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Living related liver transplantation in children with hypoxemia related to intrapulmonary shunting

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Abstract Living related liver transplantation (LRLT) was performed in seven children with hypoxemia related to intrapulmonary shunting. Based on the degree of the shunt ratio calculated by technetium ^{99}m macroaggregated albumin (MAA) scintigraphy, the seven patients were classified in the moderate (shunt ratio under 40 %, $n = 4$) or severe group (shunt ratio over 40 %, $n = 3$). While PaO_2 was maintained over 60 mmHg in the moderate group, that in the severe group continued at a low level of under 40 mmHg in the early postoperative period. However, 48 h after surgery the arterial ketone body ratio recovered to a safe level of 1.0 in both groups. Values of aspartate aminotransferase and serum total bilirubin decreased at a constant rate in both groups. Six patients survived, but one died of portal vein thrombosis on the 53rd postoperative day. Five of six surviving patients recovered from hypoxemia. We concluded that the transplanted liver can tolerate the stress of severe hypoxemia after LRLT.

Key words Living related liver · transplantation Hypoxemia · Intrapulmonary shunting

Introduction

Indications for liver transplantation in patients with hypoxemia related to intrapulmonary shunting have been controversial. Some authors consider severe hypoxemia as an absolute contraindication for liver transplantation [1, 2]. In contrast, it has been documented that hypoxemia in patients with cirrhosis may improve after successful liver transplantation [3, 4]. It would be reasonable to speculate that organs other than the transplanted liver can tolerate the stress of hypoxemia even after transplantation because prolonged hypoxemia existed before transplantation. However, the transplanted liver is suddenly exposed to hypoxemia after liver transplantation. Therefore, the success of liver transplantation in patients with hypoxemia may depend on whether the transplanted liver can function well under hypoxic conditions.

Patients and methods

Seven pediatric patients (one male, six female) with a mean age of 9.8 years (2.4–14.4 years) underwent living related liver transplantation (LRLT) between December 1994 and July 1995. The original liver disease was biliary atresia in all cases. All patients had portal hypertension defined by esophageal varices with previous episodes of bleeding or splenomegaly with hypersplenism. Three patients previously underwent partial splenic embolization (two patients) or splenectomy (one patient) for hypersplenism. Three patients previously underwent distal splenorenal shunt (one patient) or endoscopic sclerotherapy (two patients) for esophageal variceal bleeding. Jaundice was less severe (serum total bilirubin under 4 mg/dl) in these six patients compared to nonhypoxic patients with biliary atresia treated during this period. Only one patient had a moderate degree of jaundice (serum total bilirubin: 28.5 mg/dl).

All patients had cyanosis and digital clubbing. Five had dyspnea on effort and three often required oxygen. Table 1 shows the results of preoperative respiratory tests. Patients were divided into two groups according to the degree of the intrapulmonary shunt ratio calculated by technetium ^{99}m macroaggregated albumin scintigraphy (MAA scintigraphy). The severe group consisted

Table 1 Respiratory test prior to living related liver transplantation (LRLT). Values are mean ± SD (*MAA scintigraphy* technetium ^{99}m macroaggregated albumin scintigraphy)

Group	MAA scintigraphy (%)	PaO_2 at room air (mmHg)	PaO_2 under 100 % O_2 (mmHg)
Moderate ($n = 4$)	25.0 ± 9.4	56.5 ± 4.4	215.9 ± 61.6
Severe ($n = 3$)	54.1 ± 9.0	40.6 ± 6.5	57.3 ± 12.5

Table 2 Changes in aspartate aminotransferase and serum total bilirubin. Values are mean ± SD (*AST* aspartate aminotransferase, *T-Bil* serum total bilirubin, *POD* postoperative day)

	1	2	3	7	14 (POD)
AST (IU/l)					
Moderate	132 ± 24	120 ± 31	64 ± 12	42 ± 15	48 ± 17
Severe	102 ± 8	113 ± 13	58 ± 2	28 ± 9	25 ± 7
T-Bil (mg/dl)					
Moderate	8.9 ± 3.0	5.8 ± 2.2	5.4 ± 3.2	3.3 ± 2.9	1.8 ± 1.4
Severe	6.0 ± 3.1	3.1 ± 0.7	3.0 ± 0.6	2.2 ± 0.6	1.5 ± 0.8

of three patients with a high shunt ratio of over 40 % (44.0–61.1 %), while the moderate group consisted of four patients with a shunt ratio under 40 % (16.1–35.0 %). Increase in the PaO_2 after 100 % oxygen breathing was marked in the moderate group, but the severe group only showed a slight increase.

LRLT was performed electively in all patients. Segmental liver grafts (six left lobe and one lateral segment) were obtained from the patients' parents (three fathers and four mothers). Viability of the liver after transplantation was evaluated by the arterial ketone body ratio (AKBR). As long as the AKBR was maintained over a safety level of 1.0 and vital signs were stable, FiO_2 was not increased over 0.6 and positive end-expiratory pressure (PEEP) was maintained at under 2 cm H_2O. Patients were extubated as early as possible. Immunosuppressive therapy consisted of Tacrolimus (FK 506) and low dose steroids.

