PAPERS AND SHORT REPORTS

Results of surgical treatment for extrahepatic biliary atresia in United Kingdom 1980-2

Survey conducted on behalf of the British Paediatric Association Gastroenterology Group and the British Association of Paediatric Surgeons

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Abstract

A postal survey identified 114 infants with biliary atresia (roughly one in 21 000 live births). Biliary operations were performed on 107. Of the 105 infants who were followed up, 35 were free of jaundice at 10 months to 3½ years. Good results occurred most often in those operated on by 12 weeks and were also related to the number of cases operated on in each centre. Only two of 18 infants treated in centres dealing with one case a year were free of jaundice compared with 11 of 38 at centres treating two to five cases a year and 22 of 49 in a centre treating more than five cases a year.

Jaundice in an infant of more than 2 weeks associated with yellow urine or pale stools is never physiological and requires urgent investigation to identify causes for which effective treatment may be possible. Identification of suspected cases by 4 weeks of age and a greater concentration of investigative and surgical skills should improve the short term results of surgery and the long term prognosis of biliary atresia.

Introduction

Jaundice in an infant of more than 2 weeks of age associated with yellow urine or acholic stools indicates potentially serious hepatobiliary disease. Urgent investigation is essential to prevent complications and to identify causes for which effective treatment may be available.[1] Among these causes should now be considered extrahepatic biliary atresia, a disorder in which inflammatory destruction of the extrahepatic bile ducts is rapidly followed by a biliary type cirrhosis. Such infants in the first two months of life are often well nourished and have no extrahepatic features of cirrhosis but in untreated cases have a mean age at death of 11 months and a four year survival of 2%.[2,3]

Jaundice free survival after surgery for extrahepatic biliary atresia of the "non-correctable" form—that is, in which there is occlusion of the proximal portion of the extrahepatic bile ducts in the porta hepatis—was first reported by Kasai and Suzuki in 1959.[4] They excised the residual bile duct tissue, exposing bile channels of 50-300 μm in the porta hepatis at the level of the liver capsule, and anastomosed the cut surface to a Roux-en-Y loop of jejunum.[5] By 1983 Kasai could report 41 jaundice free survivors (27% of treated patients) who were well grown and normally active at ages ranging from 5 to 28 years, with 21 more than 10 years of age.[6] The radical surgical procedure employed by Kasai gained acceptance slowly in Japan, but by 1970 a national scheme of management of biliary atresia had evolved.[7] Such surgery has been accepted even more slowly outside Japan, but in the past decade prolonged survival without recurrence of jaundice has been reported in roughly 40% of cases from the United States,[8] Australia,[9], Europe,[10] and the United Kingdom[11] by centres which have concentrated resources on the management of this disorder. All reports have emphasised the importance of early surgery, ideally by 60 days of age and certainly by 90 days of age, in obtaining a satisfactory bile flow. These studies also confirm that the pathology of biliary artresia and the response to surgery are no different from those observed in Japan.

The aim of this study was to ascertain the incidence of biliary atresia in the United Kingdom over the three years 1980-2, assess the short term results of surgical treatment, and determine the age at which surgery had been performed.

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Methods

The data were obtained by a postal survey of members of the British Paediatric Association Gastroenterology Group and the British Association of Paediatric Surgeons, the survey having been endorsed by these organisations. A member who reported cases was identified in each area. A short questionnaire was sent asking for age at surgery, findings at laparotomy, surgical procedure used, lowest subsequent serum bilirubin concentration, presence or absence of jaundice, hepatomegaly, and splenomegaly, and results of the most recent standard biochemical tests of liver function. Complications were to be listed and the age at death recorded. Yearly reminders seeking new cases were accompanied by a form on which follow up data on identified cases were recorded. This report includes data on children born between 1 January 1980 and 31 December 1982. Results were analysed using the χ^2 test with Yates's continuity correction factor.

Results

A total of 114 cases of biliary atresia were reported. Two paediatric surgeons were unable to cooperate in the study. Eight infants were born outside the United Kingdom, giving an incidence of biliary atresia of one in 21 000 to one in 23 000 live births in the United Kingdom (number of births reported to the Office of Population Censuses and Surveys). Seven infants did not have biliary surgery owing to decompensated cirrhosis or congenital anomalies in other systems—for example, cyanotic heart disease. Table I shows the operations performed and the state of the infants at most recent follow up.

