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Letter to Editor

Initial Experience of "Mujib Protocol", Therapeutic Plasma Exchange in Acute on Chronic Liver Failure: A Tribute to Father of the Nation of Bangladesh in his Birth Centennial

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Acute and acute-on-chronic liver failure (ACLF) is the consequence of acute insult of the liver on the background of underlying compensated chronic liver disease and may result from a wide variety of causes. The short-term mortality may be as high as 65% at 3 months [1]. This is the result of multi-organ failure involving both liver as well as extra hepatic organs as a consequence of bizarre systemic inflammation [2].

Progression of compensated cirrhosis to ACLF is due to systemic inflammatory response. This response is characterized by elevated serum levels of cytokines namely, TNF-α, IL-2, IL-4, IL-6, IL-8, IL-10 and interferon. As a result of this systemic inflammatory response inflammation, apoptosis and necrosis of hepatocytes occur. This is further supplemented by cholestasis and fibrosis.

Available therapeutic options are limited for ACLF. Current medical therapy is non-specific and mainly supportive. Standard of care for ACLF patients today involve management of the precipitating event, end organ support and management of complications. Liver transplantation is the only curative option for ACLF. However, the limited availability of donor organs, high cost, limited expertise and lack of wide spread availability limits its usefulness.

Plasma exchange (PLEX) can be employed as a bridging therapy to liver transplantation. It eliminates toxins and facilitates hepatic regeneration. PLEX involves discarding of separated plasma, while cells are reinfused. PLEX offers multiple benefits. It removes bilirubin, endotoxin and complement activators and at the same time

replenishes albumin, coagulation factors etc. These help to correct metabolic derangements.

Endothelial activation is triggered as a result of the acute inflammatory cascade. This leads to high plasma levels of Von Willebrand factor (VWF), which is an endothelium derived platelet adhesive protein. This rise in VWF leads to occlusion of microcirculation by aggregated platelets. As a result multi-organ failure ensues. Similar picture is seen in patients with thrombotic thrombocytopenic purpura (TTP) who also develop primary thrombotic microangiopathies. It has been observed that markedly raised plasma VWF levels can predict mortality in ACLF and is comparable to MELD scoring system.

ADAMTS13 is a disintegrin and metalloproteinase. It has a thrombospondin type 1 motif with supplementation of member 13. When fresh frozen plasma (FFP) is transfused, it provides ADAMTS13. This in turn cleaves VWF multimers. VWF is thus reduced in size and losses activity. PLEX basically works both by removing VWF from plasma as well as by supplying ADAMTS13.

During 'Mujib Borsho' - birth centennial of Father of the Nation of Bangladesh Bangabandhu Sheikh Mujibur Rahman, we introduced PLEX in Bangladesh for ACLF, as a tribute from the Hepatologists of the country which he visioned and liberated. This treatment is dedicated to him and is designated "Mujib Protocol".

Around 1 - 1.5L plasma exchange with fresh frozen plasma for 1 hour daily for 3 consecutive days were performed. The patients also received standard medical care including antiviral, diuretics, albumin, beta blocker, lactulose and proton pump inhibitor. Enteral or parenteral nutrition was provided if calorie requirement was not fulfilled by mouth. Patients were followed up for 3 months or till their death. Patients with hepatocellular carcinoma or any other malignancy, sepsis, severe cardio and/or pulmonary disease and pregnancy were not considered for PLEX.

Our initial experience with PLEX is encouraging with improvement of liver function noted in our first 3 patients (Table 1). We unfortunately lost the third patient from COVID-19. There are several comparable reports in the published literature. A study in 2011 reported 46.7% 30-day survival in PLEX group opposed to 28.7% in standard of care group only [3]. High volume PLEX is also found to be associated with increased survival in non-transplanted patients after three months [4]. The cumulative survival rate at week 4 in the PLEX and control groups was 37 and 18% respectively in entecavir-treated hepatitis B infected patients with hepatic decompensation and ACLF, which further justifies PLEX [5].

PLEX is a new concept for management of ACLF with promising outcome reported from different studies. Here we report our initial experience with PLEX, which is at par with that in published literature. Our study is ongoing and we look forward to presenting data from larger sample size in the future.

Case-1 (HBV flair)	**Before PEX**	**After 1st session**	**After 2nd session**	**After 3rd session**	**After 3 months**
SGPT (U/L)	155	184	113	110	39
Bilirubin (mg/dL)	12.9	10.02	8.67	7.07	4.2
INR	1.72	1.87	1.95	1.78	1.35
Case-2 (DILI on AIH)					
SGPT (U/L)	155	184	113	110	39
Bilirubin (mg/dL)	12.9	10.02	8.67	7.07	4.2
INR	1.72	1.87	1.95	1.78	1.35
Case-3 (DILI on NASH)					
SGPT (U/L)	26	-	-	48	-
Bilirubin (mg/dL)	30.8	-	-	18.1	-
INR	1.41	-	-	1.38	-

Table 1: Outcome of PLEX in three ACLF patients.

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