Clinical Resource Guide: Pruritus

INTRODUCTION TO PRURITUS

Pruritus, or itching, is a particularly distressing and often refractory symptom which patients may experience at the end of life. Scratching associated with itching may damage the skin and compromise its function as a barrier. In addition to superficial skin irritation or infection, many pruritic conditions have underlying systemic causes. Patients may describe pruritus as burning, tingling, numbness, or crawling in the skin. Itch may be mediated by histamine, serotonin, and pro-inflammatory cytokines. Patients may experience worsening agitation, fatigue, insomnia, and reduced quality of life as a result.

Pharmacist Corner Objectives

1.) Review the common causes of pruritus
2.) Describe pruritus associated with advanced liver and kidney disease
3.) Outline the non-pharmacological and pharmacological management of pruritus

COMMON CAUSES OF PRURITUS	
Allergens	Detergents, latex, soaps
Dermatologic	Irritation, dryness, eczema, psoriasis
Drug-Induced	Opioids, aspirin, drug reactions
Hematologic	Iron deficiency, polycythemia, leukemia, lymphoma, thrombocytosis
Infections	*Candida*, cellulitis, folliculitis, HIV, scabies, lice
Malignancy	Breast, CNS, leukemia, lung, melanoma, carcinoid syndrome
Metabolic	Hepatic failure, renal failure, hypothyroidism, electrolyte disturbances
Psychogenic	Psychological

CHRONIC LIVER DISEASE-ASSOCIATED PRURITUS

Pruritus is a common comorbidity in liver disease. Patients will frequently complain of intense itching that is unrelieved by scratching. Often, there are no discernable rashes or skin findings. Several potential mechanisms have been proposed, including bile acid accumulation, elevation of lysophosphatidic acid levels, and activation of specific neuronal pathways. Itching may be generalized or localized, particularly to the hands and soles of feet. The severity of itching does not typically correlate with the severity of the underlying liver disease. In the case of primary biliary cholangitis, disease-specific treatment of the underlying disorder using ursodeoxycholic acid (ursodiol) may be initiated. Mild pruritus may be treated with emollients and antihistamines. Moderate to severe pruritus may be treated with a bile acid sequestrant such as cholestyramine.

CHRONIC KIDNEY DISEASE-ASSOCIATED PRURITUS

Patients with chronic kidney disease may experience what is frequently called “uremic pruritus,” although this type of itch may occur in the absence of other symptoms associated with uremia. The pathophysiology is incompletely understood, but may include skin atrophy and dryness due to secondary hyperparathyroidism, accumulation of pruritogenic metabolites, and abnormal mast cell proliferation in skin. CKD-associated pruritus may involve the back, arms, abdomen, and head. Some patients may experience more generalized itching. Symptoms tend to be worse at night and result in sleep disruption. Patients with CKD should utilize topical emollients. Additional therapy may include topical analgesics such as pramoxine, oral antihistamines, gabapentin, and SSRIs.

NON-PHARMACOLOGICAL MANAGEMENT OF PRURITUS

- Treat dry skin through the topical application of moisturizing emollients such as Aquaphor®, EpiCeram®, or CeraVe®
- Cool compresses and oatmeal baths may provide temporary relief
- Encourage the use of gentle, fragrance-free detergents and soaps
- Avoid spicy foods, hot, water, excessive seating, caffeine, and alcohol
- For refractory cases, phototherapy using ultraviolet B light may be useful in pruritus associated with uremia, malignant skin infiltrations, and cholestasis

PHARMACOLOGICAL MANAGEMENT OF PRURITUS

Medication	Usual Adult Dose	Formulations	Notes
TOPICAL – ANESTHETICS & PROTECTANTS			
Camphor + menthol (Sarna®, Mentholatum®)	Apply as needed	Cream, gel, lotion, ointment	• Cooling and antipruritic • May act as a counterirritant • Avoid contact with open wounds, mucous membranes, burns
Calamine (Caladryl®)	Apply as needed	Lotion	• Astringent & protectant
Lidocaine + prilocaine (EMLA®)	Apply as needed	Cream	• Anesthetic used to reduce itching and irritation • Avoid contact with open wounds
Pramoxine	Apply as needed	Lotion	• Anesthetic used to reduce itching and irritation
TOPICAL STEROIDS			
Hydrocortisone (Cortaid®)	Apply BID	Cream, ointment, gel, lotion	• Helpful for inflammation • Ointment formulation preferred to alleviate dryness • Low potency
Triamcinolone (Kenalog®)	Apply BID	Cream, ointment, lotion	• Helpful for skin inflammation • Moderate potency
TOPICAL - ANTIFUNGALS			
Clotrimazole (Lotrimin AF®)	Apply BID	Cream, ointment, lotion	• Reassess if no improvement within 7 days
Nystatin (Nystop®)	Apply BID-TID	Cream, ointment, powder	• Use powder for moist topical lesions
ANTIHISTAMINES			
Hydroxyzine (Atarax®, Vistaril®)	25mg Q8H PRN	Tablets, capsules, oral liquid	• Antihistamine with anxiolytic properties • Anticholinergic side effects: sedation, dry mouth,

