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PHARMACOLOGICAL MANAGEMENT OF HEPATIC ENCEPHALOPATHY: THE IMPACT OF AMMONIA DRUGS ON COGNITIVE FUNCTION IN HEPATIC ENCEPHALOPATHY

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Hepatic encephalopathy (HE) is a severe neuropsychiatric complication arising from liver dysfunction, characterized by elevated ammonia levels in the blood and brain. This metabolic disorder manifests through a spectrum of symptoms, including cognitive impairment, personality changes, and motor disturbances, resulting from the liver's inability to detoxify ammonia via the urea cycle. The accumulation of ammonia disrupts cellular energy metabolism, neurotransmission, and causes astrocyte swelling, leading to progressive neurological decline.

Current therapeutic strategies focus on two primary approaches: reducing ammonia production and enhancing its elimination. Lactulose remains the cornerstone of treatment, acidifying the colon to trap ammonia and promote its excretion. Upon reaching the colon, gut microbiota metabolizes this compound into acetic and lactic acid, creating an acidic environment that suppresses urease-producing bacterial populations, reduces luminal pH, and limits systemic ammonia absorption. Antibiotics such as rifaximin are used adjunctively to suppress ammonia-generating gut bacteria. Other interventions include ammonia scavengers (sodium benzoate, phenylbutyrate) and adsorbents like AST-120, which binds neurotoxic compounds. Protein restriction is an option for cirrhotic patients to prevent a rise in gut-derived blood ammonia. This approach is no longer recommended because it promotes protein degradation, decreases muscle mass, and can cause deterioration in the patient’s nutritional status. Within the small intestine, phosphate-activated glutaminase plays the dominant role in breaking down glutamine, with research showing this single enzyme generates the majority (85%) of ammonia produced in intestinal tissues.

Emerging treatments aim to improve ammonia clearance, including branched-chain amino acids (BCAAs) to reduce muscle catabolism, L-ornithine-L-aspartate (LOLA) to stimulate residual urea synthesis, and acetyl-L-carnitine to support neuronal function. Experimental therapies targeting inflammation and alternative metabolic pathways, such as taurine and TNF-α inhibitors, show promise but require further validation.

In conclusion, ammonia-reducing drugs are essential in the management of hepatic encephalopathy. Lowering ammonia improves brain function leading to mental clarity and lessen the symptoms such as, confusion, disorientation, and coma. However, there are limitations to these drugs, namely, lactulose can cause diarrhoea and abdominal discomfort, while rifaximin may lead to nausea or other gastrointestinal issues. Also, these drugs are not a complete cure for HE and should be used in conjunction with other supportive measures and management of the underlying liver disease.