

A Case of Acute Hepatic Insufficiency Treated with Novel Plasmapheresis Plasma Diafiltration for Bridge Use Until Liver Transplantation

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Abstract: A patient with acute hepatic insufficiency induced by a drug presented to our institution, and we performed a novel plasmapheresis that we call plasma diafiltration (PDF). The patient was a 36 year old woman. She underwent 11 sessions of PDF for a duration of about 9 h for each procedure using the Evacure EC-2A filter together with 20 units of fresh frozen plasma and dialysate simultaneously. Serum levels of total bilirubin and prothrombin time were significantly improved after she underwent each procedure. However, after the third procedure the levels returned to the same level as on the previous day. Encephalopathy improved after the first

procedure, and this improvement was maintained until the ninth procedure. The patient prepared to undergo liver transplantation after the tenth procedure because of the development of hepatic coma, but she died of respiratory insufficiency before undergoing the procedure. Accordingly in this case, PDF worked to maintain liver function in acute liver failure and may act as bridge therapy until the patient can undergo liver transplantation. **Key Words:** Bridge use—Fresh-frozen plasma—Hemodiafiltration—Hepatic insufficiency—Liver transplantation—Plasma exchange.

Plasma exchange (PE) has been recognized as a method for extracorporeal immunomodulation in patients with hyperbilirubinemia without the obstruction of the biliary tract, such as occurs in patients with septic hyperbilirubinemia, fulminant hepatitis, and liver failure after undergoing hepatectomy (1–3). In liver transplantation, PE as an artificial liver support is used mainly as bridge therapy until the performance of liver transplantation.

Recently, PE plus continuous hemodiafiltration (CHDF) in series or in parallel (i.e., therapy with PE plus CHDF) has been performed in patients with hyperbilirubinemia caused by postoperative hepatic insufficiency or septic hepatic dysfunction and is considered to be more effective for the removal of cytokines and the avoidance of adverse effects such as metabolic alkalosis and hypocalcemia (4–6). How-

ever, the system for performing this therapy is more complicated and more expensive than others.

The Evacure filter (Kuraray Medical Inc., Tokyo, Japan) is a membrane plasma separator. Bilirubin (Bil) was effectively removed when the Evacure filter was used for the treatment of patients with septic hyperbilirubinemia and plasma diafiltration (PDF) using the Evacure filter alone for PE plus CHDF simultaneously may be useful for the treatment of patients with hyperbilirubinemia with sepsis (unpublished results).

In this report, we describe our experience with a patient who had acute hepatic insufficiency that was treated with PDF as bridge therapy until liver transplantation.

PATIENTS AND METHODS

Patients

The patient was a 36 year old woman who was admitted to our hospital with general malaise and jaundice. She had taken an herbal medicine to lose

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weight 3 months before. On hospital admission, an elevated serum level of transaminase was recognized and increased every day. She was suspected to have hepatitis, however, neither hepatitis B nor hepatitis C was detected in laboratory tests. At that point a liver biopsy was performed, and testing of the specimen revealed drug-induced liver injury. A few weeks later, her platelet count decreased remarkably, her ascite level increased, and she fell into a coma.

Methods

The column (Evacure EC-2A filter, Kuraray Medical Inc.), a membrane plasma separator, had been used conventionally as a secondary column for PE and had been made into an ethylene-vinyl alcohol copolymer with a film area of 1.0 m². The sieving coefficient for albumin is about 0.3. This column tends to compensate for the removal of the middle-molecular-weight substance by the pouring of the dialysis liquid on the hollow fiber outside.

To perform PDF using the Evacure EC-2A filter, the rates of blood flow (QB), dialysate flow (QD), and filtrate flow (QF) were kept at 70 ml/min, 600 ml/h, and 500 to 640 ml/h, respectively, and the unit was supplied with Sublood-B (Fuso Pharmaceutical Co., Osaka, Japan). The patient was infused with 100

ml of a 25% albumin solution at 200 ml/h and 20 units of fresh frozen plasma (FFP) as supplement liquid. The filtration pump was set at a rate of 1,200 ml/h. Futhan (Torii Pharmaceutical Co., Tokyo, Japan) was used as the anticoagulant at a rate of 30 mg/h. The patient underwent the PDF procedure 11 times for a duration of 8 to 9 h per procedure. Between the sessions of PDF, CHDF was performed using the Hemofeel-CH-1.0L device (Toray Co., Tokyo, Japan) which was supplied with Sublood-B at rates of 70 ml/min for QB, 300 ml/h for QD, and 480 ml/h for QF.

Statistical analysis was performed using a paired *t*-test, and $p < 0.05$ was considered to be statistically significant. Values are reported as mean \pm SD.