TABLE I—*Surgical procedures and outcome*

Biliary surgery	Total No of patients	No not followed up	No jaundice free	No with jaundice	Dead
Hepaticojejunostomy	8	1	3	1	3
Portoenterostomy	65	1	20	16	28
Portoenterostomy plus stoma	22	—	8	9	5
Portogastrostomy	5	—	1	1	3
Portocholecystostomy	2	—	2	—	—
Others*	5	—	1	—	4
No biliary surgery	7	—	—	2	5
Total	114	2	35	29	48

*Portoduodenostomy, hepaticocholecystectomy, hepaticoduodenostomy, cholecystoduodenostomy, choledochoduodenostomy.

TABLE II—*Centres treating biliary atresia in United Kingdom*

	1980	1981	1982
(A) Centres with one case per year	10	5	4
(B) Centres with two to five cases per year	4	5	6
(C) Centres with more than five cases per year	1	1	1
Total No of centres	15	11	11
Total No of cases	37	37	40

Ninety five patients (83%) were treated by Kasai portoenterostomy or a variant, and 12 underwent a conventional anastomosis between residual elements of the bile ducts and bowel—for example, hepaticojejunostomy. The age at surgery ranged from 4 to 36 weeks (median 9·0, mean 10·7 (SD 5·5) weeks). Thirty five children were free of jaundice at ages ranging from 10 months to 3½ years (mean 2 years 3 months (SD 10 months)). Of 27 children operated on between 4 and 7 weeks, 10 (37%) were free of jaundice, as were 18 of 48 (38%) operated on between 8 and 11 weeks; only seven of 30 (23%) operated on after 11 weeks were jaundice free. These differences were not statistically significant.

The 114 patients were treated in 16 different centres by at least 16 different surgeons. The centres were divided into three groups to assess whether the outcome of treatment was influenced by the number of cases seen. Group A centres treated one case a year, group B two to five cases a year, and group C more than five cases a year (table II).

Nineteen infants were reported from centres in group A, and two of 18 (11%) who underwent surgery were free of jaundice. In group B 38 of 41 had surgery, and in 11 (29%) this was successful. Surgery was performed in 51 of 54 infants in the single centre of group C; two were lost to follow up but 22 (43%) were jaundice free. The difference in jaundice free survival rate between this last centre and centres treating only one case a year was statistically significant ($p < 0.05$; χ^2 test). The mean ages at surgery in the three categories of centres were: group A 8·4 (SD 4·7) weeks, group B 9·7 (3·1) weeks, and group C 12·2 (6·9) weeks. Jaundice free survival in group A centres occurred in one of nine children operated on at less than 8 weeks of age, one of six operated on at 8-11 weeks of age, and none of three operated on later. Jaundice free survivals in group B centres at the same age intervals were one of seven, nine of 22, and one of nine, and in the group C centre eight of 11, eight of 20, and six of 18.

The record of complications in the 64 survivors was incomplete, but at least 12 had cholangitis and 21 presumed cholangitis. None bled from oesophageal varices. Fluid loss from a cutaneous stoma caused death in one child and profound shock in another. Prolapse of the jejunum required surgical correction in another child. Four were reported to have bled from their stoma. Rickets was reported in 12 infants.

Discussion

The incidence of biliary atresia found in this survey (roughly 0·5/10 000 live births) was lower than in other series (0·8-1·0/10 000 live births),[12-14] suggesting a degree of underreporting. Furthermore, infants with biliary atresia in the United Kingdom may not necessarily have been managed by paediatricians or surgeons affiliated to either reporting group. Nevertheless, the magnitude of the problem created by extrahepatic biliary atresia, with an incidence comparable to that of phenylketonuria,[15] is confirmed.

