ACLF Patient Treated with Plasma Exchange

Professor Mamun Al Mahtab (Shwapnil)
MBBS, MSc (Gastro.), MD (Hepato.), FICS (India)
FRCP (Ireland), FRCP (London), PhD (University of Malaya)
Head, Interventional Hepatology Division
Bangabandhu Sheikh Mujib Medical University
Member, Strategic Technical Advisory Group on Viral Hepatitis
WHO-SEAR

Particulars of the Patient

- Age: 41 years
- Sex: Male
- Occupation : Private service
- Date of admission: 4 March, 2020
- No previous history of liver disease
- No family history
- Chief Complaints:
  - Jaundice for 28 days
  - Abdominal distension for 15 days

General Examination

- Well alert, cooperative
- Appearance - Ill looking
- Body built - Normal
- Nutrition - Average
- Decubitus - On choice
- Anaemia - Moderate
- Jaundice - Present
- Cyanosis - Absent
- Clubbing - Present
- Koilonychia - Absent
- Leukonychia - Absent
- Oedema - Present

- Pulse - 72 bpm, regular
- Blood Pressure - 110 / 70 mm Hg
- Respiratory Rate - 16 / min
- Temperature - 99 F
- Lymph Nodes - No lymphadenopathy
- JVP - Not raised
- Flapping Tremor - Absent
- KF Ring - Absent
- Bony Tenderness - Absent
- Skin Condition - Normal
- Dehydration - Absent

Alimentary System Examination

Mouth and oral cavity : Normal

Per-abdominal examination :

Inspection :-

- Abdomen distended
- Umbilicus centrally placed and everted
- Flanks full
- No visible lump, peristalsis, engorged veins or scar mark

Palpation :

- **Liver -** Not palpable.
- **Spleen -** Palpable, 3cm from left costal margin along it's long axis
- **Kidneys -** Not ballotable
- **Abdominal lymph nodes -** Not palpable
- **Hernial orifices -** Intact

Percussion :

Ascites is present, positive shifting dullness

Auscultation :

Bowel sound present

No hepatic bruit or rub

- Examination of other systems show no abnormality

Complete Blood Count

	4 March, 2020
Hb (g/dL)	11.2
ESR (mm in 1st hour)	30
WBC (cells/cu.mm)	13,500
Neutroplils	83 %
Lymphocytes	13 %
Eosinophils	02 %
Platelets (cells/cu.mm)	250000

Liver Function Tests

	4 March, 2020
SGPT (U/L)	981
SGOT (U/L)	1478
Bilirubin (mg/dL)	38.7
Prothrombin Time (sec) INR	44.2 3.43
Alkaline Phosphatase (U/L)	112
Albumin (g/dL)	2.2

Serum Electrolyte

	4 March, 2020
Electrolytes Na + (mmol/L) K + (mmol/L)	 126 4.49
Creatinine (mg/dL)	0.55
GGT (U/L)	88

Viral Markers

	2 March, 2020
HBsAg	Positive
Anti HCV	Negative
Anti HAV IgM	Negative
Anti HEV IgM	Negative

HBV Profile

	22 February, 2020
HBeAg	Positive
Anti- HBc IgM	Positive
HBV DNA	$7.59X10^5$ IU/ml

USG of HBS

- Evidence of cirrhosis of liver
- No SOL in liver
- Splenomegaly
- Ascites

Endoscopy

- Grade-II oesophageal varices
- Portal hypertensive gastropathy
- Gastric Erosion

Diagnosis

- Acute on Chronic Liver failure
  - Chronic: CHB
  - Acute: HBV Flair

Plan of Management

- General management
- Antiviral against HBV
- Management of ascites
- Management of portal hypertension
- Plasma exchange

Mechanism in Liver Failure

- PLEX mitigates the proinflammatory response responsible for many of the complications of liver failure
- PLEX not only removes bilirubin, endotoxin and complement activators, but also replenishes albumin, coagulation factors and hepatic regenerative stimulating substance, which can correct metabolic disorder
- In critically ill patients, SIRS contributes to disseminated intravascular coagulation, development of microvascular thrombosis and consequent multiorgan failure
- Von Willebrand factor (vWF), released from activated endothelium in very high molecular weight forms, is an adhesive protein to which platelets stick
- In patient with sepsis, development of organ failure and systemic inflammation is linked to imbalance of vWF–ADAMTS13, high vWF levels and low levels of ADAMTS13 (a vWF-cleaving protease)