RESULTS

The mean serum levels of total Bil (T-Bil) and direct Bil (D-Bil) before the procedure were 9.60 ± 1.79 mg/dl and 7.23 ± 2.78 mg/dl, respectively, and the levels after the procedure were 7.26 ± 0.76 mg/dl and 5.17 ± 1.61 mg/dl, respectively, which were significant reductions ($p = 0.0003$ and $p = 0.0017$, respectively) (Fig. 1A and 1B). In comparing all procedures, the first procedure was the most effective yielding a remarkable improvement in the level of consciousness. Encephalopathy was not observed af-

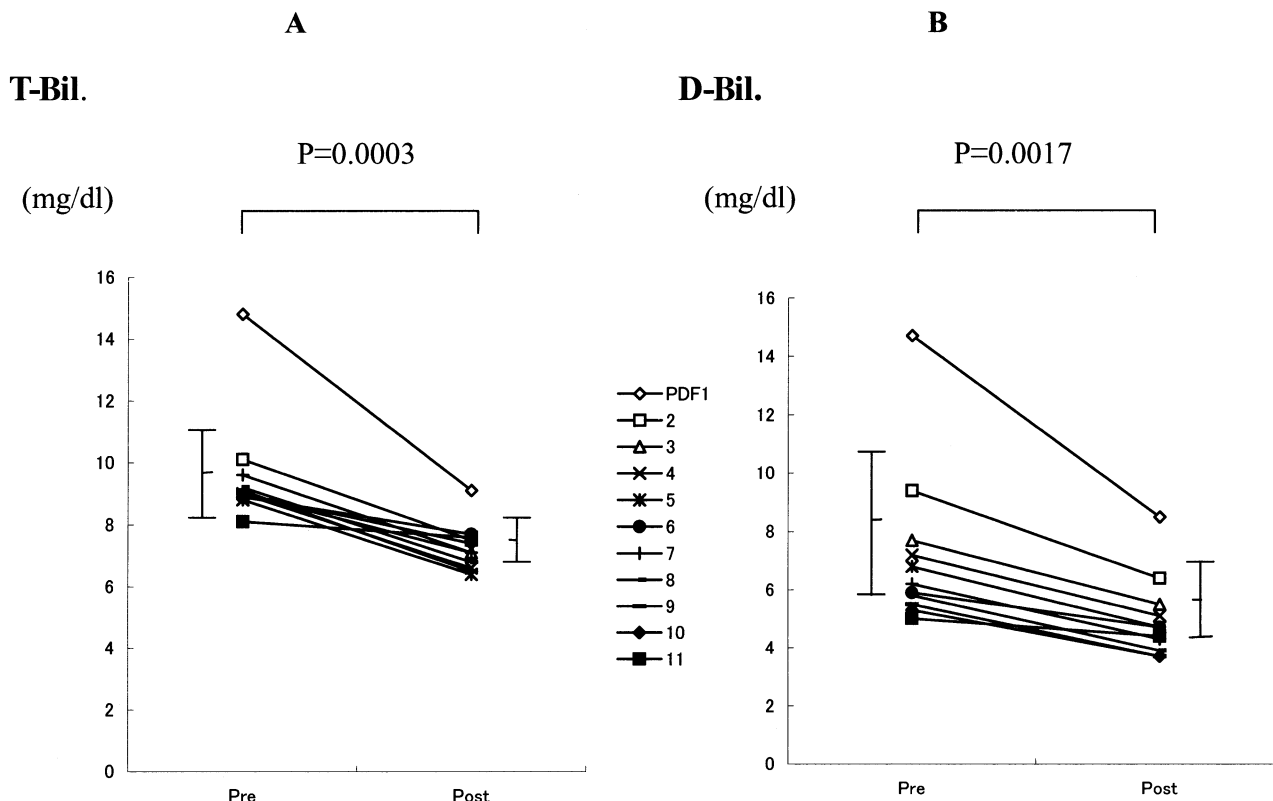


FIG. 1. Changes are shown in the mean values of T-Bil (A) and D-Bil (B) during plasma diafiltration.

ter the ninth procedure, then a worsening of symptoms and hepatic coma developed before the eleventh procedure. The eleventh procedure was not effective in reducing the level of T-Bil, and, indeed, clinically the patient's encephalopathy did not improve.

The mean serum values for prothrombin time (PT) and total protein (TP) level before the procedure were 20.97 ± 2.07 s and 6.03 ± 0.74 mg/dl, respectively, and those after the procedure were 16.89 ± 1.47 s and 6.75 ± 0.571 mg/dl, respectively, which reflected significant improvement ($p = 0.061$ and $p = 0.034$, respectively) (Fig. 2A and 2B).

