Pediatr Nephrol (2000) 14:856–858 

BRIEF REPORT

**Michel Tsimaratos · Sylvie Cloarec**
**Bertrand Roquelaure · Karine Retornaz**
**Gérard Picon · Brigitte Chabrol · Jean-Michel Guys**
**Jacques Sarles · Hubert Nivet**

# Chronic renal failure and portal hypertension – is portosystemic shunt indicated?

Received: 18 May 1999 / Revised: 8 November 1999 / Accepted: 9 November 1999

**Abstract** We report two girls with histories of recessive polycystic kidney disease. Both were on maintenance hemodialysis. They had undergone surgical distal portocaval shunt because of portal hypertension. Later, bilateral nephrectomy was performed, and they presented with hepatic encephalopathy (HE) and evolution towards irreversible hepatic coma and death. Portosystemic shunt is the treatment of choice of portal hypertension. The kidney plays a pivotal role in ammonia disposal during portosystemic shunt. Thus, we stress the risk of HE after portosystemic shunt followed by bilateral nephrectomy in patients with end-stage renal failure and suggest that combined liver-kidney transplantation should be considered.

**Key words** Autosomal recessive polycystic kidney disease · End-stage renal failure · Portal hypertension · Portocaval shunt · Encephalopathy

## Introduction

Autosomal recessive polycystic kidney disease (ARPKD) accounts for 1%–2% of cases of end-stage renal failure (ESRF) in children [1]. In children surviving the neonatal period, the probability of survival with functioning kidneys at 15 years of age is about 70% [2–4]. Hepatic involvement is frequent and comprises proliferation of dilated biliary ducts, resulting in portal fibrosis and symptomatic portal hypertension (PH) [4, 5]. Portosystemic shunt is the treatment of choice for PH [6, 7]. Hepatic encephalopathy (HE) following portosystemic shunt is rare in childhood [6]. Experimental models of intra- and extra-hepatic portosystemic shunting lead to hyperammonemia and an increase in renal ammonia disposal in response to diminished hepatic ammonia detoxification [8, 9]. We report two pediatric patients with ARPKD on maintenance hemodialysis who died because of HE. Both had portosystemic shunting because of PH, followed by bilateral nephrectomy because of hypertension and chronic pyelonephritis. There was no liver insufficiency. Evolution of encephalopathy was rapidly fatal for both patients despite treatment. The aim of this paper is to discuss the pathophysiology of HE in anephric patients. In this rare situation, and before every therapeutic decision, pediatric nephrologists and hepatologists should be aware of the risk of HE and choose their strategy accordingly.

Presented at the IPNA meeting, London 1998

M. Tsimaratos (✉) · B. Roquelaure · K. Retornaz · G. Picon
J. Sarles
Department of Multidisciplinary Pediatrics,
La Timone Children's Hospital, 13385 Marseille, France
e-mail : gpicon@ap-hm.fr
Tel.: +33-491386742, Fax: +33-491384936

B. Chabrol
Department of Pediatric Neurology,
La Timone Children's Hospital, Marseille, France

J.-M. Guys
Department of Pediatric Surgery, La Timone Children's Hospital,
Marseille, France

S. Cloarec · H. Nivet
Department of Pediatric Nephrology, Clocheville Hospital,
Tours, France

## Case reports

Case 1

Patient 1 was a 6-year-old girl with a history of ARPKD discovered immediately after birth. Hepatic involvement consisted of congenital hepatic fibrosis (CHF) with PH and hypersplenism. Gastrointestinal bleeding and cholangitis were not observed. Liver function tests, including serum bilirubin, transaminases, and prothrombin time, were normal. Progressive evolution towards ESRF necessitated hemodialysis at the age of 5 years. Left nephrectomy was performed in order to reduce the abdominal mass. At the same time, because of hypersplenism and thrombocytopenia, a surgical splenorenal shunt was performed. No overt sign of encephalopathy was observed in the post-operative period. Three months later she had an inversion of portal blood flow on Doppler examination. The shunt was patent. Four months later, she had worsening confusional episodes during the course of pyelonephritis. Serum am-

