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Review Article

Management of adults with paediatric-onset chronic liver disease: Strategic issues for transition care☆

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ABSTRACT

Advances in the management of children with chronic liver disease have enabled many to survive into adulthood with or without their native livers, so that the most common of these conditions are becoming increasingly common in adult hepatology practice. Because the aetiologies of chronic liver disease in children may vary significantly from those in adulthood, adults with paediatric-onset chronic liver disease may often present with clinical manifestations unfamiliar to their adulthood physician.

Transition of medical care to adult practice requires that the adulthood medical staff (primary physicians and subspecialists) have a comprehensive knowledge of childhood liver disease and their implications, and of the differences in caring for these patients. Pending still unavailable Scientific Society guidelines, this article examines causes, presentation modes, evaluation, management, and complications of the main paediatric-onset chronic liver diseases, and discusses key issues to aid in planning a program of transition from paediatric to adult patients.

1. Introduction

In the last few decades, a considerable increase in survival and improvement in quality of life have been observed among children with chronic hepatobiliary diseases [1–6]. An increasing number of patients who were previously treated only in paediatric settings now reach adulthood, and a transition period in which the transfer of their care from the paediatric staff to adulthood specialists needs to be facilitated. This "transfer" from a department with paediatric expertise to an adult program has now been replaced by the term "transition," stressing the need for a process driven by therapeutic and educational standards rather than by purely administrative ones [7]. These strategies have been the object of increasing attention (Fig. 1) for a number of paediatric-onset chronic diseases such as diabetes, cystic fibrosis, rheumatic, gastroenterological and renal diseases [8–12], but are still poorly available in the field of chronic liver diseases [13–15].

Paediatricians in general do not routinely offer transition support services, only one-third of them report making referrals to adult physicians for any of their patients, and less than 15% provide transition education materials to adolescents and their parents [16]. Although many agree that adolescent services need to be enhanced, few empirical data exist on which approaches they can be based on. In all cases, any strategy aiming to implement an effective transition of hepatopatic adolescence to an adult care system calls for acquaintance of the adult hepatologist at least with the most common causes of chronic hepatobiliary diseases, namely those that have an exclusively paediatric-onset or have some peculiar aspects. Here we aim to lay emphasis on a number of circumstances which might find the adult primary physician and hepatologist hesitant in terms of disease knowledge or specific care, and to discuss the possible adaptation of general and/or specific transfer guidelines already proposed for conditions other than liver disease.

2. Paediatric-onset chronic hepatobiliary diseases

The spectrum of chronic liver diseases in childhood is wider than that seen in adults. In addition to infectious, autoimmune, and

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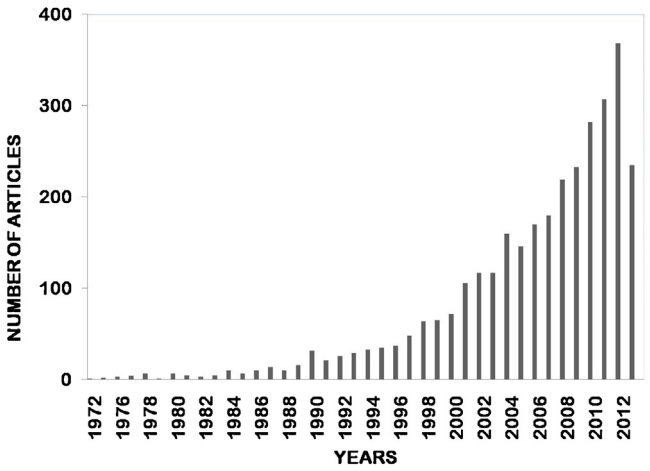

Fig. 1. Increasing number of publications on the topic of '*transition to adult care*' in recent decades.
Source: pubmed.gov (15 September 2013).

iatrogenic conditions, an extraordinarily increasing large number of genetic and metabolic aetiologies are also encountered. In general, these diseases are singularly quite rare, but when considered as a group they represent a considerable cluster. The clinical presentation, diagnosis, treatment, and management of complications also vary. Adult hepatologists should be familiar with these conditions to provide the best possible care at and after the time of transition, including basic genetic counselling [13–15] (Table 1).

