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• BRIEF REPORT •

Liver transplantation and artificial liver support in fulminant hepatic failure

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INTRODUCTION

Fulminant hepatic failure (FHF) is a severe disease with devastating consequences; the incidence is high in China. Before the availability of liver transplantation, the mortality rate was more than 80%[1,2]. The advent of liver transplantation revolutionized the outcome of FHF[3,4]. However, many patients were unwilling to accept liver transplantation until very late, hence most of them died because of donor shortage and urgency of the disease[5-7]. To overcome the problems, we performed orthotopic liver transplantation (OLT) in combination with artificial liver support (ALS) in the treatment of FHF in the past 2 years with satisfactory results. Our experience was reported below.

PATIENTS AND METHODS

Patients

All eight patients were male with a mean age of 40 (range 32 -49) all had hepatitis B with acute absolute liver failure on admission. These patients had a history of hepatitis for 7 days to 12 weeks, with acute onset of severe hepatic disfunction, rapidly progressive jaundice, abdominal distention, asthenia, ascites, coagulopathy and encephalopathy. Two of them were complicated with acute hepatorenal syndrome and acute necrotizing pancreatitis respectively. Seven patients had stage II-IV coma. All 8 patients received artificial liver support for 2-20 times before transplantation.

Artificial liver support therapy

All patients received artificial liver support treatment with Plasmaflo KM8800 (Kuraray Co. Japan). Plasma exchange (PE), hemodiafiltration (HDF) or bilirubin absorption were singly or jointly selected to treat the patients respectively[8]. On the first treatment, anconeus venous or femorali catheterization was established. Plasma exchange given was 2000mL - 4000mL, plasma transfusion or plasma substitute of 2500 mL - 4500 mL and albumin infusion of 20 g - 40 g each time. The rate of plasma seperation and the flow rate of plasma exchange were controlled at the speed of 20-30mL/ min and 60 - 100mL/min, respectively. The whole course took 3-5 hours.

Procedure of liver transplantation

The 8 patients underwent orthotopic liver transplantation under veno-venous bypass[9,10], of whom 7 underwent standard orthotopic liver transplantation[11] and 1 modified Piggyback liver transplantation[12]. The transplantation was successfully performed with a median anhepatic phase of 78 minutes and operation lasted averagely 5 hours and 30 minutes, but the 2 patients with preoperative renal failure had oliguria during operation. An average bleeding of 5600mL (2000mL-10000mL) was recorded during the operation and the blood lost was collected with Cellsaver.

RESULT

Recipient's survival

All patients became conscious soon after liver transplantation and one in stage IV coma also awoke 2 hours postoperatively. Six of 8 recipients have survived for 2-20 months with good hepatic function, of whom 3 had returned to normal work for more than 18 months. Three days after transplantation, 2 patients died of multi-organ failure (MOF), one with acute necrotic pancreatitis that was unnoticed. Acute rejection occurred in one patient who recovered after anti-rejection treatment of methylprednisolone.

Effect of artificial liver support on FHF

After treatment with artificial liver support the ascites and coagulopathy, decreased serum bilirubin declined, encephalopathy relieved and hepatic function improved (Table 1).

Table 1 Changes of hepatic function before and after ALS

Treatment	N	ALT(U/L)	AST(U/L)	TBil(μmol/L)	IBil(μmol/L)	PT(second)
Before	8	125.4+55.9	132.0+42.9	559.2+209.3	310.8+151.8	40.9+6.7
After	8	120.3+35.5	119.0+29.6	423.7+157.0	252.3+118.5	36.7+6.2
t		0.574	1.336	6.187	4.206	1.959
P		>0.50	>0.20	<0.001	<0.005	>0.05

DISCUSSION

Fulminant hepatic failure progresses rapidly with high mortality and liver transplantation has emerged as an effective therapy for whom do not responded to the standard treatment[13-16]. All patients with FHF must be considered as potential transplantation candidates[17,18]. At King's College Hospital in England, the criteria used for liver transplantation are dependent on the cause of FHF[19,20]. In patients with paracetamol-induced FHF, a pH of less than 7.3 at 24 hours or more after overdose, with concurrent presence of a serum creatinine level greater than 300 μmol/L (>3.4 mg/dL), hepatic encephalopathy of grade III or IV, and a prothrombin time greater than 100 seconds are considered indications for liver transplantation. In non-paracetamol-induced FHF, the decision is based on the occurrence of three of the following: a prothrombin time greater than 50 seconds; jaundice proceeding to encephalopathy more than 7 days; non-A, non-B hepatitis or drug-induced hepatitis; age younger than 10 years or older than 40 years; bilirubin level greater than 300 μmol/L (>17.5 mg/dL); or an isolated finding of prothrombin time of greater than 100 seconds. The indications of 8 patients in our group met with the criteria of King's College Hospital. But in China, where brain death has not been accepted as a criterion for human death, most of the patients with FHF died before the organ became available because not only of the organ donor shortage but also of the rapidity of the course. Thus, it is necessary to develop artificial liver support system as a bridge to cross over to liver transplantation[21,22]. In our study, 8 patients with FHF underwent artificial liver support, then 6 of them survived the most critical period and returned to normal life. Liver transplantation plus artificial liver support creates a new avenue for treatment of FHF.

Artificial liver support system can remove the toxic substances by way of plasma exchange[23], hemodialysis[24], hemo-infiltration[25] and absorption[26], in order to substitute the hepatic function of detoxication[27-31]. Perhaps ALS can remove the toxic substances causing encephalopathy, improve the patients' consciousness, prevent and treat multi-organ failure[32,33]. Why ALS is effective in preventing brain edema is also unelucidated, perhaps by change in permeability of the blood-brain barrier and by raising the osmolality of neural cells[34-36]. ALS, particular the hemodialysis, may prevent the brain edema[37-41]. Our experience showed that pretransplant ALS may not only help the patients to tide over critical period but also increase the chance for liver the transplantation

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