In this study the various surgical procedures utilised indicate that Kasai's radical surgical approach to biliary atresia has been adopted by most paediatric surgeons in Britain who are dealing with this problem. Portoenterostomy, portogastrostomy, or portocholecystostomy had been performed in 94 (88%) of the 107 infants in whom bile drainage procedures were attempted. The overall results of surgery with a jaundice free survival rate of 33% suggest that the pathology of biliary artresia and its response to surgery are no different in the United Kingdom from those in other parts of the world.[8-10]

Infants who underwent surgery at centres seeing only one case a year were significantly less likely to have a successful outcome than those having treatment in a centre operating on more than five cases a year, while the outcome in centres treating two to five cases a year was intermediate. This study, based on a very simple questionnaire, could not identify the pathological factors or aspects of preoperative, intraoperative, or postoperative management that might have contributed to this difference in outcome. Nevertheless, in view of the radical and unorthodox nature of the surgery of biliary atresia and the fact that most major surgical procedures have a learning period in which results are less than optimal, probably the experience of the surgeon and the standard of perioperative care were major factors.

The age at which surgery was performed was similar in all centres and therefore did not account for the observed differences in outcome. In the group as a whole, however, the incidence of successful surgery fell with increasing age at the time of operation, but the effect of age did not reach statistical significance. A similar trend was observed in a survey of cases in North America with survival rates being higher when surgery was performed before 90 days of age.[16] The influence of age at surgery on outcome is more clearly seen in series reporting the experience of one surgeon. In a recent report from Kasai's unit 27 of 33 infants (82%) operated on at less than 60 days of age had good bile flow, as compared with 26 of 47 (55%) operated on between 61 and 90 days and five of 13 (38%)

operated on later.[6] In the single centre in our series treating more than five cases a year the jaundice free survival rate with surgery before 8 weeks was 72% compared with 33% after 12 weeks. In this series three quarters of the infants were treated after 60 days of age and one third after 90 days.

These observations and the progressive nature of biliary atresia as evidenced by pathological studies[17 18] suggest that if more infants are to benefit from treatment they must have surgery by 8 weeks of age. This will be possible only if suspected cases are identified earlier and referred to centres with the diagnostic skills to distinguish biliary atresia from the many intrahepatic causes of complete cholestasis, conditions for which surgery is contraindicated.[19] Observations at King's College Hospital suggest that the major cause of delay in diagnosis is a failure to appreciate the importance of jaundice in infancy, particularly in a well grown, healthy looking baby. Parents should be advised that any jaundice persisting into the third week of life is unusual and requires referral to a paediatrician for investigation and possible treatment.

Family and community physicians, health visitors, and district nurses need reminding that persistently yellow or orange urine or stools with reduced pigment accompanying jaundice invariably indicates hepatobiliary disease, which in infants requires urgent investigation. Paediatric referral is often not initiated until review in the infant clinic at 6 weeks of age. If this examination was advanced to 4 weeks of age earlier treatment would be possible. At 4 weeks of age detection of other structural abnormalities and assessment of developmental or nutritional problems and of emotional difficulties in the child-parent interaction—the main objectives of the examination—should be no more difficult than at 6 weeks of age. In Japan infant review is at 1 month of age and the investigation of suspected biliary atresia has been concentrated in a few centres, in each of which the vast majority of operations are done by one surgeon.[7] This survey suggests that a similar approach in the United Kingdom would increase the number of infants who become free of jaundice after surgery and may improve the long term prognosis in biliary atresia.

