ACUTE LIVER FAILURE
PRINCIPALS OF MANAGEMENT

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Format

- Definition
- Etiology
- Investigations
- Liver support
- Treatment of complications
ALF Definition (PALF Study group)

The summation of clinical and biochemical parameters:

1. The onset of liver disease with no known evidence of CLD

2. Biochemical and/or clinical evidence of severe liver dysfunction:
   - Hepatic based Coagulopathy with PT >20 secs or INR >2.0 +/- Hepatic encephalopathy. uncorrectable by parenteral Vit K
   - PT >= 15.0-19.9 secs or INR 1.5-1.9 in the presence of Hepatic encephalopathy
Etiologies

- Infectious: HAV, HBV, Herpes, indeterminate hepatitis
- Metabolic: Galactosemia, Tyrosinemia, Wilsons disease
- Drugs: Valproate, INH, Acetaminophen
- Toxins: mushroom
- Autoimmune: Hepatitis
- Ischaemia: Asphyxia, Cong Heart Dz
Acute Liver Failure: Etiology

- Acetaminophen: 39%
- Indeterminate: 17%
- Idiosyncratic drug: 13%
- Hepatitis A: 10%
- Hepatitis B: 7%
- Ischemic: 6%
- Autoimmune: 4%
- Other: 4%

• Acute liver failure in children: The first 348 patients in the pediatric acute liver failure study group  Squires R, Schneider B, et al
Management

- Management involves:
  1. Support liver functions
  2. Prevention and treatment of complications

Until Liver Fully recovers OR Replaced (Transplant)

Ideally in ICU setting
Functions of the Liver

- Nutrition - regulation of uptake and processing from intestinal tract
- Synthetic - Ptns, CHOś, Lipids
- Excretion Bile and hydrophobic compounds
- Energy metabolism
- Endocrine
- Immune regulation
- Drug metabolism
- Fluid balance
History

- Full h/o to help establish appropriate risk factors
- Drugs use, iv medications, transfusions,
- OTC meds especially acetaminophen
- Herbal meds & foods/teas

Examination

- Assess all systems
- Complete neuro exam including coma status
- Evidence/signs of CLD eg cataracts, Keiser-Fleischer rings, needle marks etc
Labs

Baseline
• CBC
• LFTs
• Coagulation profile
• U/E/Crea
• BGAs
• Septic screen
• Imaging

Diagnostic
• Acetaminophen
• Ceruloplasmin
• Immunoglobulins
• TORCHES
• Urine – Reducing sugars, amino acids
Fluid Balance

- Aim is to maintain balance between hydration and renal function without provoking cerebral edema
- Maintenance fluid - 75% of normal,
- 10% Dextrose in N/Saline
- Sodium 0.5-1mmol/Kg/Day
- Potassium 2-4mmol/l
- Maintain urinary output with Lasix & Colloid/FFPs
- Maintain Hb > 10g/dl
Nutritional support

• Aim:
  • To Maintain blood glucose >4mmol/l ensure sufficient CHOs to energy metabolism
  • To reduce ptn intake to 0.5-1 gm/kg/day
  • To provide enough energy to reverse catabolism
Hypoglycaemia

• Causes
• Failed gluconeogenesis
• Hyperinsulinaemia due to failed degradation
• Increased utilization – anaerobic metab
• Secondary bacterial infection
• 2-4hrly monitoring
• Target >4 mmol/l
• Refractory hypoglycaemia is a poor prognostic sign
Coagulopathy

• Causes:

• Failure of Synthesis of clotting and Fibrinolytic factors

• Low platelets – hypersplenism, DIC or aplastic anemia

• Factors I, II, V, VII, IX, X

• leads to raised PT and PTT

• Only treat PROFOUND COAGULOPATHY
- Mild coagulopathy PT <25 secs no treatment needed except support
- Severe coagulopathy PT > 40 secs give
- FFPs, cryoppt & platelets
- Double volume exchange transfusion
- For Haemorrhage:
  - High dose PPI (10-20 mg/Kg/day) or H2RA
  - Sucraflate/Alginate
Encephalopathy

- Defn: Brain dysfunction resulting from acute hepatic dysfunction
## Clinical grading of HE

<table>
<thead>
<tr>
<th>Clinical grade</th>
<th>Clinical signs</th>
<th>Flapping tremor</th>
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<tbody>
<tr>
<td>Grade 1 (prodrome)</td>
<td>Alert, euphoric, occasionally depression. Poor concentration, slow mentation and affect, reversed sleep rhythm.</td>
<td>Infrequent at this stage</td>
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<tr>
<td>Grade 2 (impending coma)</td>
<td>Drowsiness, lethargic, inappropriate behavior, disorientation.</td>
<td>Easily elicited</td>
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<tr>
<td>Grade 3 (early coma)</td>
<td>Stuporose but easily rousable, marked confusion, incoherent speech</td>
<td>Usually present</td>
</tr>
<tr>
<td>Grade 4 (deep coma)</td>
<td>Coma, unresponsive but may respond to painful stimulus</td>
<td>Usually absent</td>
</tr>
</tbody>
</table>
Management

• Restriction of dietary protein
  0.5-1 gm/Kg/day enterally or parenterally
• Enteral antibiotics
• Enteral Cathartic
  Lactulose 1-2mls/Kg/day &/or Magnesium sulphate
• Controlling complications of ALF that may contribute to ammonia accumulation
Cerebral Edema

• The most frequent cause of mortality
• Develops between stage III & IV of encephalopathy
• Etiology: unknown
• Iatrogenic factors: fluid overload
• Failed glucose mnx
• Failure to maintain systemic BP
• Management:
• Prevention
• Fluid restriction to <75% of maintenance
• Colloids – to maintain circulatory volume
• Mannitol 0.5 gm/Kg 4-6hrly
• Others:
  • Hyperventilation
  • Controlled hypothermia
  • ps: Steroids & Barbiturate coma have No role in ALF
Ascites

Due to

• Decreased oncotic pressure
• Lobular collapse
• Vasodilatation

• Care for secondary Bacterial / fungal infection:
Renal dysfunction

- May be due to:
- Pre-renal – uraemia
- Acute tubular necrosis
- Functional renal failure
Secondary Bacterial and Fungal infections

• Up to 50% children will develop significant infection
• Failed cellular and humoral immunity
• Mainly gram positive (S. aureus, epidermidis Strept.)
• Regular surveillance cultures & swabs
• Amoxil, cefuroxime, and metronidazole
• Amphotericin B or Fluconazole prophylactically
• **Pancreatitis**
  Rare seen in valproic acid toxicity

• **Aplastic Anaemia**
  Seen in non, Parvovirus B19, HSV-6
  Potentially fatal
Specific Therapies

- Acetaminophen ingestion
  N-acetyl cysteine
- Aminata phalloides (mushroom) poisoning
  Benzyl penicillin, Thiocytic acid, Haemodialysis, MARS removes Amatoxin
- Double volume exchange transfusion (<15Kg)
- Molecular adsorbent recirculating system (MARS)
- Hepatocyte transplant
- Liver transplant
Summary

• Is it ALF?
• Detailed history and examination
• What's the Probable etiology
• Admit ICU
• Hepatic support
• Prevention and treatment of complications
• Early referral to Transplant centre