PORTAL SYSTEMIC ENCEPHALOPATHY (PSE)

Pages with reference to book, From 25 To 33

Huma Qureshi, Anjum Shahid, Fatima Nizami, Sarwar J. Zuberi (PMRC Research Centre, Jinnah Postgraduate Medical Centre, Karachi.)

Abstract

Sixtynine cases of portal systemic encephalopathy (PSE) (45 cirrhosis, 24 hepatitis) were seen during 15 months. Coma due to acute viral hepatitis occurred in a younger age group as compared to cirrhosis. Upper gastrointestinal bleeding and hepatic necrosis were the main precipitating factors. Most of the patients were in grade Ill (37.6%) and IV (34.7%) coma when first seen.

Blood ammonia nitrogen was raised in all hepatitics and 85% cirrhotics. Serum and urinary electrolytes were deranged in both the groups, while renal function tests were disturbed in more than 50% cases in the two groups.

Steroids, diuretics, “Prophylactic” use of broad spectrum antibiotics and intra muscular pitressin might have played an adverse role in the management of coma.

The caloric intake prior to and during coma was drastically low in most of the cases. Overall mortality in the series was 74% (JPMA 37:25 ,1987).

INTRODUCTION

Portal systemic encephalopathy, commonly known as hepatic coma, is a syndrome comprising of foetor hepaticus, flapping tremors, FEG changes and hyperventilation. Presence of raised blood ammonia levels completes the syndrome.[1]

Ammonia enters the gastrointestinal tract either by bacterial degradation of urea[2] or by deamination of proteins. On reaching the liver, it is extracted[3-5] and stored as glutamine unless utilised for urea or protein synthesis[6]. Liver[7] and kidneys, not only remove ammonia from the circulation but also contribute to its formation by the degradation of aminoacids and other nitrogenous compounds[8]

Severe electrolyte derangements occur in advanced liver disease[9-10] Hypokalaemia[10-12] and marked reduction in sodium excretion[10-13-17] have been observed in fulminant hepatic failure. In hepatorenal syndrome sodium excretion is often lessthan 15 meq/day’[18-19]

Renal failure is a common complication of advanced liver disease. [20-24] Abnormalities in renal function get môie pronounced as the liver disease worsens.[25]

Inadequate nutrition in liver disease worsens the severity and prolongs the convalescence[26-27].

Vegetable proteins, milk, and egg contain far less amount of ammonia as compared to meat[18] and so are less likely to precipitate or worsen coma.

Patients with PSE were seen in different hospitals of Karachi, to find out the etiology presentation, common precipitating factors and causes of death in PSE.

MATERIAL AND METHODS

Sixtynine cases of portal systemic encephalopathy were seen on request of their treating physicians. History, physical examination, haematological findings, nutritional status and different treatment regimens prior to and during coma, were entered in a standard proforma.

Patients with hepatic coma either due to cirrhosis (Group .1) or hepatitis (Group II) were graded into 4

grades following Conn's criteria, and a daily follow up and grading of coma was done till death or discharge.
Most of the patients were treated by their respective physicians and therefore no intervention was made in the treatment regimens.
Daily recording of nutritional status and treatment given was done in all the cases.

RESULTS

Of 69 cases of PSE, 45 had coma due to cirrhosis (Group -I) and 23 due to acute viral hepatitis (Group II). Most of the group I cases were in 3rd or 4th decade of life while those of group II were a decade or two younger. Male to female ratio for group .1 was 2:1 while no sex difference was noted in group II. Following Conn's criteria, 38% cases were in grade III and 34.7% in grade IV coma when first seen, showing that almost 71% cases were brought to the hospital in deeper states of coma (Table I).

TABLE – I
Grades of Coma.

Grading		Group I (45) No (%)	Group II (24) No (%)	Total (69) No (%)
Grade 0 :	No abnormality detected			
Grade I:	Trivial lack of awareness, euphoria or anxiety, shortened attentionspan. Impairment in performing addition or substraction.	3 (66)	2 (8.3)	5 (8.6)
Grade II :	Lethargy or apathy. Disorientation for time. Obvious personality change, inappropriate behaviour.	10 (22.2)	4 (16.6)	14 (20.2)
Grade III:	Somnolence to semistupor, but responsive to stimuli. Confused. Gross disorientation.	16 (35.5)	10 (41.6)	26 (37.6)
Grade IV:	Mental slate not testable.	16 (35.5)	8 (33.3)	24 (34.7)

