

Pruritis in Cholestatic Liver Disease

Antihistamines tend to be ineffective and should be avoid in patients with Hepatic Encephalopathy

Treatment

Ursodeoxycholic acid (Ursodial, Actigal®)

- Indicated for the treatment of PBC. Treatment of the primary disease should ameliorate the pruritis but generally patients need an additional agent to manage pruritis associated with PBC.
- Ursodeoxycholic acid is a naturally occurring bile acid that lowers BA levels in cholestatic disorders. Unclear whether this mechanism works by competing with intestinal absorption of endogenous bile or if it increases hepatic clearance of the BA.
- Effect of ursodiol on pruritis is uncertain. Seems to work well in cholestasis associated with pregnancy (safe in third trimester only).
- **Dose: 13-15mg/kg/day orally in 2-4 divided doses (300 mg PO TID).**
- Common side effects: headaches and constipation (~25%)
- Decreased effect with OC, aluminum containing antacids and colestipol.

Cholestyramine (Colestipol®)

- Most widely used agent for pruritis associate with cholestatic disease.
- A non-absorbable, anion exchange resin that binds BA from the terminal ileum to prevent their absorption and enterohepatic circulation.
- No randomized trials for effectiveness but clinical experiences shows that cholestyramine alleviates pruritis within first 2 weeks of treatment, although this response can be transient.
- Dose: Should be given in escalating divided doses starting 2-4gm/day up to 16gm/day. Manufactured as 5gm packets of powder or 1gm tablets. Mix with juice or water.
- Greatest amount of BA available for binding is in the gall bladder right before breakfast. Ideally give medication 30min before and 30 min after breakfast and then a third dose following lunch.
- **Drug interaction: NEED to separate other medications and cholestyramine. Give all other medication 1-2 hours before or 4 hours after giving colestipol.**

Rifampin (Rifadin®)

- Generally considered as a second line agent in patient who cannot tolerate cholestyramine.
- Acts as a strong inducer of microsomal drug-oxidizing system and promotes the metabolism of endogenous pruritogens. Also competes with hepatocytes for the uptake of BA.
- Dose: Recommendation is to begin at 150mg/day orally and can maximize to 150 mg PO BID. Available in suspension, capsule or intravenous formulation.
- Drug interactions: **STRONG** inducer of many cyp enzymes which results in the liver chewing up your other drugs. Anticipate these interactions before starting rifampin.
- Common side effects: hepatotoxicity (~7% reported when rifampin used alone), hemolytic anemia and thrombocytopenia (generally high doses), dark urine.
- Liver function tests, especially in the first two months of initiating therapy.