

# PHARMACIST CORNER

## Hepatic Encephalopathy Management

Hepatic Encephalopathy (HE) is a neuropsychiatric disorder associated with liver failure and is very common in hospice patients. The exact cause of HE is not understood but is believed to be related to the build up of excess ammonia usually removed by the liver. Knowing what contributes to the cause of HE and recognizing the symptoms allows for early treatment at the lowest possible doses for the shortest duration. This is essential to ensuring the highest quality of life possible as treatment does have significant risks.

### Precipitants of hepatic encephalopathy in patients with cirrhosis

#### Drugs

- Benzodiazepines
- Nonbenzodiazepine
- hypnotics (e.g., zolpidem)
- Narcotics
- Alcohol

#### Increased ammonia production, absorption or entry into the brain

- Excess dietary intake of protein
- Gastrointestinal bleeding
- Electrolyte disturbances (e.g., hypokalemia)
- Constipation
- Metabolic alkalosis
- Infection

#### Dehydration

- Large volume paracentesis
- Hemorrhage
- Vomiting
- Diarrhea

#### Portosystemic shunting

- Radiographic or surgically placed shunts
- Spontaneous shunts

#### Vascular occlusion

- Hepatic vein thrombosis
- Portal vein thrombosis

#### Primary hepatocellular carcinoma

**Grading of the symptoms of hepatic encephalopathy is performed according to the so-called West Haven classification system, as follows:**

**Grade 0** - Minimal hepatic encephalopathy; lack of detectable changes in personality or behavior; minimal changes in memory, concentration, intellectual function, and coordination; asterixis is absent.

**Grade 1** - Trivial lack of awareness; shortened attention span; impaired addition or subtraction; hypersomnia, insomnia, or inversion of sleep pattern; euphoria, depression, or irritability; mild confusion; slowing of ability to perform mental tasks.

**Grade 2** - Lethargy or apathy; disorientation; inappropriate behavior; slurred speech; obvious asterixis; drowsiness, lethargy, gross deficits in ability to perform mental tasks, obvious personality changes, inappropriate behavior, and intermittent disorientation, usually regarding time.

**Grade 3** - Somnolent but can be aroused; unable to perform mental tasks; disorientation about time and place; marked confusion; amnesia; occasional fits of rage; present but incomprehensible speech.

**Grade 4** - Coma with or without response to painful stimuli.

## BetterRX Clinical Services

Clinical studies comparing treatment options are minimal and small. That being said, the comparative studies done have not found one treatment significantly superior over another. Rifaximin (Xifaxin®) gained favor over neomycin or metronidazole due to its lower risk-benefit profile with long term use. This is less of a concern in hospice where life expectancy is less than 12 months. One treatment note: when using antibiotics to treat HE, they are to be ADDED to a current Lactulose regimen; not replace it. The chart below is a useful tool to aid in deciding the most appropriate treatment for a patient.

|                      | Lactulose   | Metronidazole (Flagyl)   | Neomycin   | Rifaximin (Xifaxin)  |
|----------------------|---|--|--|--|
| Dose                 | 15ml-45ml 2-3 times a day (titrate up to 2-3 soft stools daily) | 250mg-500mg twice daily  | 500mg-1000mg 2-4 times daily                         | 400mg 3 times daily or 550mg twice daily                   |
| Adverse Effects      | Excessive sweet taste, GI upset, hypernatremia                  | GI upset, metallic taste, headache, loss of appetite, diarrhea | Clumsiness, diarrhea, dyspnea, thirst, increased gas | Edema, dizziness, nausea, diarrhea, muscle spasms, dyspnea |
| Warnings             |   | Renal dosing required  | N/A  | N/A  |
| Long term use risk   |   | Neurotoxicity  | Nephrotoxicity, ototoxicity                          | N/A  |
| Long term use risk   |   | Alcohol, Warfarin, Phenytoin, Diflucan + many others           | Warfarin   | N/A  |
| Studies vs Lactulose |   | =  | =  | =  |
| Studies vs placebo   | +   | ND   | ND   | +  |
| Cost/month           | 45ml/day=\$41<br>135ml/day=\$122                                | \$20   | 500mg 4 times a day = \$100                          | 200mg = \$4400<br>550mg = \$2700                           |

+: superior to control; =: equal to lactulose; -: no effect; ±: conflicting results; ND: not done.

### References

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