GOVERNMENT OF KERALA

Abstract

Health & Family Welfare Department - "Standard Operating Procedure for Plasma Exchange (PLEX) to treat patients with Severe Hepatitis A" - orders issued.

HEALTH & FAMILY WELFARE (F) DEPARTMENT

G.O.(Rt)No.1311/2024/H&FWD Dated,Thiruvananthapuram, 31-05-2024

Read:- Letter No. K3-3403/2024/DME dated 22.05.2024 from the Director of Medical Education, Thiruvananthapuram.

ORDER

In view of the current outbreak of Hepatitis A in the state, Government are pleased to issue a "Standard Operating Procedure for Plasma Exchange (PLEX) to treat patients with Severe Hepatitis A", as annexed to this order.

(By order of the Governor)
RAJAN NAMDEV KHOBRAGADE
ADDITIONAL CHIEF SECRETARY

To:
The State Mission Director - National Health Mission, Thiruvananthapuram.
The Director of Health Services, Thiruvananthapuram.
The Director of Medical Education, Thiruvananthapuram.
The Executive Director, Kerala State Organ and Tissue Transplant Organization.
Principal Accountant General (A&E/Audit) Kerala, Thiruvananthapuram.
Information & Public Relations (Web & New Media) Department.
Stock File/ Office Copy to file F2/162/2024-HEALTH.

Forwarded /By order

Signed by
Vilasini K V
Date: 31-05-2024 21:30:42

Section Officer

Annexure

STANDARD OPERATING PROCEDURE FOR PLASMA EXCHANGE (PLEX) TO TREAT PATIENTS WITH SEVERE HEPATITIS A

Preamble:

The spectrum of acute hepatitis A(HAV) infection can be acute hepatitis, acute liver injury, acute liver failure and acute on chronic liver failure (acute liver insult being HAV).

Acute liver injury is defined as acute liver dysfunction with coagulopathy, without encephalopathy. There is no consensus on the definition of severe acute liver injury. Acute liver failure is the presence of acute liver dysfunction, coagulopathy and encephalopathy.

Prognosis in patients with severe liver damage caused by HAV

Patients with uncomplicated acute hepatitis A do not die. However, deaths are seen in patients with HAV induced severe acute liver injury, death rate further increases in patients with acute liver failure.

In a recent study from Kolkota, 3 of 33 patients hospitalised with severe acute liver injury (ie. INR > 1.5) due to HAV progressed to ALF, one of the 3 patients died. This hospital based study suggests that about 10% of patients with HAV induced severe acute liver injury will progress to acute liver failure.[1]

More severe illness may be seen in pregnant women, older age, patients with cirrhosis and patients on immunosuppressive medications.

ALFA score (derived specifically for HAV —ALF), King's college criteria to list for urgent liver transplantation and MELD score are prognostic scores used to predict survival in patients with HAV - ALF. [2] In this study which enrolled patients from 2007 - 2014, spontaneous survival rate was 59.2% (in 294 patients in the derivation cohort) and 58.9% (in 56 patients in the validation cohort) of HAV induced ALF patients.[2]

Treatment

Effective anti-viral medicines are not available at present to treat hepatitis A.

Treatment of cerebral edema in patients with HAV- ALF.

Cerebral edema is a serious complication in HAV - ALF. Anti-cerebral edema measures are needed to treat this.[3] Treatment should be done in accordance with currently accepted guidelines.

Caution on use of sedative drugs in patients with acute liver dysfunction

Sedative drugs are given in patients with acute hepatotoxicity and cerebral edema primarily to reducing surges in intracranial pressure. In patients with hepatic dysfunction, metabolism of sedative drugs is likely to be impaired (most sedative drugs are metabolized in the liver). This can lead to prolonged half-life of the sedative and precipitate drowsiness/respiratory depression.[4] Thus, in patients with hepatotoxicity, without encephalopathy, it is preferable to avoid sedative drugs. Cerebral edema is an event in the later stages of liver failure, and judicious use of sedatives in patients already in encephalopathy needs to be made.

It is preferable to avoid sedation in patients with hepatotoxicity and absence of encephalopathy.

Urgent liver transplantation to treat HAV induced acute liver failure

Urgent liver transplantation needs to be considered in patients who worsen. Patients who meet listing criteria for urgent liver transplantation are best managed by liver transplantation.[3] It is important to discuss the option of urgent liver transplantation with patient/ family members.

The patient and his/her family members need to be counselled regarding urgent liver transplantation in a patient with encephalopathy or with worsening INR. If transplantation is feasible, liaison with a hospital where urgent liver transplantation is performed and decide on patient transfer for the same.