The major symptoms prior to going into coma, for group .1 were abdominal pain (57.7%), haemetemesis (51 .1%),malena (46.6%) and jaundice (51.1%). In group II, all the cases were jaundiced, majority having associated prodromal symptoms of hepatitis. Twelve per cent cases had a history of upper G.I. bleeding.
On examination more than 50% cirrhotics had ascites or oedema ,while hepato-splenomegaly was seen in 31.1% and 26.6% cases respectively. Oesophageal varices were demonstrated on endoscopy in 333% cirrhotics prior to going into coma. Other signs of cirrhosis like palmer erythema, purpuric rashes, duputerens contractures and foetor hepaticus were less frequently seen. Five patients with acute viral hepatitis had an associated pregnancy.
Twentyseven per cent (Group I) and 33.3% (group II) cases gave a history of repeated blood transfusions inthe past, while 31.1% and 4.1% had jaundice. Past history of ascites (17.7%), upper G.l. bleeding (11.1%) and hepatic coma (13 .3%) was only present in cirrhotics. Four cases of acute viral hepatitis gave history of contact with hepatitis, while 2 received blood transfusions with in 45 days of the onset of coma.
Three cirrhotics went into coma consequent to surgical procedures to control variceal bleeding. The

operations included a splenorenal shunt a porta caval shunt and variceal ligation.
Blood ammonia nitrogen was raised in all group I cases and 85% group II cases. The levels in two groups are shown in Figures 1 and 2.

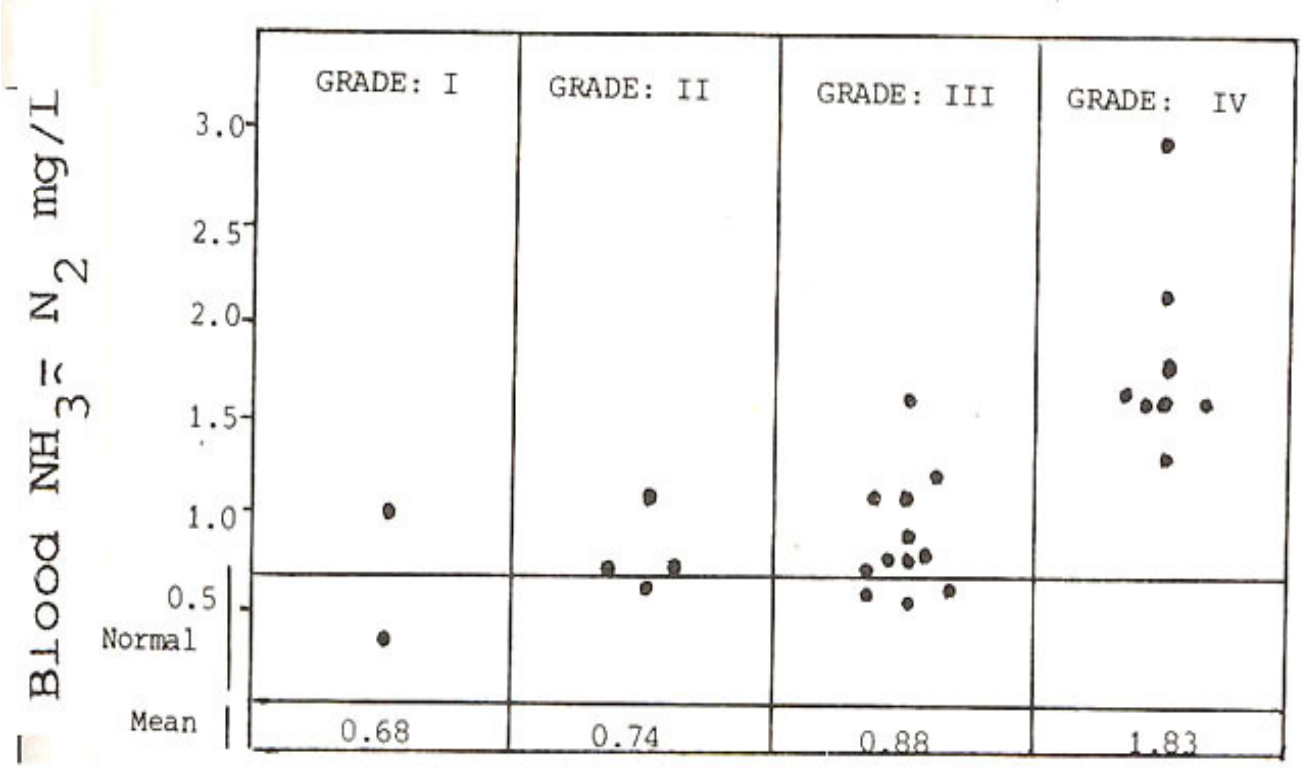

Figure 1. Blood Ammonia Nitrogen (mg/L) in various Grades of Group I Coma.

