

**SCOT Forum**

**Single Pass Albumin Dialysis in Hepatorenal Syndrome**

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**ABSTRACT.** Hepatorenal syndrome (HRS) is the most appalling complication of acute or chronic liver disease with 90% mortality rate. Single pass albumin dialysis (SPAD) can be considered as a noble liver support technique in HRS. Here, we present a case of a young healthy patient who developed hyperacute fulminant liver failure that progressed to HRS. The patient was offered SPAD as a bridge to liver transplantation, however, it resulted in an excellent recovery.

**Riyadh Nephrology and  
Transplantation Club**

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Sponsored by : Novartis Pharmaceutical  
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Transplantation

technique that has been underestimated up till now. In comparison to the conventional liver support devices such as molecular adsorbent recirculation system (MARS), SPAD is less expensive and involves use of a regular hemodialysis machine.

**Case Report**

**Introduction**

Single pass albumin dialysis (SPAD) is a unique and effective form of liver support

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A 24-year-old Saudi man was admitted with a two days complaint of diffuse abdominal pain and yellow discoloration of the sclera. His past medical history was unremarkable. There was no history of animal contact, alcohol abuse, or recent travel. The physical examination was remarkable for fever, jaundice, and severely tender epigastrium with positive shifting dullness in the abdomen. However, it was not remarkable for hepatosplenomegaly or signs of hepatic encephalopathy. Initial laboratory investiga-

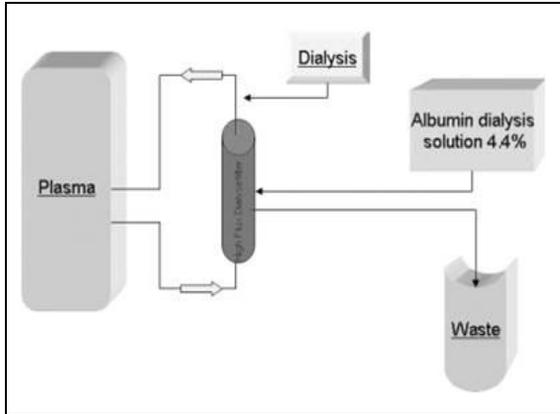


Figure 1. The SPAD circuit design

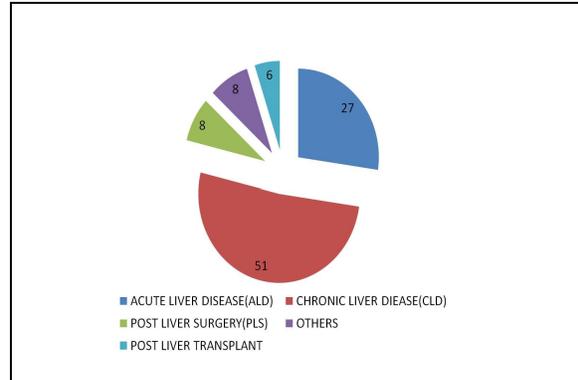


Figure3. Indications for the liver support system

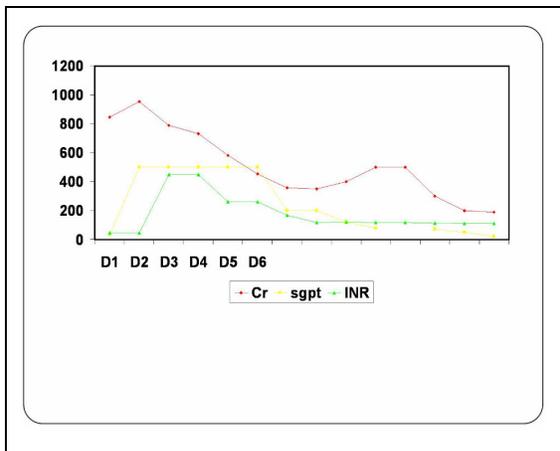
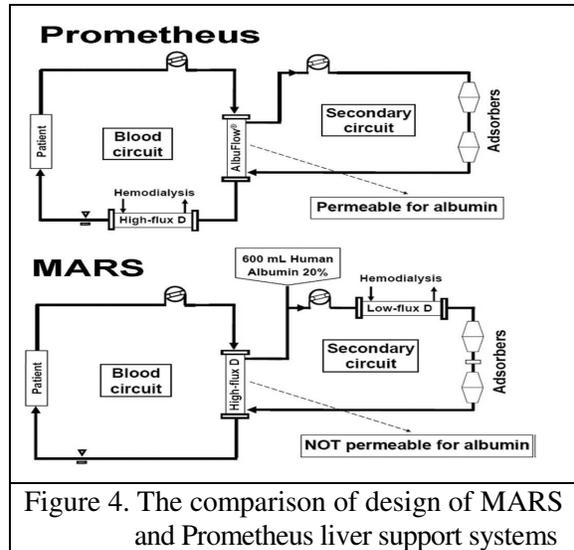