- In patients with cirrhosis (of varied etiology, including viral and alcohol), vWF levels correlate with hepatic fibrosis, hepatic vein pressure gradient, and predict survival over next 2–3 years.
- In acute liver failure, vWF–ADAMTS13 imbalance predicts survival.
- Therapies to lower VWF levels are available like N-acetyl cysteine (NAC), fresh frozen plasma (FFP) infusions, and plasma exchange (PLEX).
- NAC reduces disulphide bonds in VWF, thus decreases the size of VWF multimers and hence their prothrombotic potential.
- FFP transfusion provides ADAMTS13 supplementation.
- ADAMTS13 is an enzyme which cleaves VWF multimers and reduces its size and activity.
- PLEX works both by removing VWF from patient's plasma as well as supplying ADAMTS13

Reference from Previous Studies

- APASL ACLF 2019 recommended PLEX as a promising and effective bridging therapy to LT and spontaneous regeneration
- Also mentioned it as a specific therapy for Wilson's disease and flare of AIH
- In a study conducted by Yue-Meng et al (2015) found that cumulative survival rate 3 months was 29% in the PLEX group and 14% in control group ($p<0.05$)
- Larsen et al (2016) observed significant improvement in transplant free survival after High Volume Plasma exchange (HVP)

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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

Mamun Al Mahtab[1]*, Ahmed Lutful Moben[2], Md Abdur Rahim[3], Md Ashraful Alam[4], Sheikh Mohammad Noor-E-Alam[1], Faiz Ahmad Khondaker[5], Most Rokshana Begum[5], Dulal Chandra Das[1], Md Atikul Islam[6], Partho Pratik Roy[7], Md Zahurul Huq[8], Mohammad Helal Uddin[9] and Musarrat Mahtab[10]

[1]Department of Hepatology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh

[2]Department of Medicine, Kurmitola General Hospital, Dhaka, Bangladesh

[3]Department of Hepatology, Abdul Malek Ukil Medical College, Noakhali, Bangladesh

[4]Department of Hepatology, Shaheed Tajuddin Ahmed Medical College, Gazipur, Bangladesh

[5]Department of Hepatology, Shaheed Suhrawardy Medical College, Dhaka, Bangladesh

[6]Sheikh Russel GastroLiver Institute and Hospital, Dhaka, Bangladesh

[7]Department of Anatomy, Shaheed Suhrawardy Medical College, Dhaka, Bangladesh

[8]Department of Anesthesiology, National Institute of Cardiovascular Diseases, Dhaka, Bangladesh

[9]Forum for the Study of the Liver, Dhaka, Bangladesh

[10]Department of Biochemistry and Biotechnology, North South University, Dhaka, Bangladesh

***Corresponding Author:** Mamun Al Mahtab, Professor, Chairman, Department of Hepatology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh.

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Plasma Exchange Strategy

- 3 sessions for consecutive 3 days
- 1-1.5L plasma in each session
- Femoral vein was used as port
- Followed up for up to 3 months

LFT During PLEX

	Before PEX	After 1st session	After 2nd session	After 3rd session
SGPT (U / L)	293	186	121	91
Bilirubin (mg / dL)	33.0	23.1	21.12	18.4
PT (sec) INR	31.8 2.59	23.0 1.87	24.0 1.96	20.5 1.73
Calcium (mg/dl)	8.0	8.7	8.61	8.6
Phosphate (mg/dl)	2.3	2.6	2.3	1.4

Post PLEX Follow up after 3 Month

	Pre PLEX Value	After 3 month
Hameoglobin (gm/dl)	12.6	14.8
WBC (/cmm)	18,000	6,500
Platelet (/cumm)	296000	310000
Na (mmol/L) **K (mmol/L)**	124 4.4	141 5.3
S. Albumin (mg/dl)	2.3	3.4

	Before PLEX	After 3 month
SGPT (U / L)	293	58
Bilirubin (mg / dL)	33.0	1.8
PT (sec) INR	31.8 2.59	16.3 1.17
Calcium (mmol/l)	2.0	2.4
Phosphate (mg/dl)	2.3	2.0
Creatinine (mg/dl)	0.55	1.1
APTT (Control) Patient	26 34.50	37.1 29.5
Ferritin (ng/ml)	549	356

Follow up after 1 year (March, 2021)

- General status improved
- Patient non icteric
- Mild ascites in USG
- HBV-DNA undetected.

Comparative Study between Plasma Exchange and Standard Care

- Total 28 patients were divided in 2 groups in 1 year.
- At 90 days, 46.43% patient survived.
- 57.1% survived in Plasma Exchange group and 35.7% in standard medical therapy group.
- Serum bilirubin and ALT declined significantly after 7 days, 30 days but not after 90 days in Plasma Exchange group.
- Significant ($p<0.05$) improvement of MELD, MELD-Na and AARC score were observed in each group from base line

Issues to be Resolved

- Plasma volume exchanged in each session?
- Number of sessions, a fixed number or up to improvement?
- Appropriate time to start?
- Selection of cases?

Thank You