

PALLIATIVE PEARLS

BY ENCLARA PHARMACIA

Management of Pruritus in Primary Biliary Cholangitis November 2016

Patient Case

GH is a 56-year-old woman admitted to hospice 4 months ago with a diagnosis of primary biliary cholangitis (PBC) and cirrhosis. Her comorbidities include hyperlipidemia and chronic urinary tract infection. She has no known drug allergies and lives at home with her husband.

GH is experiencing itching all over her body that developed prior to her admission to hospice and has become increasingly intolerable. During physical exam, jaundice with hyperpigmentation of her skin is noted except for a “butterfly area” of normal pigmentation in the upper back. Xanthelasmas, which are yellowish painless plaques caused by deposition of lipids underneath the skin, are seen on her eyelids.

The diphenhydramine regimen (25mg PO Q.I.D PRN) prescribed prior to hospice admission is no longer keeping her symptoms at bay despite routine dosing. She also has no relief of her pruritus on a corticosteroid regimen of dexamethasone titrated to 8mg BID. GH states, “I just want to be comfortable” and asks if there are any other therapies she could try.

WHAT IS PRIMARY BILIARY CHOLANGITIS (PBC) AND WHY DOES PRURITUS OCCUR IN THIS CONDITION?

PBC, formerly known as primary biliary cirrhosis, is a chronic disease of the liver that leads to progressive cholestasis and end-stage liver disease.¹ Cholestasis is defined as a decrease in bile flow causing accumulation of bile acids in the serum. A common clinical consequence of cholestasis is pruritus, but the underlying mechanism of action is not fully understood as the degree of serum and tissue bile acid retention does not always correlate with the degree of pruritus.² Several links have been proposed in end-stage liver disease:^{2,3}

- Breakdown of endogenous opioids
- Increased peripheral release of serotonin hormones
- Histamine release, but to a lesser extent

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WHAT OTHER CONDITIONS ARE ASSOCIATED WITH PRURITUS?

- Dermatological (dryness, wetness, irritation, eczema, psoriasis)
- Metabolic (hepatic failure, renal failure, hypothyroidism)
- Hematologic (iron deficiency, polycythemia, thrombocytosis, leukemia, lymphoma)
- Infectious (scabies, lice, candida)
- Allergy (urticaria, contact dermatitis, drug reactions)
- Psychogenic

WHAT MEDICATIONS MAY PRECIPITATE PRURITUS?

- Opioids
- HAART (highly active antiretroviral therapy) drugs
- Antibiotics

HOW IS PRURITUS COMMONLY MANAGED?

Nonpharmacological

- Remove offending agent(s)
- Control temperature of environment (avoid heat, promote cool, humidified area)
- Avoid intake of caffeine, application of fragrant topicals
- Lukewarm bathing with unscented products

Topical (localized areas)

- Moisturizers/emollients (dry skin)
- Capsaicin, lidocaine, menthol (pain)
- Corticosteroids (inflammation) (i.e., hydrocortisone, betamethasone)

Oral (systemic therapy)

- Antihistamines (diphenhydramine)
- Corticosteroids (dexamethasone, prednisone, methylprednisolone)
- Serotonin modulators (paroxetine, sertraline, mirtazapine, ondansetron)
- Opioid antagonists (naloxone)
- Bile acid agents (rifampin, cholestyramine, colestipol)

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Click [here](#) for the comprehensive management tables from Alshammary, et al: Pruritus in palliative care published in *J Health Spec* 2016.3

PHARMACIST ASSESSMENT

Antihistamines have a role in cholestasis-induced itching for mild cases in the early stages of PBC. Corticosteroids may alleviate symptoms in all stages, however GH is not responding despite dose titration.

Opioid antagonists, such as naloxone have been shown to significantly reduce the sensation of cholestasis-induced itching. Potential disadvantages of this therapy include opioid withdrawal in patients using opioids for pain, the burden of frequent dosing as naloxone has a short half-life, and the need to administer parenterally. GH is currently prescribed an “as needed” regimen of morphine that she uses 1-2 times per day with relief, so this is not a viable option for her.

Considering the proposed causes of pruritus in cholestasis, there may be a role for a serotonin modulator and/or a medication that affects bile acid.

RECOMMENDATIONS TO REDUCE PRURITUS FOR GH

- Discontinue dexamethasone
- Keep diphenhydramine as PRN
- Continue morphine
- Consider cholestyramine powder, 4 grams PO Daily mixed in 2-6 ounces fluid, to bind bile acids

AND/OR

- Paroxetine 20mg PO Daily to inhibit reuptake of serotonin and keep it circulating centrally

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FOR ADDITIONAL INFORMATION ON THIS TOPIC, PLEASE REVIEW THESE REFERENCES:

Enclara Pharmacia's On Demand Educational Webinar, "Management of Less Common but Troubling Symptoms in Hospice: Pruritus, Hiccups, Cough, Muscle & Bladder Spasm". Click here to log in.

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6. Bergasa NV, Talbot TL, Alling DW, Schmitt JM, Walker EC, Baker BL, Korenman JC, Park Y, Hoofnagle JH, Jones EA. A controlled trial of naloxone infusions for the pruritus of chronic cholestasis. 1992 Feb;102(2):544-9.
7. Bergasa NV, Alling DW, Talbot TL, Swain MG, Yurdaydin C, Turner ML, Schmitt JM, Walker EC, Jones EA. Effects of naloxone infusions in patients with the pruritus of cholestasis. A double-blind, randomized, controlled trial. Ann Intern Med. 1995 Aug 1;123(3):161-7.
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9. Zylitz Z; Stork N; Krajnik M. Severe pruritis of cholestasis in disseminated cancer: developing a rational treatment strategy. J Pain Symptom Manage. 2005 Jan;29(1):p 100-103.