

Treatment of hepatic diseases

Lecture 8

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Treatment of hepatic encephalopathy

Lifestyle modification

1. **Very** small & frequent meals (& proteins).

2. Proteins: 1.2 - 1.5 gm/Kg/day.

More of vegetable & dairy sources.

Also non absorbed vegetable fibers ↑nitrogen clearance.

3. ↑carbohydrates.

4. Probiotics & prebiotics.



Drug therapy of hepatic encephalopathy

A) Treatment of Precipitating factors

1. Electrolyte & acid base balance.
2. Evacuant enema & ↓ protein intake.
3. H₂ antagonists & PPIs.
4. Macrolides stimulate motilin receptors in GIT smooth muscles → ↑ motility. Used to ↑ gastric emptying of blood.
5. Drugs decreasing portal pressure (for esophageal varices):
 - a. Octreotide.
 - b. β blockers.
 - c. Vasopressin.
 - d. Nitrates.
 - e. Ca⁺⁺ channel blockers.(For bleeding : 3 – 5)



B) ↓ ammonia

1. Lactulose:

1st line ttt & prophylaxis in all cases.

2. Antimicrobial therapy:

Non absorbed antibiotics against urease - producing & glutaminase - producing gut bacteria.

a. Rifaximin:

Antimicrobial of 1st choice because it is not absorbed, broad spectrum, with low adverse effects. 550 mg twice daily.

b. Neomycin:

4 gm daily in divided doses.

But → ototoxicity & nephrotoxicity.

c. Metronidazole: against gram -ve anerobic gut bacteria.



3. Spherical carbon:

Adsorbs ammonia from GIT.

4. Branched -chain ammonia - lowering agents:

a. L- Ornithine L- Aspartate:

Provides metabolic substrates for urea cycle in liver and glutamine synthesis in skeletal muscle → ammonia detoxication & ↑ skeletal muscle protein synthesis.

b. Phenylbutyrate.

5. Zinc: cofactor for ammonia detoxication.

C) Flumazenil

Mechanism: ↓ neuro-inhibitory effect of GABA-A / benzodiazepine receptor complex.

Disadvantages: short - term (minutes) benefits.



Treatment of liver cirrhosis

1. Cholchicine : inhibits mitotic spindles → inhibition of fibroblasts.
2. Methotrexate : inhibits mitotic spindles.
3. Penicillamine : softens fibrous tissue.
4. Corticosteroids : affect fibrinolysis.
5. Captopril : affects fibrinolysis
6. Ursodiol : improves liver function in cholestatic disorders.



Ursodiol (ursodeoxycholic acid)

Mechanism:

Bile acid, orally absorbed, conjugated in liver, excreted in bile with extensive enterohepatic circulation →

1. ↑bile acid pool in bile → dissolution of cholesterol gall stones.
2. ↓hepatic cholesterol secretion in bile.
3. Stabilization of hepatocyte canalicular membrane.

Uses:

1. Small cholesterol gall stones.
2. Biliary cirrhosis.
3. Improvement of liver function & histology.

