HEPATIC ENCEPHALOPATHY

Dr. Muhammad Sarfraz

Abstract: Hepatic encephalopathy is neuropsychiatric disorder, in which there is alteration in sensorium and cognitive functions due to liver failure or cirrhosis. It can be acute and reversible or chronic and irreversible. There are number of causes leading to hepatic encephalopathy in cirrhotic patients such as uremic encephalopathy, encephalopathy due to glucose metabolism impairment, encephalopathy due to impairment of respiratory gaseous exchange, high dietary protein, spontaneous bacterial peritonitis, gastrointestinal hemorrhage, constipation, any central nervous system depressants drugs, hypokalemic alkalosis, procedures include; TIPS (trans-jugular intrahepatic portocaval shunt), portosystemic shunt operations and paracentesis. Diagnosis of hepatic encephalopathy is made clinically. The main aim of management is to identify and remove the possible precipitants and suppress the production of neurotoxins in the gut. Depending on grades treatment is started. General measurements includes supplemental oxygen is given and strict intake output record established to determine CNS, renal and fluid status.

Key words: Cirrhosis, Hepatic Encephalopathy, Lactulose, Rifaximin.

DEFINITION:

Hepatic encephalopathy is neuropsychiatric disorder, in which there is alteration in sensorium and cognitive functions due to liver failure or cirrhosis. It can be acute and reversible or chronic and irreversible.

CAUSES & PRECIPITATING FACTORS:

There are number of causes leading to hepatic encephalopathy in cirrhotic patients such as uremic encephalopathy, encephalopathy due to glucose metabolism impairment, encephalopathy due to impairment of respiratory gaseous exchange, high dietary protein, spontaneous bacterial peritonitis, gastrointestinal hemorrhage, constipation, any central nervous system depressants drugs, hypokalemic alkalosis, procedures include; TIPS (trans-jugular intrahepatic portocaval shunt), portosystemic shunt operations and paracentesis.

PATHOPHYSIOLOGY:

Due to liver failure, the portal circulation bypasses the liver, occurs through collaterals. The nitrogenous toxic substances produced in gut are not metabolized in liver, directly leading to brain. These nitrogenous toxic substances mainly ammonia, include others false neurotransmitters (octopamin), gamma amino butyric acid (GABA) and mercaptans accumulates in brain. These substances causes neurotoxicity and called neurotoxins,

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disturb the normal brain activity leading to hepatic encephalopathy.

DIFFERENTIAL DIAGNOSIS:

Several other diseases can presents in a similar way as hepatic encephalopathy, including:

- Intracranial bleeding (subdural and extradural hematoma)
- Wernicke's encephalopathy
- Wilson's disease
- Delirium tremens
- Space occupying lesion in brain
- Sepsis

CLINICAL FEATURES:

Acute onset has definitive precipitating factor and patient become increasingly drowsy, comatose and his sleep rhythm disturbed. Confusion is followed by coma.

Chronically patient develop mood swing, personality disorder and intellectual problems with reversal of sleep rhythm. Initially symptoms may be mild but when condition become worse patient develop irritability, inability to concentrate, disorientation, drowsiness slurring of speech and eventually coma.

On the basis of personality disorder, intellectual problems and neurological signs hepatic encephalopathy divided into five grades by which we can assess patient response to therapy.

Examination findings include fetor hepaticus (a sweat smell to the breath), asterixis

GRADES	CLINICAL SIGNS			
	Concentration and Speech	Personality	Sleep rhythm and Memory	Neurological Signs
Grade 0	Minimal change only on psychometric analysis	Normal	Normal	Asterixis ABSCENT
Grade 1 Prodrome	Poor concentration and slurred speech	Mild confusion and agitation	Inverted sleep pattern and impairment of calculation ability	Asterixis may be present but not consistently
Grade 2 Impending Coma	Drowsy but easily arrousable and lethargic & disorientation regarded time	Inappropriate behavior but occasional aggressive	-	Asterixis present consistently & hypoactive reflexes
Grade 3 Stupor	Somnolence but arrousability, confusion and disorientation regarded place	Aggressive behavior (Bizarre behavior)	Sleepy but respond to pain and voice	Asterixis present, Positive Babinski's sign & hyperactive reflexes
Grade 4 Coma	Coma (un-response to voice, may or may not respond to painful stimulus)			Decerebration

(coarse flapping tremors seen when hands are outstretched and wrists hyperextended), constructional apraxia (patient unable to draw five pointed star), decrease mental functions which can be assess by trail making test and hyper-reflexia.

INVESTIGATIONS:

Diagnosis of hepatic encephalopathy is made clinically.

Electroencephalogram (EEG) is used to determine stages of encephalogram, it shows decrease in frequency of the normal αwaves which eventually developed into delta waves. The arterial blood ammonia level is usually 2-8 times elevated (>100iu/l). Conjugated bilirubin and serum aminotransferases (ALT, AST) markedly very high. Other investigations to rule out precipitating factors include viral markers, coagulation profile, arterial blood gases, blood urea, serum creatinine, CT scan and abdominal ultrasound.

MANAGEMENT:

The main aim of management is to identify and remove the possible precipitants and suppress the production of neurotoxins in the gut.

Depending on grades treatment is started. General measurements includes supplemental oxygen is given and strict intake output record established to determine CNS, renal and fluid status. Dietary protein restriction is not recommended because it is difficult to put up and can cause worsening of nutritional state in malnourished patients.

Non-absorbable disaccharides such as lactulose (15-30mL 3 times daily) is mainstay of treatment, goal is to produce 2-3 stools per day. Lactulose in gut reduces the ammonia absorption and increase the entry of nitrogen into bacteria by osmotic laxative effects (reduce water absorption in the stool to soften the stool and increasing the number of bowel movements) and colonic acidification.

Rifaximin (400 mg 3 times daily) is poorly absorbed semisynthetic antibiotic based on rifamycin reduces the bacterial contents of bowel recently shown very effective and use alternative, to lactulose when diarrhea worsen. Metronidazole is alternative to rifaximin, neomycin and diuretics should be avoided. Sometimes zinc supplementations with rifaximin proved very helpful.

If necessary maintain nutrition via fine bore nasogastric tube.

Refractory encephalopathy is only major indication and development of irreversible brain damage is a major contraindication of liver transplantation.

PROGNOSIS:

Acute encephalopathy in acute hepatic failure and Grade IV encephalopathy have very poor prognosis. Jaundice more than 7 days before onset of encephalopathy, prothrombin time greater than 50 seconds and bilirubin level greater than 17.5 mg/dl are poor prognostic factors. These patients require liver transplantation.

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