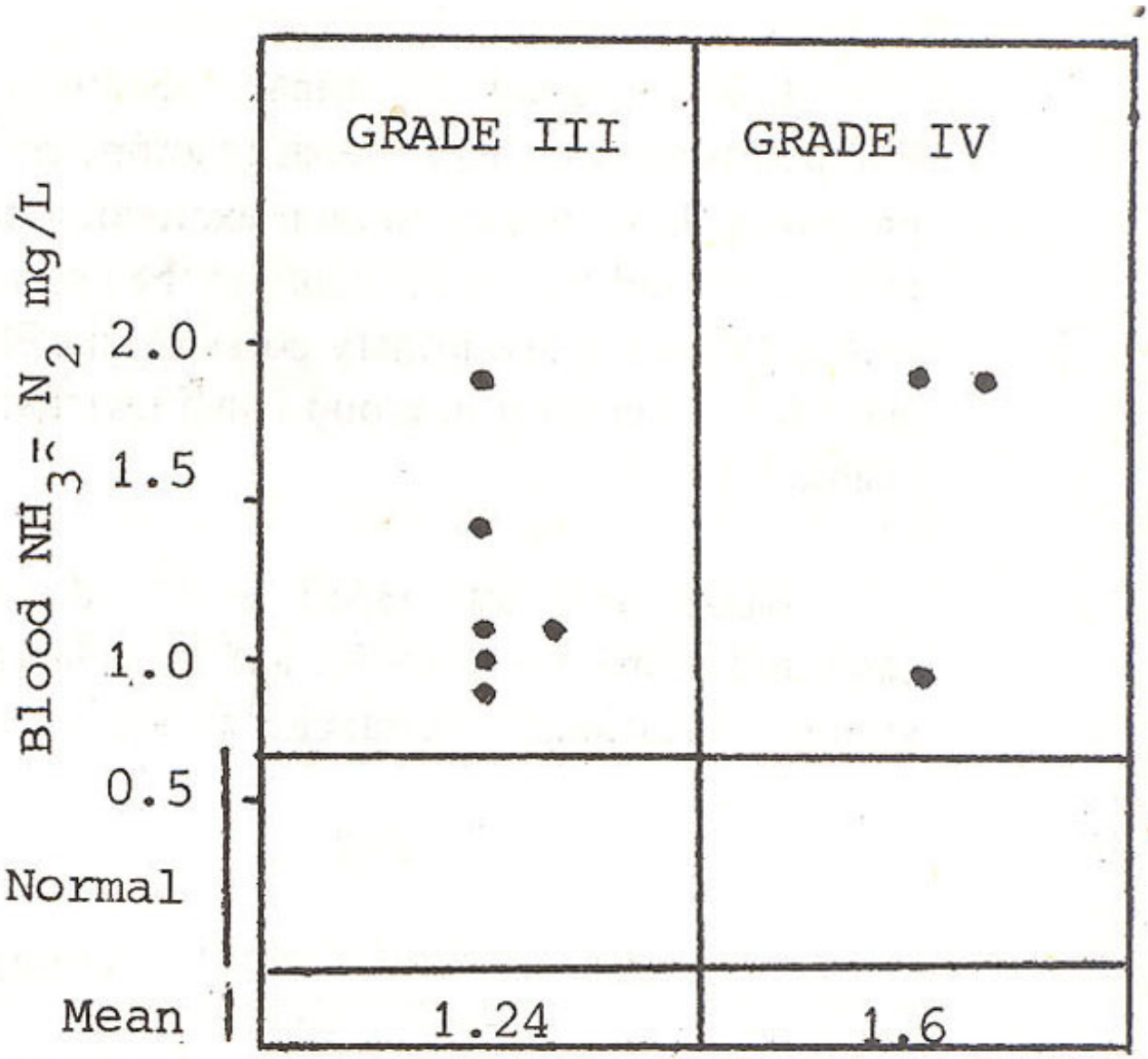

Figure 2. Blood Ammonia Nitrogen (mg/L) in grades of Group II Coma.

