Liver failure, either acute or chronic, leads to the accumulation of toxic products in the blood stream that normally would be cleared by the liver. These toxic products affect the central nervous system, resulting in a myriad of symptoms from mild (lessened cognitive abilities, suppression, or heightening of emotions) to severe (lethargy, coma, and death). These symptoms may result from numerous other afflictions. Confirmation of liver disease, usually by laboratory analysis, diagnostic imaging, and/or biopsy, can identify a particular cause as hepatic encephalopathy.

Once the diagnosis of hepatic encephalopathy is made, the goal is to lower the toxic blood stream products (primarily ammonia). Conventional treatment has previously focused on continual diet restriction of protein. It was thought that by restricting protein consumption, blood ammonia levels may be lowered. Protein breaks down into amino acids, which are converted into ammonia byproducts. Current diet modifications include protein restriction to 20 or more grams per day during acute hepatic encephalopathy exacerbations. Continual protein restrictions are no longer fully supported because there is a risk of initiating catabolic processes that will also increase ammonia levels.

Diet Protein Restriction
Dietary restrictions of protein are often a first-line treatment for hepatic encephalopathy, but little evidence exists to support its efficacy in symptomatic hepatic encephalopathy patients. Diet restriction alone cannot be the sole treatment. The continual exploration of optimal treatments has led to the use of probiotics, nonabsorbable disaccharides, and minimal to nonabsorbable antibiotics (Gerber & Schomerus, 2000; Seymour & Whelan, 1999).

Probiotics
In addition to limiting the protein intake that normal intestinal flora breaks down into ammonia, probiotics may be prescribed to support intestinal bacteria that are less likely to create this byproduct. Probiotics are gaining much interest and many food products, nutraceuticals, and prescriptive medications may already contain these beneficial microbes. Multiple studies have shown some benefit of probiotics for minimal hepatic encephalopathy (McGee, Baken, Riley, Riddell, & Webster, 2010; Sharma, Sharma, Puri, & Sarin, 2008; Solga, 2003) as well as other conditions affecting bowel function such as lactose intolerance, irritable bowel syndrome, and colitis. Studies of the effectiveness of...
probiotics to lower ammonia levels compared with other treatments such as nonabsorbable disaccharides have been promising. Consensus does not exist as to which microbes are most effective for lowering ammonia levels in patients with hepatic encephalopathy, but a systematic review of available studies is under way (McGee et al., 2010). It is generally believed that probiotics are most effective for minimal degrees of hepatic encephalopathy, but not for advanced or severe cases (McGee et al., 2010; Sharma et al., 2008; Solga, 2003).

Nonabsorbable Disaccharides

Nongastrointestinal absorbable lactulose is composed of indigestible sugar. Lactulose has been prescribed to bind ammonia in the intestinal tract and remove it via the feces. Lactulose is thought to be broken down in the intestine into lactic acid and acetic acid, which lowers the pH of the colon. This lowered pH has the effect of trapping ammonia (NH₃) in its ionized nondiffusible form (NH₄⁺). Other theories of its action are the promotion of beneficial bacteria growth and inhibition of undesirable ammonia-producing bacteria (Patil et al., 1987; Vince, Zeeger, Drinkwater, O’Grady, & Dawson, 1974). Regardless of its specific action, the net effect of lactulose is lowering ammonia levels and it remains a primary drug treatment.

A systematic review by Als-Nielsen, Gluud, and Gluud (2004) found lactulose to have a “modest” effect on improving hepatic encephalopathy and it was inferior to antibiotic use. Modest findings of effectiveness have caused some to question these treatments for more aggressive therapy (Shawcross & Jalan, 2005).

Nonabsorbable Antibiotics

Nonabsorbable antibiotics administered orally are intended to kill gut bacteria that are responsible for producing ammonia. Unfortunately, metronidazole, vancomycin, paromomycin, and oral quinolones have been found to have a degree of systemic absorption and side effects. The most serious include ototoxicity and nephrotoxicity (Cash et al., 2010). A rifampin antibiotic derivative antibiotic, rifaximin (Xifaxan; Salix Pharmaceuticals, Inc., Morrisville, NC), offers significantly less side effects, while showing effectiveness to lower blood ammonia levels (Bass et al., 2010).

Rifaximin

Rifaximin is a nonaminoglycoside semisynthetic antibacterial derived from rifamycin (Salix Pharmaceuticals, 2010). Rifaximin is minimally absorbed from the intestinal tract with less than 0.2% found in the liver or kidneys. This amount represents significantly less intestinal tract absorption compared with other antibiotics. The majority of rifaximin is excreted unchanged in feces. The most common side effects (<10% occurrence) are peripheral edema, nausea, dizziness, fatigue, ascites, diarrhea, and headache (Salix Pharmaceuticals, 2010). The lower systemic absorption of rifaximin compared with other antibiotics, lower side effect profile, and effectiveness as good as or better than lactulose makes rifaximin a viable treatment for hepatic encephalopathy.

Conclusion

Advanced degrees of hepatic encephalopathy require more aggressive treatments. The use of rifaximin to diminish ammonia-producing bacteria in the gut offers a treatment with little systematic effects, owing to its minimal absorption from the intestinal tract. ♦

REFERENCES