The changes in the serum levels of T-Bil and D-Bil, and PT and TP before each procedure are shown in Fig. 3A and 3B, respectively. The improvements of T-Bil levels and PT were observed until the third procedure, and after that the serum levels of T-Bil did not change and PTs tended to be worse. Before the sixth procedure, the PT was 21.6 s which was longer than the PT before the first procedure (21.2 s)

After the tenth PDF session, the patient fell into a coma again. She was prepared to undergo a liver transplantation, but her respiratory function continued to decline. The patient died of respiratory insufficiency before undergoing liver transplantation.

DISCUSSION

In this report, PDF was performed in a patient with acute hepatic insufficiency induced by a drug, and the procedure was able to maintain liver function. Recently, PE plus CHDF in series or in parallel (i.e., PE plus CHDF) has been performed in patients with fulminant hepatitis as bridge therapy to liver transplantation and is considered to be more effective compared with the performance of PE alone. It has been reported that PDF, a novel plasmapheresis procedure, works in the same manner as PE and is as effective or more effective than PE for decreasing serum Bil levels postoperatively in patients with hyperbilirubinemia despite using half the volume of FFP. These observations together with the information in this report concerning the use of PDF indicate possible cost reductions and reductions in the risk management of adverse effects from FFP with its use (7). Nevertheless, if the same volume of FFP is used for PDF, the duration for plasmapheresis may be longer, resulting in greater usefulness for patients with liver failure.

In our case, liver transplantation was not performed because of the patient's respiratory insufficiency. Before the sixth procedure, when encephalopathy was not observed, the serum level of T-Bil

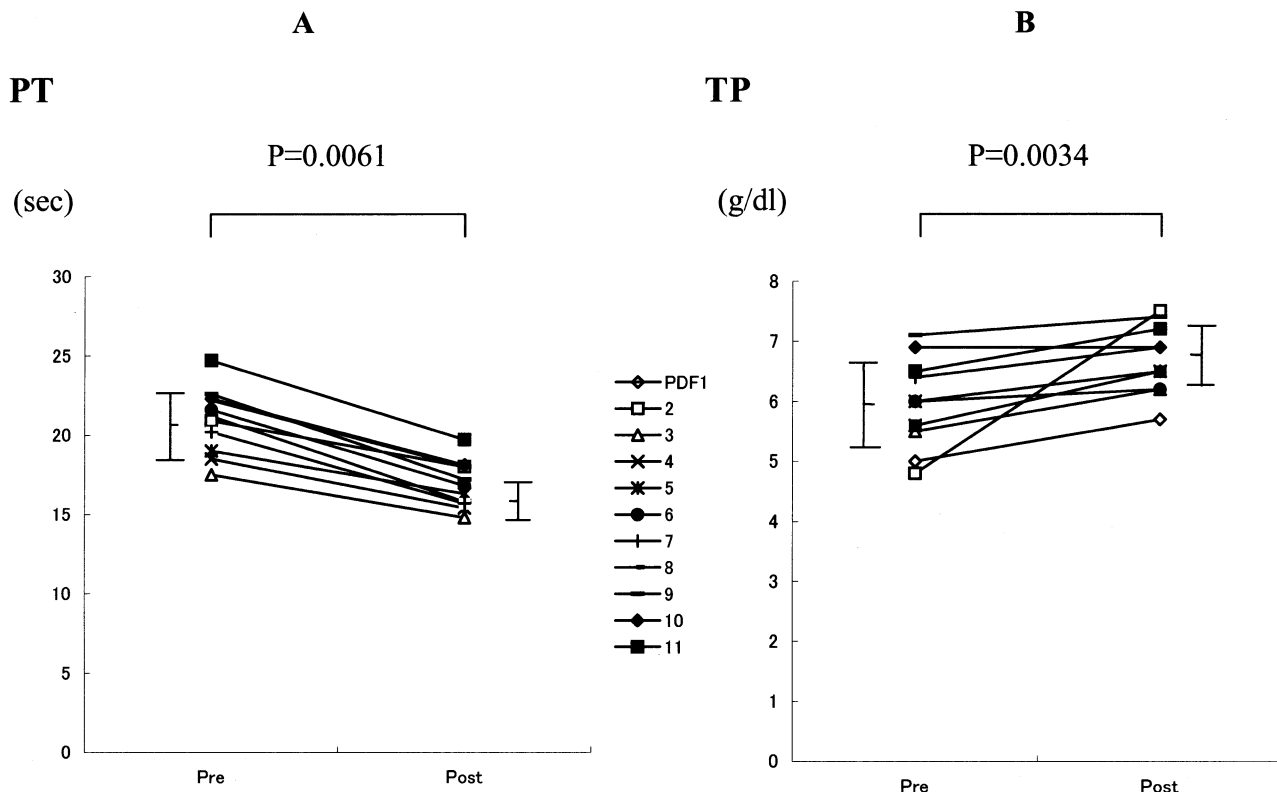


FIG. 2. Changes are shown in the mean values of PT (A) and TP (B) during plasma diafiltration.