Electrolytes were deranged in the form of hyponateremia in 783% and 73% (Table II)

TABLE – II
Serum Sodium in Hepatic Coma.

	Coma Cirrhosis Group I	Mortality Rate %	Coma Hepatitis Group II	Mortality Rate %
No. of cases	23	–	11	–
Severe: <120meq/L	7 (30.4%)	100%	1 (9.1%)	100%
Moderate: 120-126meq/L	2 (8.7%)	100%	3 (27.3%)	100%
Mild: 127-134 meq/L	9 (39.1%)	89%	4 (36.4%)	25%
Hyponatraemia	78.3%	–	73%	
Normal. 135-145 meq/L	5	–	3	–
>145 meq/L	–	–	–	–

and hypokalaemia in 69.5% and 63.6% cases in group I and II, (Table III).

TABLE – III
Serum Potassium in Hepatic Coma.

	Coma Cirrhosis group I	Mortality Rate %	Coma Hepatitis group II	Mortality Rate %
No. of cases	23	–	11	–
Severe: <3.1 meq/L	11 (47.8%)	81.8%	6 (54.5%)	66.6%
Moderate: 3.1-3.29 meq/L	–	–	–	–
Mild: 3.3-3.49 meq/L	5(21.7 %)	100%	(1 (9.1%)	–
Hypokalaemia	69.5%	–	63.6%	–
Normal: 3.5-4. 5meq/L	7	–	3	–
>4.5 meq/L	–	–	1	–

Mortality in the two conditions was directly related to the degree of biochemical derangement.
Low excretion of urinary electrolytes in PSE points towards hepatorenal syndrome and bad prognosis.
Low urinary sodium excretion resulted in a 93.3% and 83.3% mortality in the two groups (Table IV)

TABLE – IV
Urinary Sodium in Hepatic Coma.

	Coma Cirrhosis Group I	Mortality Rate %	Coma Hepatitis Group II	Mortality Rate %
No. of cases	19	–	8	–
Severe: <25meq/24 hrs	11 (58 %)	91	6 (75 %)	83.3
Moderate: 25-51meq/24hrs	2 (10.5%)	100	–	–
Mild: 52-79meq/24 hrs.	2 (10.5%)	100	–	–
Low urinary sodium	79%	–	75%	–
Normal: 80-290 meq/24hrs	1	–	2	–
>290 meq/24 hrs	3	–	–	–

while low urinary potassium had a 90% and 66.6% mortality in group I and II respectively (Table V).

TABLE – V
Urinary Potassium in Hepatic Coma.

	Coma Cirrhosis Group I	Mortality Rate (%)	Coma -Hepatitis Group II	Mortality Rate (%)
No. of cases	19		8	–
Severe: < 8 meq/24 hrs	5 (26.3%)	80.0	3(37.5%)	66.6
Moderate: 8-15meq/24hrs	2(10.5%)	100	1(12.5%)	100
Mild: 16-24meq/24 hrs	3 (15.8%)	100	2 (25%)	50
Low urinary potassium	52.6%	–	75%	–
>100 meq/24 hrs	1	–	–	–
Normal: 25-100 meq/24hrs	8	–	2	–

Blood urea was raised in 50% and 61% cases and creatinine in 69.5% and 73% in the two groups. Creatinine clearance was significantly impaired in all the cases.

The common practices for a comatosed in various hospitals was to pass a ryles tube, cathetense and put an I.V. Line. Ryles tube was passed to keep the stomach empty, mostly by active aspiration.

The average caloric intake of all the patients, prior to going in to coma, was about 50% less than that of a healthy individual belonging to the same socioeconomic group. Caloric intake for males in the two groups was 960 and 1100 and for females 620 and 655 respectively.

Dextrose in water 5% mostly and occasionally 10% with injection B complex was the only source of calories and vitamins in these patients. On this therapy the caloric intake during coma varied from starvation to 1500 calories/day. (About 58% cases were taking 200-400 calories/thy and 25% 500-800 calories day).