Figure 2. Patient's course in the hospital following use of single pass albumin dialysis (SPAD). There was improvement of prothrombin international normalizing ratio (INR) and serum transferase (SGPT). INR is shown at 100 multiple to be plotted in a common curve. The SGPT is fractionated 5 times for the same reason

tions revealed hemoglobin 10.4 g/dl, White cell count  $6.1 \times 10^3/\mu\text{L}$ , platelets  $104 \times 10^3/\mu\text{L}$ , serum  $\text{Na}^+$  level: 127mmol/L,  $\text{K}^+$ : 4.4 mmol/L, Urea:17.2 mmol/L, Creatinine: 850  $\mu\text{mol/L}$ , ALT: 5225 U/L, AST: 2922 U/L, and Gamma GT:195 U/L. Other investigations revealed positive Hepatitis A (Hep A) IgM, negative serological tests for Brucella, Epstein Barr virus (EBV), Hepatitis B, Hepa-

titis C, and HIV; negative toxicology screen for paracetamol; negative serological tests for autoimmune disease; serum IgA level was within normal; 24-hour urinary volume 744 ml with a total Protein of 0.34 g and creatinine clearance of 8 ml/dl. On 2<sup>nd</sup> day after admission to hospital, the patient's condition deteriorated, and he developed hepatic encephalopathy, but maintained normal hemodynamic signs. Both the computerized tomography scan (CT scan) of brain and the ultrasound of the kidneys were normal. The INR of prothrombin increased to 4-5. The patient was diagnosed as hyperacute fulminant hepatic failure secondary to hepatitis A viral infection and complicated by hepatorenal failure. Although, the patient received fluid challenge, the renal function did not improve. Liver transplantation was contemplated but unfortunately no donor could be arranged. In the meanwhile, conventional hemodialysis was provided to treat the metabolic derangement and fluid overload associated with anuria. However, the patient continued to deteriorate. Hence, an alternative supportive technique was required, and SPAD was selected as a mode of therapy with the following protocol: we used Aquarius Platinum CRRT machine with Aquamax 19 solutions (Baxter Health systems) with access



to circulation through a femoral double lumen catheter without heparin. We adopted continuous venovenous hemodialysis (CV-VHD) mode with 2 Liters/hour dialysate flow and albumin added in alternate dialysate infusion bags to produce a concentration of 4% albumin per liter of dialysate. We modified ultrafiltration to maintain balance of input and output of fluids. We applied the albumin dialysate in 6-hours daily sessions and continued the CRRT without albumin for the rest for the day, hence we named our protocol SPAD. The circuit design is shown in Figure 1. We changed dialyzers every 48 hours as recommended by manufacturer. After 4 days of SPAD and CRRT, the patient had excellent bio-chemical profile, reduction of INR and dramatic improvement of liver function as shown in the Figure 2.

## Discussion

Hepatorenal Syndrome (HRS) is a reversible functional renal impairment that occurs in patients with advanced liver cirrhosis or those with fulminant hepatic failure.<sup>1</sup> Our patient presented all major

diagnostic criteria of HRS.<sup>2</sup> Our patient fitted into type 1 HRS, which has higher mortality than type 2.

Figure 3 summarizes the indications of liver support.<sup>3</sup> Standard management of HRS includes maintenance of MAP 85-90 mmHg by volume expansion with albumin.<sup>4</sup> Various pharmacological agents such as terlipressin,<sup>5,6</sup> ornipressin, midodrane,<sup>7,8</sup> pentoxifylline,<sup>8,9</sup> and octreotide,<sup>7,8</sup> have also been used with success.

Transjugular intrahepatic portosystemic shunt (TIPS)<sup>8</sup> is a better method of treatment of ascitis than controlled paracentesis or the obsolete Denver or Leveen's Shunt that cause increased mortality and morbidity. However, TIPS is contraindicated in patients with severe encephalopathy and patients with high prothombin time >100. As our patient had minimal ascitis, with severe coagulopathy, and grade 4 encephalopathy, paracentesis or TIPS were not indicated. Of the liver systems, we selected the readily available hemodialysis modality SPAD with CRRT modification.<sup>17-21</sup> Recently, similar finding with the use of SPAD has been described, and also the results of SPAD and MARS were comparable.<sup>22</sup> However, SPAD has a simpler circuit compared to MARS, Table 1. Though, the principal of both methods is the same (ie. to remove albumin bound toxins), in SPAD albumin is not recirculated. Fractionated plasma separation (Prometheus system) has also been introduced,<sup>20</sup> which is based on patients' albumin separation through an albumin permeable membrane, and then the albumin bound toxins are removed by the raisin chambers. Here, the patients albumins are cleaned and returned back. This process does not require any exogenous albumin in the circuit. Initial studies are promising. The circuit sign is in comparison with

