used to assess the quality of the nonrandomized studies included in the systematic review/meta-analysis, whereas Delphi list was used to assess the quality of randomized studies included in the systematic review/meta-analysis.

2.6. Statistical methods

Odds ratios (OR) with 95% confidence intervals were calculated for the jaundice-free and cholangitis rates and were compared between patients who received adjunct steroid treatment (steroid group) and those who did not receive adjunct steroid treatment (control group). Meta-analysis of survival rate was not performed due to the lack of appropriate/sufficient data. Heterogeneity among the studies was assessed by calculating the Cochran Q and the I [2] statistic. For the Q statistic, $P < 0.10$ was considered to indicate statistically significant heterogeneity. The I^2 statistic indicates the percentage of the observed between-study variability caused by heterogeneity. Heterogeneity determined using the I^2 statistic was defined as follows: 0–24% = no heterogeneity; 25–49% = moderate heterogeneity; 50–74% = large heterogeneity; and 75–100% = extreme heterogeneity. If either the Q statistic ($P < 0.1$) or I^2 statistic (>50%) indicated heterogeneity existed between studies, a random-effects model of analysis (DerSimonian-Laird method) was used. Otherwise, a fixed-effects model of analysis (Mantel-Haenszel method) was used. Pooled ORs were calculated and two-sided P value <0.05 was considered to indicate statistical significance. Sensitivity analysis was performed for jaundice-free and cholangitis rates based on the leave-one-out approach. All statistical analyses were performed using the statistical software Comprehensive Meta-Analysis, version 2.0 (Biostat, Englewood, NJ).

3. Results

3.1. Literature search

A total of 481 studies were identified in the literature search (Fig. 1). Of these, 18 underwent full-text review and 8 were subsequently excluded. Hence, 10 studies [7,9–16] were included in the systematic review (8 of these studies were included in the meta-analysis). One study [13] was excluded from the meta-analyses because there was a large difference in patient numbers in each group, while the other [7] was excluded because the patients involved partially overlapped with those included in a later study [16].

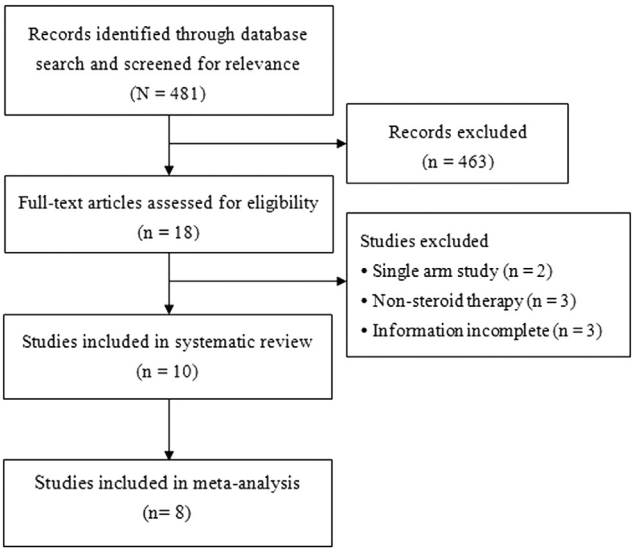

Fig. 1. Flowchart of study selection.