PLEX to treat severe acute liver injury or acute liver failure caused by HAV

Recent studies report an increase in survival with the native liver in patients with acute liver failure, after treatment with PLEX.[5] The American Society for Apheresis recommends high-volume PLEX to be considered a Category I indication (i.e., stand alone first line treatment or along with other treatments) to treat acute liver failure.[6] Based on the volume of plasma exchanged during each session, PLEX for acute liver failure can be classified into high volume, standard volume, and low volume.[7] Recent reports suggest improved survival with PLEX in patients with ALF caused by viral hepatitis.[8] PLEX may be used both as a stand-alone treatment and as a bridge to liver transplantation in patients with viral hepatitis induced ALF. PLEX may also be used to treat patients with underlying chronic liver disease/ cirrhosis (i.e., HAV as the acute liver insult in patient with acute on chronic liver failure). The efficacy/survival benefit of PLEX to treat patients with ALF may be superior to that in patients with acute on chronic liver failure.[10]

PLEX may be initiated as stand-alone treatment or as a bridge to liver transplantation (Level of evidence: Low; Grade of recommendation: Strong).

A recent meta-analysis has shown mortality benefit for PLEX in acute liver failure patients, irrespective of the volume exchanged.[9] Thus, low-volume PLEX provides equivalent benefit with lower risk of transfusion related lung complications[10] and lesser strain on blood bank resources.

Indications for plasma exchange

The Tamil Nadu chapter of Indian Society of Gastroenterology Guidelines for management of rodenticidal hepatotoxicity has given recommendations as to when PLEX is to be initiated in patients with acute liver injury/acute liver failure.[11] Early institution of PLEX in patients meeting criteria for the same (as mentioned in these guidelines) may favourably alter the course of the illness in patients with severe acute liver injury / acute liver failure.

The indications for PLEX in patients with severe acute hepatitis A

(adapted from TNISG Rodenticidal poisoning guidelines) are;

Presence of deranged LFT, AND any of the following three criteria:

1. INR ≥ 4
2. worsening INR on serial tests (After 2 doses of Vitamin K 4 hours apart and repeat INR)
3. depressed consciousness/ altered behaviour (Level of evidence: Low; Grade of recommendation: weak).

Contra-indications for plasma exchange

The contra-indications for PLEX in patients with acute hepatitis A are presence of either of the following two criteria:

1. Hemodynamic instability
2. Active sepsis (Level of evidence: Low; Grade of recommendation: Strong).

Pregnancy is not a contra-indication for PLEX to treat acute hepatitis A. PLEX has been used to treat acute liver failure in children.[12]

Details of PLEX procedure[13]

1. Obtain informed consent for PLEX treatment from patient / next of kin who opt for this treatment after counselling about all the treatment options.
2. It is preferable to insert venous access line for PLEX and to perform PLEX at the bedside in monitored setting like HDU/ ICU.
3. Femoral vein is the preferred access for PLEX port insertion, this is done under ultrasound guidance. This venous access is kept exclusively for PLEX and should not be used for other purposes like taking blood samples, administering medicines etc. Avoid prophylactic platelet or fresh frozen plasma transfusion for line insertion.
4. Start prophylactic intravenous antibiotic (to be chosen as per local hospital antibiotic policy) after sending blood culture.
5. Start Tab Prednisolone 10 mg or equivalent as soon as decision to

PLEX is made, and continue for further 1 to 4 weeks after stopping PLEX, based on clinical assessment. Prednisolone reduces the cytokine storm.

6. Low volume plasma exchange (50% of plasma volume exchanged per PLEX session) is recommended.
7. The preferred replacement fluid is synchronously administered blood group specific fresh frozen plasma at 1:1 volume.
8. Centrifugal type PLEX is preferred over membrane type PLEX.
9. PLEX is performed daily, for at least 3 days. Decision to do PLEX is reviewed each day by the treating team; total number of PLEX sessions is decided based on tolerability and clinical condition. During PLEX, maintain strict asepsis, avoid hemodynamic instability and give calcium supplementation. Calcium supplementation may be given as 1000 mg orally before PLEX and 20ml slow IV infusion of Calcium gluconate towards the end of PLEX in separate line. The venous access is removed once decision is made to terminate PLEX, in view of either improvement or futility. This is to reduce the risk of line related sepsis, which increases with number of days in situ, esp. after 5-7 days.
10. It is preferable to do PLEX during daytime, when experienced personnel are likely to be available. However, for encephalopathic/ sick patients (i.e., acute liver failure), PLEX can be undertaken at anytime.
11. In case of clinical signs of sepsis while on PLEX, it is necessary to withhold/discontinue PLEX until sepsis is controlled. Antibiotics may be escalated awaiting culture / sensitivity report.
12. Organ-specific standard of care for critically ill patient should be continued. (Endorsed by ISG, Kerala)

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