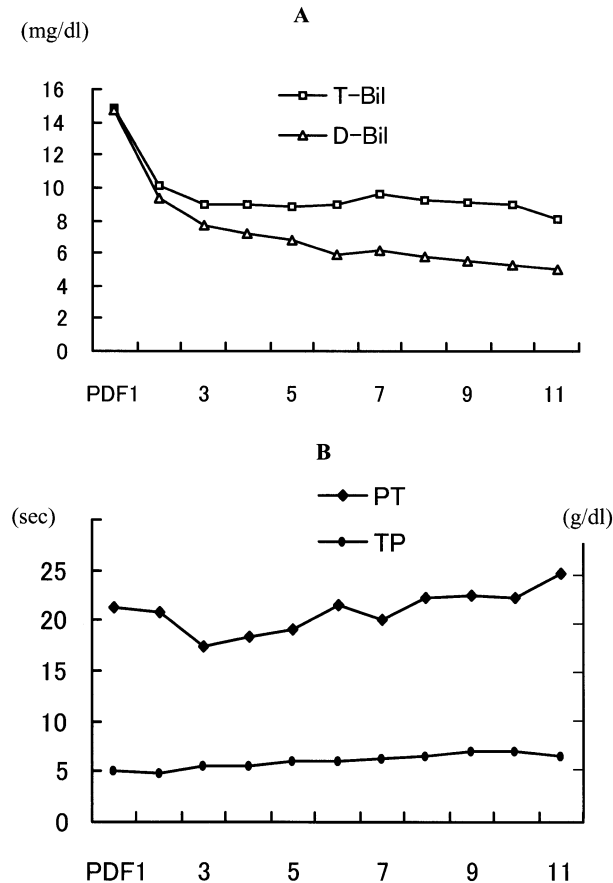


FIG. 3. Changes are shown in the serum levels of T-Bil and D-Bil (**A**), and PT and TP (**B**) before each PDF procedure. (PT: prothrombin time, TP: total protein, PDF: plasma diafiltration.)

slightly increased in comparison with the previous day and the PT was greater than that before the first procedure. These observations may indicate that the patient should begin to be prepared for liver transplantation after the sixth PDF procedure.

In conclusion, the novel plasmapheresis procedure PDF, using the Evacure EC-2A filter alone with a half volume of FFP, is sufficient to maintain patients with acute hepatic insufficiency, and its use is suggested as bridge therapy to liver transplantation.

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REFERENCES

1. McLaughlin BE, Tosone CM, Custer LM, Mullon C. Overview of extracorporeal liver support systems and clinical results. *Ann NY Acad Sci* 1999;875:310-25.
2. Iwai H, Nagaki M, Naito T, Ishiki Y, Murakami N, Sugihara J, Muto Y, Moriwaki H. Removal of endotoxin and cytokines by plasma exchange in patients with acute hepatic failure. *Crit Care Med* 1998;26:873-6.
3. Usami M, Ohyanagi H, Nishimatu S, Kasahara H, Shiroiwa H, Ishimoto S, Ueda T, Saitoh Y. Therapeutic plasmapheresis for liver failure after hepatectomy. *ASAIO Trans* 1989;35:564-7.
4. Sadahiro T, Hirasawa H, Oda S, Shiga H, Nakanishi K, Kitamura N, Hirano T. Usefulness of plasma exchange plus continuous hemodiafiltration to reduce adverse effects associated with plasma exchange in patients with acute liver failure. *Crit Care Med* 2001;29:1386-92.
5. Matsubara S. Combination of plasma exchange and continuous hemofiltration as temporary metabolic support for patients with acute liver failure. *Artif Organs* 1994;18:363-6.
6. Yoshiba M, Sekiyama K, Iwamura Y, Sugata F. Development of reliable artificial liver support (ALS): plasma exchange in combination with hemodiafiltration using high-performance membranes. *Dig Dis Sci* 1993;38:469-76.
7. Sasaki N, Ando Y, Yoshida I, Tabei K, Kusano E, Yoshida M, Asano Y. Differential effect of double filtration plasmapheresis and standard plasma exchange on Guillain-Barré syndrome. *J Artif Organs* 1998;1:15-22.