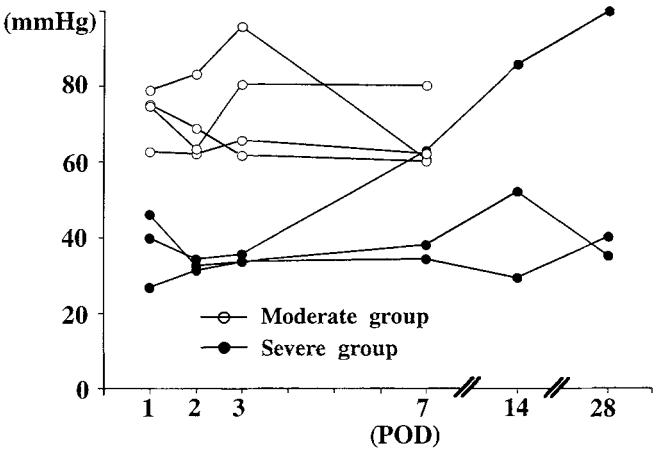

Fig. 1 Changes in PaO_2 after transplantation

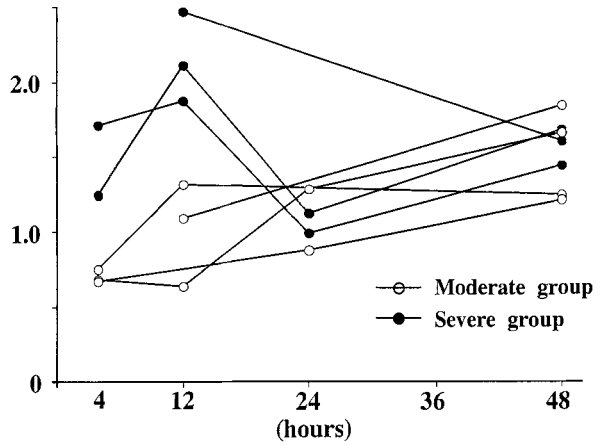

Fig. 2 Changes in arterial ketone body ratio (AKBR) after transplantation

Results

Six patients were extubated on the first postoperative day (1 POD), and one on the 2 POD. Figure 1 shows the changes in PaO_2 after transplantation. In the moderate group, PaO_2 was maintained over 60 mmHg during the first postoperative week, and none of the patients required any more oxygen 2 weeks after transplantation. In contrast, low PaO_2 values (under 40 mmHg) persisted in the severe group. One patient aged 2.4 years in the severe group demonstrated recovery from hypoxemia on the 7 POD, and did not require any more oxygen 2 weeks after transplantation.

Figure 2 shows the changes in the AKBR after transplantation. The AKBR recovered to 1.0 in five patients 12 h after transplantation and remained over 1.0 in all patients 48 h after transplantation. Postoperative peak values of aspartate aminotransferase (AST) were minimal (under 200 IU/l) in all cases, and decreased at a constant rate. There was no significant difference between the two groups. Serum total bilirubin also decreased at a constant rate in the two groups (Table 2). The hematocrit in the two patients in the severe group remained elevated (over 40 %); however, the other patients demonstrated a decrease in the hematocrit (29 %) on the 14 POD concomitant with an improvement in hypoxemia.

One patient in the severe group did not recover from hypoxemia, and the elevated hematocrit persisted. This patient developed portal vein thrombosis on the 37 POD and underwent a second operation to remove thrombi from the portal, superior mesenteric, and splenic veins. However, the patient died of hepatic failure on the 53 POD. Six patients survived, with follow-up periods ranging between 3 and 10 months. Five patients recovered from hypoxemia clinically, and demonstrated

normal blood gas analysis. Closure of the intrapulmonary shunting on MAA scintigraphy was shown in two patients 3 months after transplantation. Another three patients did not undergo this examination. One patient in the severe group had not recovered from hypoxemia 3 months after transplantation.

Discussion

One of the advantages of LRLT is that highly viable liver grafts can be obtained with shorter cold ischemia compared to that in cadaveric liver transplantation. In this study, the AKBR clearly demonstrated that transplanted segmental liver in LRLT functioned well under severe hypoxemia, even when the PaO_2 was under 40 mmHg. Maintenance of good liver function was confirmed by very low values of AST and a steady decrease in serum total bilirubin after transplantation.

Hobeika et al. reported that of nine pediatric patients with hypoxemia three died from worsening hypoxemia after liver transplantation [5]. However, in our series none of the patients died of respiratory insufficiency and all patients were extubated by the 2 POD. We believe that patients with long-term hypoxemia can survive severe decreases in PaO_2, even under 40 mmHg, and that stress on lungs and heart, such as a high PEEP or high FiO_2, can be prevented as long as patients have stable vital signs and stable liver function.

One patient developed portal vein thrombosis at a relatively late stage. The patient had not recovered from hypoxemia at that time, and polycythemia continued. It was speculated that the portal vein thrombosis was partly attributable to the polycythemia. Long-term anticoagulant treatment might be necessary to prevent thrombus formation until the patient recovers from hypoxemia and polycythemia.

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