monia was in the normal range. Electroencephalography, cerebral tomography, and magnetic resonance imaging were normal. After a third episode of pyelonephritis, she presented with regressive dysphonia secondary to a unilateral vocal cord paralysis. Eight months later, because of chronic pyelonephritis, the second kidney was removed. Blood ammonia and electroencephalography were normal. Three weeks after nephrectomy, she presented with abdominal pain, confusion, and pseudo-psychiatric delirium. Liver ultrasonography and Doppler examination showed portal venous occlusion, with no cavernous transformation or thrombosis. The splenorenal anastomosis was large and patent. The blood ammonia concentration was elevated (575 µmol/l). Electroencephalography confirmed HE. Liver function tests remained normal. Despite symptomatic treatment of HE, including continuous veno-venous hemodiafiltration, parenteral protein-free nutrition, bowel decontamination, and lactulose, evolution towards irreversible hepatic coma and death occurred within 3 days.

Case 2

Patient 2 was a 9-year-old girl with a typical history of ARPKD. The diagnosis was made on day 7 of life because of an abdominal mass. Overt signs of hepatic disease appeared at the age of 1 year. She had hypersplenism with pancytopenia, esophageal varices, and presented with episodes of bacterial cholangitis requiring antibiotics. Liver histology confirmed the diagnosis of CHF. ESRF led to hemodialysis at the age of 4 years. During the same period, a preventive mesentericocaval anastomosis was performed. Right nephrectomy was carried out to reduce the abdominal mass. Six months later, she had a first episode of coma with hyperammonemia (442 µmol/l). Symptomatic treatment led to remission. At the age of 7 years, left nephrectomy was performed during an unsuccessful cadaver kidney transplantation (venous thrombosis and transplantectomy on post-operative day 6). She then presented with several episodes of coma, all with the same clinical presentation, including confusion, flapping tremor, abdominal pain, and sometimes variceal bleeding. Liver function tests, including serum bilirubin, transaminases, and prothrombin time remained normal. Liver ultrasonography showed heterogeneous parenchyma. Doppler examination revealed inversion of portal and mesenterical flux and patency of mesentericocaval anastomosis. Electroencephalography confirmed HE. Because of the frequency of coma episodes, we considered emergency liver-kidney transplantation. Unfortunately, and despite symptomatic treatment, she died following a fatal episode of coma at the age of 9 years.

## Discussion

ARPKD is a genetic disease, with renal cysts involving exclusively collecting ducts and biliary dysgenesis comprising proliferation of dilated biliary ducts, which is responsible for PH [5, 7]. Hepatomegaly and splenomegaly are frequent (83% and 61%, respectively) [2]. Gastrointestinal bleeding occurs in 23% of patients even after portocaval anastomosis [3]. In children with isolated hepatic fibrosis and PH, the most-appropriate treatment is surgical portocaval shunt [6, 7]. HE is rare [6]. HE has been reported once in an ARPKD patient undergoing hemodialysis with a portosystemic shunt [3]. Prophylactic portosystemic shunting, followed by renal transplantation, has been described in children with ARPKD [10].