Treatment regimens consisted of parenteral steroids administered in 42.2% and 50% cases in the two groups. The mortality was 94.7% and 66.6% in steroid treated patients in 2 groups. Similarly large doses of strong loop diuretics like furosemide were used parenterally in 33.3% and 12.5% cases in the two groups to induce diuresis in those with hepatorenal syndrome. The mortality in this group was 100%.

Broad spectrum antibiotics along with neomycin were used “prophylaetically” in 42.2% and 17.1% cases with a view to combat infection following catheterization and other procedures.

PropranoloL a beta blocker was used to control variceal bleeding in 8 cirrhotics. The drug was helpful in controlling bleçding in few cases, but it is too early to draw any conclusions on such a small number.

Depot pitressin (oil soluble pitressin) was used intramuscularly in 3 cases to control variceal bleeding. Haemodialysis was done in 1 cirrhotic, though the patient recovered from coma but died while in hospital due to severe electrolyte imbalance and cardiac arrest.

The survival rate of PSE was directly related to the grade of coma. Maximum survival was seen in grade 1 (40%) and 2 coma (50%). The mortality increased with the increasing grades of coma.

The various causes of death in the two groups is shown in table VI.

TABLE VI

Causes of Death in Coma.

Causes	Group I No (%)	Group II No (%)
G.I. Bleeding	12 (26.6)	2 (8.3)
H.R. Syndrome	10 (22.2)	2 (8.3)
Pul. Congestion	6 (13.3)	5 (20.8)
Acute Liver Failure	2 (4.4)	4 (16.6)
Septicaemia	1 (2.2)	1 (4.1)
Sedation	2 (4.4)	–
Not known	4 (8.8)	–
Cardiac arrest	–	1 (4.1)
Total Deaths	36	15

Total Mortality = 73.9%

Bleeding oesophageal varices (26.5%) and hepatorenal syndrome (22.25%) were the main causes of death in cirrhotics (Group I) while acute liver failure (16.6%). hepatorena] syndrome (8.3%) and pulmonary Malnutrition and bad nursing were the common contributory causes of death in the two groups.

Mortality in cirrhotics (group 1) was 80% and in hepatitcs (group II) 62.5%. Overall mortality was 73.9%.

Duration of follow up varied from 1-6 days to more than 2 years. Maximum cases (38) were followed

up for 5 days and maximum mortality also occurred in the same period.

DISCUSSION

Portal systemic shunting is the major prerequisite in PSE, which in majority of the cases is due to cirrhosis and in a very small percentage due to viral hepatitis (Type B mostly). In cirrhosis the etiology, type and degree of decompensation differs in different countries. In Indo Pak subcontinent it is mostly post hepatitic or secondary biiary in contrast to alcoholic, haemochromatosis or cryptogenic in the West.[1] In the present study cirrhosis was the cause of PSE in 65% cases and acute viral hepatitis in 34.5% cases.

Blood ammonia levels are within normal limits in all liver diseases without coma, [29-30] but are elevated in hepatic coma,[29-31-35] though they may be within normal limits in a small percentage[29-34] regardless of the depth of coma. In this study ammonia levels were within normal limits in 15% cirrhotics.

Renal retention of sodium is often seen in cirrhosis[22-26] and PSE resulting in ascites and oedema. Hyponatraemia in such cases is due to dilutional effect and should not be treated with sodium supplements as it would worsen the condition.

Other metabolic changes in PSE are hypokalaemia and extracellular alkalosis [37-39]. Presence of blood in the gut lowers the serum potassium levels by exchanging it into the intestinal fluid[40] and therefore further deteriorates the condition. In the presence of adequate urinary output, prompt measures should be taken to replenish potassium levels by both oral and parenteral routes. A dose high as 120 meq/day of potassium may be given.[41]

Patients with PSE excrete a hypertonic salt free urine'[18]. The lesser the urinary excretion of sodium, the more grave is the prognosis, and a value as low as 20meq/day indicates a bad prognosis. In the present study 79% and 75% cases in the two groups had low urinary sodium excretion, while 91% and 833% of those with an excretion of less than 25meq/day died. Potassium excretion is though an ion exchange for sodium in the distal nephron[42]. Absence of potassium in the urine therefore indicates complete proximal reabsorption of sodium, leaving a small amount for exchange in the distal nephron.[43] Low urinary potassium excretion in 53% and 75% cases in group I and II respectively shows the extent of sodium reabsorption and also reflects bad prognosis as seen by 90.66% mortality in the two groups.