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References

1 Mowat AP. Current developments in chronic liver disease. In: Hull D, ed. *Recent advances in paediatrics*. 6th ed. Edinburgh: Churchill Livingstone, 1981:138-41.
2 Adelman S. Prognosis of uncorrected biliary atresia: an update. *J Pediatr Surg* 1978;**13**:389-91.
3 Mowat AP, Psacharopoulos HT, Williams R. Extrahepatic biliary atresia versus neonatal hepatitis. A review of 136 prospectively investigated infants. *Arch Dis Child* 1978;**51**:763-70.
4 Kasai M, Suzuki S. A new operation for "non-correctable" biliary atresia; hepatic portoenterostomy. *Shujitsu* 1959;**13**:733-9.
5 Howard ER. Extrahepatic biliary atresia. In: Maingot R, ed. *Abdominal operations*. 7th ed. New York: Appleton-Century-Crofts, 1980:1176-85.
6 Kasai M. Advances in treatment of biliary atresia. *Jpn J Surg* 1983;**13**:265-76.
7 Hayes DM, Kimura K. *Biliary atresia—the Japanese experience*. Cambridge, Massachusetts: Harvard University Press, 1980.
8 Altman RP. Long-term results after the Kasai procedure. In: Daum F, ed. *Extrahepatic biliary atresia*. New York: Marcel Dekker Inc, 1983:91-8.
9 Jones PG, Danks DM, Smith A. Post-operative monitoring in biliary atresia. In: Kasai M, ed. *Cholestasis in infancy*. Tokyo: University of Tokyo Press, 1980:355-8.
10 Valayer J. Biliary atresia and portal hypertension. In: Daum F, ed. *Extrahepatic biliary atresia*. New York: Marcel Dekker Inc, 1983:105-10.
11 Howard ER, Driver M, McClement J, Mowat AP. Results of surgery in 88 consecutive cases of extrahepatic biliary atresia. *J R Soc Med* 1982;**75**:408-13.
12 Shim WKT, Kasai M, Spence MA. Race and biliary atresia. In: Kasai M, ed. *Cholestasis in infancy*. Tokyo: University of Tokyo Press, 1980:5-10.
13 Psacharopoulos HT, Mowat AP, Williams R. Epidemiological study of the hepatitis syndrome in England—incidence and early course. In: Kasai M, ed. *Cholestasis in infancy*. Tokyo: University of Tokyo Press, 1980:11-7.
14 Silverman A, Roy CC, Casetto FJ. *Pediatric clinical gastroenterology*. St Louis: C V Mosby Company, 1971:293-300.
15 Nyhan WL. Phenylketonuria. In: Rudolf AM, ed. *Pediatrics*. 17th ed. Norwalk, Connecticut: Appleton-Century-Crofts, 1982:258-60.
16 Hayes DM, Altman P, Hitch DC, Lilley JR, Smith EI, Urceda JE. Biliary atresia in the United States: the survey of the surgical section of the American Academy of Pediatrics. In: Kasai M, ed. *Biliary atresia and its related disorders*. Amsterdam, Oxford, Princeton: Excerpta Medica, 1983:161-6.
17 Gautier M, Elliot N. Extrahepatic biliary atresia: morphological study of 98 biliary remnants. *Arch Pathol Lab Med* 1981;**105**:379-404.
18 Lawrence D, Howard ER, Tsannotis C, Mowat AP. Hepatic portoenterostomy for biliary atresia; a comparative study of histology and prognosis after surgery. *Arch Dis Child* 1981;**56**:461-3.
19 Markowitz J, Daum F, Khan EI, *et al*. Arterio-hepatic dysplasia. Pitfalls in diagnosis and management. *Hepatology* 1983;**3**:74-6.

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Use of anti-inflammatory drugs by patients admitted with small or large bowel perforations and haemorrhage

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Abstract

The intake of anti-inflammatory drugs by 268 patients with colonic or small bowel perforation or haemorrhage was compared with that by a group of patients, matched for age and sex, with uncomplicated lower bowel disease. Patients with perforation or haemorrhage were more than twice as likely to be takers of anti-inflammatory drugs, but no association was detected with the intake of other types of drugs, particularly cardiovascular drugs.

The association between complicated lower bowel disease and intake of anti-inflammatory drugs may be causal.

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Introduction

The causes of perforation of the gut below the duodenum, except perforation occurring in association with ischaemia, are poorly understood. Slow release enteric coated potassium supplements are known to cause solitary ulcers in the lower small intestine,[1] and it has recently been suggested that the controlled release indomethacin preparation Osmosin may be particularly likely to cause perforation of the lower bowel.[2] Whether other pharmaceutical preparations of non-steroidal anti-inflammatory drugs can damage the lower bowel wall is unknown, although anecdotal reports suggest that they may,[3-5] and no general search has been made to determine if the use of potassium supplements in general or of other cardiovascular drugs is associated with intestinal damage. We therefore examined the drug histories of patients admitted to hospital