Under physiological conditions, renal ammoniagenesis results from the de-amination of glutamine, mainly (90%) by mitochondrial phosphate-dependent glutaminase. Brush border membrane-bound γ-glutamyltransferase is also partly responsible for renal ammoniagenesis (10%) [8, 9, 11]. Of the total ammonia produced by the kidney, 70% is released into the renal vein, the remainder being excreted into the urine [11]. During the course of mild liver-induced encephalopathy, the renal blood ammonia release stops while urinary ammonia excretion increases, reversing the role of the kidney from net ammonia addition to the body pool to net ammonia disposal [8, 9]. During severe liver-induced encephalopathy, hyperammonemia by far exceeded renal ammonia disposal, contributing to progressive hyperammonemia [8, 9]. This suggests that the normal kidney plays a pivotal role in ammonia disposal during liver insufficiency. In experimental chronic renal failure, kidney γ-glutamyltransferase activity increases to allow an increase in renal net ammonia production [12]. During severe liver insufficiency-induced hyperammonemia, the ammonia disposal capacity appears to be exceeded [8, 9, 13]. Overall, these observations provide evidence that the kidney is a major site of ammonia disposal during mild hyperammonemia. Its capacities are exceeded during severe hyperammonemia. In ARPKD patients, portosystemic shunting is required when PH occurs, regardless of the existence of renal failure. Our patients had portosystemic shunting because of PH. After bilateral nephrectomy, hyperammonamia exceeded net ammonia disposal capacities and resulted in HE. The subsequent evolution was rapidly fatal.

We suggest that in ESRF patients, portosystemic shunting is no longer the treatment of choice for PH, except when following successful renal transplantation. We therefore propose that portosystemic shunting should not be considered in anephric patients with severe PH. In this population, liver-kidney transplantation should be considered early in the course of PH, before the onset of HE.

## References


1. Broyer M, Brunner FP, Brynger H, Fassbinder W, Guillou PJ, Oulès R, Rizzoni G, Selwood NH, Wing AG, Challah S, Dykes SR (1986) Demography of dialysis and transplantation in children in Europe, 1984. Report from the European Dialysis and Transplant Association Registry. Nephrol Dial Transplant 1:9–15
2. Gagnadoux MF (1995) Maladies kystiques des reins. Encycl Med Chir (Paris-France), Pédiatrie, 4-084-C-90, p 4
3. Roy S, Dillon M J, Trompeter RS, Barratt TM (1997) Autosomal recessive polycystic kidney disease: long-term outcome of neonatal survivors. Pediatr Nephrol 11:302–306
4. Kaplan BS, Fay JS, Shah V, Dillon MJ, Barratt TM (1989) Autosomal recessive polycystic kidney disease. Pediatr Nephrol 3:43–49
5. Blyth H, Ockenden BG (1971) Polycystic disease of kidneys presenting in childhood. J Med Genet 8:257–284
6. Alvarez F (1997) Long-term treatment of bleeding caused by portal hypertension in children. J Pediatr 131:798–800
7. Alvarez F, Bernard O, Brunelle F, Hadchouel M, Leblanc A, Odievre M, Alagille D (1981) Congenital hepatic fibrosis in children. J Pediatr 99:370–375

8. Cornelis HC, Dejong CH, Nicolaas EP, Deutz NE, Soeters PB (1993) Renal ammonia and glutamine metabolism during liver insufficiency-induced hyperammonemia in the rat. J Clin Invest 92:2834–2840
9. Cornelis HC, Dejong CH, Nicolaas EP, Deutz NE, Soeters PB (1993) Metabolic adaptation of the kidney to hyperammonemia during chronic liver insufficiency in the rat. Hepatology 18:890–902
10. McGonigle RJ, Mowat AP, Bewick M, Howard ER, Snowden SA, Parsons V (1981) Congenital hepatic fibrosis and polycystic kidney disease; role of porta-caval shunting and transplantation in three patients. Q J Med 50:269–278
11. Halperin ML, Kamel KS, Ethier JH, Stinebaugh BJ, Jungas R (1992) Biochemistry and physiology of ammonium excretion. In: Seldin DW, Giebiesh G (eds) The kidney; physiology and pathophysiology. Raven, New York, pp 2645–2679
12. Dass PD, Martin D (1990) Renal ammoniagenesis in chronic renal failure. Ren Physiol Biochem 13:259–263
13. Hubl W, Druml W, Roth E, Lochs H (1994) Importance of liver and kidney for the utilization of glutamine containing dipeptides in man. Metabolism 43:1104–1107