Table 1. Comparison between MARS and SPAD

Trait	SPAD	MARS
Albumin recirculation	Not done	Done
Amount of albumin used	1 L 20% albumin for 1 Rx of 6 hours duration	600 ml of 20% albumin for 1 Rx of 6 hours duration
Number of coils	one	Four. One high flux MARS albumin dialyzer, one low flux hemodialyzer, two adsorbers
Modality of dialysis	CVVHDF or CVVHD	CWHDF or CWHD
Circuit	Requires no special circuit other than hemodialysis machine	Requires MARS circuit and a hemodialysis machine

MARS in Figure 4. The different methods and devices used as liver support systems is summarized in Table 2. Recently, there is further modification of SPAD in the form of single pass albumin extended dialysis (SPAED) that requires two dialyzers connected one over the other. The first one being a hemodialysis dialyzer, and the second one is for albumin dialysis where the albumin is passed along the dialyzer side at a rate of 30 ml/hr. This modality is currently under review.<sup>23</sup> Nevertheless, when it comes to cost effectiveness, the cost per treatment by SPAD is far less than MARS in US dollar (USD); each MARS treatment costs

approximately 1700 USD, where as SPAD costs only 600 USD.

We conclude that SPAD is an extremely simple technique, as it can be used with the existing hemodialysis machine, can be operated by nursing staff who can handle routine hemodialysis machine and a cheaper option as compared to MARS. It has been shown to reverse HRS in case studies including ours. Moreover, it has been compared with MARS and found to be equally effective. However, its efficacy has been underestimated, hence could not get a global use as the MARS liver support system. As there is huge collection of data on MARS it is

Table 2. Different liver support systems

Biological liver support	Limitations
Cross circulation	Significant risk to the healthy partner (viral infection, sepsis, allergy, and circulatory risk) <sup>10</sup>
Bioartificial liver	No statistically significance in mortality, <sup>11</sup>
Xenoperfusion	Costly, risk of thrombocytopenia <sup>12</sup>
Hepatocyte transplantation	Available only in some centers, <sup>13</sup>
<b>Non biological liver support</b>	
Exchange Transfusion	Case reports <sup>14</sup>
Plasma exchange	Case reports <sup>15</sup>
Hemodialysis	No survival benefit <sup>15</sup>
Hemofiltration	Uncertain impact on survival <sup>10,15</sup>
Hemoadsorption	No survival benefit <sup>16</sup>
MARS	Successful bridging to transplant <sup>17-19</sup>
Fractional plasma separation and adsorption	in vitro studies, promising outcome expected <sup>20</sup>
Single pass albumin dialysis (SPAD)	Underutilized but effective as MARS <sup>21</sup>
Single pass albumin extended dialysis (SPAED)	Study design <sup>24</sup>

premature to regard SPAD superior to MARS. Nevertheless, a greater future use of SPAD will probably prove its efficacy comparable to MARS. The Newer systems such as Prometheus or SPAED are promising but are more expensive than SPAD.

### Questions and Comments

**Dr Akram Askar (King Khaled University Hospital, Chairman of the RNTC):** I would like to thank Dr. Ebadur Rahman for his presentation, and the floor is open for questions.

**Audience:** You mentioned that late application of the liver support devices has poor outcome. Do we have evidence for that?

**Dr. Ebadur Rahman:** The case and uncontrolled reports suggest that but we do not have a prospective trial yet to confirm it. I believe it will confirm the suggested notion that advanced encephalopathy secondary hepatic failure is associated with poor outcome.

**Dr. Al Swaida:** I would like to comment on the availability of liver allografts for transplantation. There is a universal shortage of organ donation that renders the need for liver support devices mandatory. The development of such devices is promising.

**Professor Jamal Al Wakeel:** What about the use of dopamine in the context of albumin dialysis in patients with hepatorenal syndrome?

**Dr. Ebadur Rahman:** There are some observations and theoretical benefit in improving the renal perfusion but prospective studies are required to confirm them.

**Audience:** Would you elaborate on the design of the single pass albumin extended dialysis (SPAED) in comparison to SPAD?

**Dr. Ebadur Rahman:** SPAED device has two dialyzers connected in series, one that runs regular dialysate in it and the following

runs the albumin. So the patient has regular and albumin dialysis at the same time, while SPAD device has one dialyzer that allows regular dialysis and albumin dialysis together.

**Dr. Askar:** Thank you for the attendance.

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