2.1. Congenital cholestatic and metabolic liver diseases

Among the most frequent conditions are biliary atresia and Wilson's disease.

2.2. Biliary atresia

Biliary atresia is a progressive fibro-sclerosing cholangiopathy of unknown aetiology, with an incidence of 0.65–0.85 per 10,000 live births in the United States [17]. After timely surgery (porto-enterostomy procedure according to Kasai, possibly within the first 2 months of life) some degree of restoration of bile flow is obtained in a variable percentage of patients (up to approximately 60%). Medical treatment includes long-term therapy with choleretics such as ursodeoxycholic acid, ion exchange resins (e.g. cholestyramine), phenobarbital, rifampicin, and nutritional supplements to avoid deficiency of fat soluble vitamins, fat malabsorption, and protein-caloric malnutrition [14,18]. Complications include bacterial cholangitis, which becomes however increasingly less probable approaching time of transition, variable degrees of portal hypertension, and liver failure [19].

Following biliary surgery only about one-third of patients will retain their livers after the first decade of life. Failure of this procedure leaves liver transplantation as the only chance for survival, and this disease is nowadays still the most common indication for orthotopic liver transplantation (OLT) in children and adolescents. With modern medical care and refinements in surgical techniques, survival after either or both of these procedures is about 90% [20]. As late adolescence in transplanted cases represents one of the most critical points of transition it becomes necessary to extend the duration of follow-up [12]. Gastroesophageal varices require attentive management and treatment at all ages [21]. A comprehensive description of other rarer congenital cholestatic and metabolic liver diseases can be found in Appendix A [22–35].

2.3. Wilson's disease

Wilson's disease is a progressive autosomic recessive (AR) disease with a prevalence of one in 30,000 in most population [36]. Presentation in children is almost exclusively hepatic: the liver disease progresses to fibrosis and then to cirrhosis. Central nervous system symptoms present later, most often during or around/after transition into adulthood if the patient remains unrecognized and untreated, or poorly treated [37,38]. Therapy is based on chronic copper chelating drugs (penicillamine and trientine hydrochloride) or zinc salts. Treatment must be pursued lifelong and may result not completely effective [39]. Except for fulminant cases and a severe course due to medical treatment interruption, Wilson's disease rarely requires OLT [1].

Table 1
Main paediatric-onset liver disorders that may require specific management at and after Transition.

Group	Disease	Specific issues
Surgical cholestasis	Biliary atresia, choledocal cyst	Pregnancy complications
Genetic-metabolic	Alagille syndrome	Cardiovascular accidents
	Progressive familial intrahepatic cholestasis; bile acid synthesis defects	Cholestatic flares during pregnancy and/or stress
	$Alpha_1$-antitrypsin deficiency	Pulmonary disease
	Wilson disease	Neurological disease; compliance to treatment
	Amino acid, carbohydrates, lipid metabolic disorders	Diet
	Other storage diseases (e.g., glycogenosis)	Hepatic adenomas
	Other (e.g., mitochondrial disease)	Systemic localizations
Caroli disease and/or congenital hepatic fibrosis		Cholangiocarcinoma
Autoimmune disorders	Autoimmune hepatitis	Compliance to treatment. Celiac disease and extra GI autoimmune diseases
		Inflammatory flares after pregnancy
	Sclerosing cholangitis	IBD
Nonalcholic fatty liver disease		Metabolic syndrome, polycystic ovary syndrome.
Viral infections	Hepatitis B and C viruses	Pregnancy (mother: HBV antiviral therapy during 3rd trimester to reduce viral load; newborn: HBV specific Ig and vaccination at birth)
Orthotopic liver transplantation		Compliance to treatment, PTLD, de novo AIH, de novo allergies

Abbreviations: AIH, autoimmune hepatitis; GI, gastrointestinal; HBV, hepatitis B virus; IBD, inflammatory bowel disease; Ig, immunoglobulins; PTLD, post transplantation lymphoproliferative disease.