## LITERATURE ABSTRACTS

**I.C. Macdougall · S.J. Gray · O. Elston · C. Breen · B. Jenkins J. Browne · J. Egrie**

### Pharmacokinetics of novel erythropoiesis stimulating protein compared with epoetin alfa in dialysis patients

J Am Soc Nephrol (1999) 10:2392-2395

Novel erythropoiesis stimulating protein (NESP) is a hyperglycosylated analogue of recombinant human erythropoietin (Epoetin) which has an increased terminal half-life in animal models. The aim of this study was to extend these observations to humans. Using a double-blind, randomized, cross-over design, the single-dose pharmacokinetics of Epoetin alfa (100 U/kg) and an equivalent peptide mass of NESP were compared following intravenous bolus in 11 stable peritoneal dialysis patients. This was followed by an open-label study to determine the single-dose pharmacokinetics of an equivalent peptide mass of NESP by subcutaneous injection in six of these patients. The mean terminal half-life for intravenous NESP was threefold longer than for intravenous Epoetin (25.3 versus 8.5 h), a difference of 16.8 h (95% confidence interval, 9.4 to 24.2 h, $P = 0.0008$). The area under the serum concentration-time curve was significantly greater for NESP (291.0 +/- 7.6 ng x h per ml versus 131.9 +/- 8.3 ng x h per ml; mean +/- SEM; $P < 0.0005$), and clearance was significantly lower (1.6 +/- 0.3 ml/h per kg versus 4.0 +/- 0.3 ml/h per kg; mean +/- SEM; $P < 0.0005$). The volume of distribution was similar for NESP and Epoetin (52.4 +/- 2.0 ml/kg versus 48.7 +/-2.1 ml/kg; mean +/-SEM). The mean terminal half-life for subcutaneous NESP was 48.8 h. The peak concentration of subcutaneous NESP was approximately 10% of that following intravenous administration, and bioavailability was approximately 37% by the subcutaneous route. The longer half-life of NESP is likely to confer a clinical advantage over Epoetin by allowing less frequent dosing in patients treated for anemia.

**G.X. Zaleski · B. Funaki · J.M. Lorenz · R.S. Garofalo M.A. Moscatel · J.D. Rosenblum · J.A. Leef**

### Experience with tunneled femoral hemodialysis catheters

AJR Am J Roentgenol (1999) 172:493-496

**Objective** The purpose of this study was to evaluate the use and complication rate of tunneled femoral hemodialysis catheters placed in patients with no remaining thoracic venous access sites.
**Methods** Over a 3-year period, 41 tunneled femoral vein catheters (35 right, six left) were placed in 21 patients (15 women, six men; 21-89 years old; mean, 52 years). Catheters ranged in length from 40 to 60 cm. Tips were positioned immediately above the iliac bifurcation, at the mid inferior vena cava (IVC), or at the junction of the IVC and right atrium. Catheters were exchanged through the existing tract if the flow rate decreased to less than 200 ml/min. Catheters were removed if an episode of bacteremia did not resolve with antibiotics or if the insertion site became infected.
**Results** Technical success of placement was 100%. The 30-, 60-, and 180-day primary patency rates were 78%, 71%, and 55%, respectively. The 30-, 60-, and 180-day secondary patency rates were 95%, 83%, and 61%, respectively. Average time of function per intervention was 61 days. Infections requiring catheter removal occurred at a rate of 2.4 per 1000 catheter days. One episode of partial IVC thrombosis occurred after a catheter infection developed 78 days after initial catheter placement. No episodes of symptomatic pulmonary embolism occurred. Total length of follow-up was 2506 catheter days.
**Conclusions** Femoral vein catheters require more frequent interventions than do thoracic catheters and are more susceptible to infection. However, in patients with difficult central venous access, the common femoral vein may be successfully used for permanent tunneled hemodialysis access.