Nontransplant surgical interventions in progressive familial intrahepatic cholestasis

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CRD summary
This review found that non-transplant surgical interventions for progressive familial intrahepatic cholestasis were generally successful in halting progression of disease and resolving symptoms. Treatment failures tended to be associated with advanced disease. The conclusions of the review should be treated with some caution as they are based on low quality evidence and the review itself had some methodological limitations.

Authors' objectives
To evaluate the efficacy and safety of non-transplant surgical interventions in progressive familial intrahepatic cholestasis.

Searching
PubMed was searched for publications in English. Search terms were reported. Search dates were not explicitly stated, but included studies were published between 1988 and 2007. The bibliography of each retrieved article was handsearched.

Study selection
Case reports, case series and clinical trials of outcomes of non-transplant surgical interventions in progressive familial intrahepatic cholestasis (PFIC) were eligible for inclusion. No clinical trials or controlled studies were identified. Interventions in the included studies were: partial external biliary diversion (PEBD); partial internal biliary diversion (PIBD); ileal bypass; and in individual studies, two variants on PEBD that used laparoscopy or an appendiceal conduit. There were two comparative case studies where PEBD was compared to either ileal bypass or transplant. All PFIC patients were diagnosed with progressive cholestasis with low serum gamma-glutamyltransferase values with variations in disease progression at time of surgery; patient ages ranged from four months to 17 years. Follow-up, where reported, ranged from 0.1 to eight years. The included outcomes varied.

One reviewer performed the selection.

Assessment of study quality
There was no formal quality assessment, but all the included studies were case series or case reports.

Data extraction
One reviewer extracted data with spot checks by two other reviewers. Individual participant data were extracted where possible; if not available, averages were extracted.

Methods of synthesis
A narrative synthesis was performed due to heterogeneity in outcomes measured. Mean values were calculated for some outcomes.

Results of the review
Eleven relevant studies were identified (n=77, range one to 24): 10 case series and one case report.

A reported 81% [sic] of patients (63 out of 77) who underwent non-transplant surgical interventions had a successful outcome, with resolution of symptoms, cessation of progression to liver failure and histological improvement. Successful outcomes were also reported for 83% (55 out of 66) of PEBD patients (laparoscopic and appendiceal PEBD patients), 60% (six out of 10) of ileal bypass patients (with one patient the initial response was not sustained) and both patients who underwent PIBD. There were underlying reasons for unsuccessful outcomes in seven patients. Improvements were reported for mean presurgical serum alanine transaminase, mean serum total bilirubin and mean serum bile salts.
Patients with presurgical and postsurgical biopsies showed markedly improved histology (seven patients in four studies), one of which was quantified. Resolution of pruritis was reported in most patients (nine studies); four studies used a 4-point scale (Whittington et al.) and noted an improvement after surgery. Four of five studies reported an improvement in growth velocity.

Complications were not reported systematically, but appeared to be present in at least 17 of 71 cases (24%). Full details were given in the paper.

**Authors' conclusions**

Patients generally had successful outcomes (81%) with cessation of progression of disease and resolution of symptoms. Treatment failures were associated with more advanced disease. There was no evidence to demonstrate superiority of any one type of non-transplant surgical intervention in PFIC patients.

**CRD commentary**

The review addressed the question in terms of participants, interventions and study design. All identified outcomes appeared to be included. Only one relevant database was searched, only studies published in English were included and unpublished studies were not apparently considered; therefore, some studies may have been missed. No formal assessment of study quality was made, but only case series and reports were identified, which have known biases. Minimal efforts appeared to be made to reduce error and bias in the review process. Relevant study details were reported. The authors performed a narrative synthesis due to study heterogeneity. Yet they also calculated mean values, which were not weighted and, therefore, unlikely to be appropriate. It was unclear what a "successful" outcome was. In view of some potential limitations that arose from the review process and low-quality evidence provided from studies with very small sample sizes, the authors’ conclusions should be treated with caution.

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

**Practice**: The authors stated that since it appeared that patients with more advanced disease were most likely to have a poor outcome with non-transplant surgical procedures, clinicians might consider a surgical intervention earlier in the disease course.

**Research**: The authors identified a need for a national registry of PFIC patients with clear inclusion and exclusion criteria and standard data collection, that included quantitative laboratory measurements, with a standard follow-up time of six months and three years, with growth measured initially and annually for at least three years reported as height and weight z-scores for age and relevant data for pruritis (including scores) and histology. A randomised trial that compared PEBD and PIBD was required (especially one that compared quality of life).

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