In hepatorenal syndrome, progressive azotemia sets in due to alterations in the renal circulation and not due to the renal parenchymal disease.[44]Hepatorenal syndrome once set in, has a mortality of close to 100%[34-45]. it was 90% in this study.

In a study the survival rate of non steroid treated patients was 13% against 12% of steroid treated group. [46] In viral hepatitis of various types, steroids failed to improve the survival[47] and in type B hepatitis they may actually worsen the condition. [48] In this series 94.7 and 66.6% steroid treated cases in the two groups died. As hepatitis B surface antigen is not usually done in our hospitals, conventional use of steroids in hepatitis must be adding to the complications and morbidity. Cerebral oedema is a major cause of death in PSE[49] but in clinical practice it is not possible to prevent cerebral oedema once it has developed and therefore steroids are of no value[1]

Diuretics are responsible for half of the episodes or PSE, precipitated by azotemia[20-50] Drugs like benzthiazides, furosemide, ethacrynic acid and carbonic anhydrase inhibitors are dangerous when used in PSE. They increase the venous levels of ammonia[51] Chlorthiazides and other kaluretic diuretics have severe ammonia elevating effects[52-56] The potassium loss on the other hand increases the extracellular intracellular ph gradient and so favours the passage of ammonia into the cells. These two actions

working synergically ‘affect adversely the ammonia balance and worsen the PSE. Spironolactone, a potassium retaining diuretic may also induce azotemia during massive diuresis[1]

Tranquillizer sedative -analgesic complex was not a major cause of PSE in the present study and only 2 cases received parenteral valium for sedation. Diphenhydramine (Benadryl) or short acting barbiturates may be given if required.

Antibiotics are used to sterilize the gut. Neomycin ‘sulphate orally or as enema is widely used. Although a large fraction is excreted but 1-3% is absorbed in blood[57-60] in those with renal insufficiency, azotemia and cirrhosis of liver. Ototoxicity[61] develops in those taking 750-2500 G/day. In the present study one case developed ototoxicity following a splenorenal shunt while on 1-2 G/day. Acute staphylococcal enterocolitis[1-61-62] monialial and fungal infections are common during neomycin therapy. Ampicillin[63], tetracycline and kenamycin are the other antibiotics of choice for lowering ammonia levels.

Acidification of the gut by lactulose or acidic enemas is effective in lowering ammonia. Enemas are only effective if administered high up and retained for 1-2 hours. Acidification of urine by potassium chloride, calcium chloride and hydrochloric acid is effective in those with UTI where urease producing organisms precipitate PSE.

Proteins are known to precipitate coma. Ammonia content of various proteinous foods varies from 0.1 4%[64] Milk has a low nitrogen and a very low amount of ammonia (0.001 -0.OOSG) and is therefore the protein of choice in encephalopathy Protein tolerance of our patients is much better than those in the West Most of our patients are hypoproteinemics to begin with; and restriction of proteins in such cases results in gross body catabolism and further deterioration of PSE. About 3.5kg of lean body tissues are catabolised/lO days to provide metabolic calories. Only one case in the present study developed protein induced encephalopathy following a spleno renal shunt and high consumption of meat. He recovered on conservative management. It is therefore suggested that vegetable proteins should not be restricted during PSE and as the recovery proceeds animal proteins may be added simultaneously.

Other pitfall in the management of PSE were lack of change of posture, resulting in hypostatic pneumonia and bed sores. Active aspiration of the gastric contents further resulted in severe electrolyte imbalance. Dependant drainage was mostly done soon after the feed, resulting in loss of calories despite good caloric intake on chart. Catheterization was not done aseptically resulting in severe U.T.I. in most of the cases. Urinalysis and urine culture were not done in those with signs and symptoms of U.T.I. Urine bags, catheters, Ryle’s tube and I.V. lines were not changed regularly. Diarrhoea produced by lactulose or magnesium sulphate was treated by antidiarrhoeals resulting in further worsening of the condition.

In case of pulmonary oedema and collection of secretions in the trachea, clearing of airway via an endotracheal tube is very effective and life saving. Two patients were saved from such a condition by prompt clearing of airway by an experienced anaesthetist. Suction through nose or mouth is ineffective in these cases.

It is therefore presumed that with good nursing care, adequate caloric intake, prompt correction of serum electrolytes, specially potassium, and limited use of drugs, the morbidity and mortality in cases with hepatic coma is likely to improve.

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