			constipation, urinary retention, confusion
Diphenhydramine (Benadryl®)	25mg Q6H PRN	Tablets, capsules, oral liquid	• Anticholinergic side effects: sedation, dry mouth, constipation, urinary retention, confusion
ORAL STEROIDS			
Prednisone	20mg QD	Tablets, solution	• Anti-inflammatory and immunosuppressant effects
Dexamethasone	4mg QD	Tablets, solution, injection	• Anti-inflammatory and immunosuppressant effects • Has less mineralcorticoid effect than prednisone
ANTIDEPRESSANTS			
Doxepin (Sinequan®)	10mg HS	Capsules, oral liquid	• Tricyclic antidepressant with significant antihistamine activity • Anticholinergic side effects: sedation, dry mouth, constipation, urinary retention, confusion
Mirtazapine (Remeron®)	7.5mg HS	Tablets, orally disintegrating tablets	• Antidepressant with antihistamine, alpha-adrenergic blocking, $5HT_3$ blocking properties • Consider for patients with comorbid depression and insomnia
Sertraline (Zoloft®)	25mg QD	Tablets, oral liquid	• Titrate to 75-100mg daily • Consider for patients with comorbid depression or insomnia
MISCELLANEOUS			
Cholestyramine (Questran®)	2-4g BID	Powder	• May decrease absorption of other medications. Separate by 2hours • Bile acid sequestrant; useful in cholestatic pruritus • Constipating; add stimulant laxative

Gabapentin (Neurontin®)	300mg HS	Tablets, capsules, solution	• Useful in neuropathic pruritus • Use with caution in advanced renal disease
Ondansetron (Zofran®)	4mg BID	Tablets, orally disintegrating tablets	• May provide benefit in refractory cases of uremic or cholestatic pruritus
Activated charcoal	Up to 6g QD	Capsules, powder	• May be useful in dialysis-related uremic pruritus
Rifampin (Rifadin®)	150mg QD	Capsules	• Risk of drug interactions; review medication profile carefully • Potent agonist of pregnane X receptor which mediates detoxification and hepatobiliary processes • Monitor liver function tests, CBC
Difelikefalin (Korsuva®)	0.5 mcg/kg IV at the end of each hemodialysis session	Injection	• Kappa opioid receptor agonist indicated for CKD-associated pruritus in patients undergoing hemodialysis • Long-term efficacy and safety data are limited
Naloxone (Narcan®)	0.25mcg/kg/hour	Injection	• Will reverse opioid analgesia • May be useful in severe cases of uremic or cholestatic pruritus

PHARMACOLOGICAL MANAGEMENT: CLINICAL PEARLS

1. Xerosis, or dry skin, can exacerbate all causes of pruritus. Ensure patients utilize a quality emollient to reduce dryness and irritation.

2. For suspected opioid-induced pruritus, consider rotating to a different opioid. Opioid-induced pruritus is less likely to occur with methadone, fentanyl, and hydromorphone.

3. Chronic pruritus is often refractory and may require combinations of topical and systemic medications to reduce symptoms.

4. Candidiasis skin rashes are bright red and macular with pustules or papules at the edges of the rash.

5. Itch may be mediated by inflammatory cytokines, peripheral histamine, or serotonin.

SUMMARY

The main causes of pruritus in the hospice and palliative care population are chronic kidney disease, liver disease, hematologic disorders, malignancies, opioids, and xerosis. If pruritus is mild, localized, or intermittent, topical therapies are preferred. When possible, systemic evaluation and treatment directed at the underlying cause of pruritus is recommended. Treatment of pruritus should be a sequential and stepwise approach based on the severity of symptoms and patient goals of care.

REFERENCES:

1. Berns, JS. Chronic kidney disease-associated pruritus. In: *UpToDate*, Taylor EN (Ed), Wolters Kluwer. (Accessed on May 10, 2024.)
2. Dalal, S. Overview of pruritus in palliative care. In: *UpToDate*, Givens J (Ed), Wolters Kluwer. (Accessed on May 8, 2024.)
3. Hegade, V. S., Kendrick, S. F. W., Rehman, J., & Jones, D. E. J. (2015). Itch and liver: management in primary care. *British Journal of General Practice*, 65(635), e418–e420. https://doi.org/10.3399/bjgp15 x685477
4. Palliative Care Network of Wisconsin. (2023, November 30). *Pruritus | Palliative Care Network of Wisconsin*. https://www.mypcnow.org/fast-fact/pruritus/
5. Poupon R, Chopra S. Pruritus associated with cholestasis. *UpToDate*. In: *UpToDate*, Lindor, KD (Ed), Wolters Kluwer. (Accessed on May 8, 2024.)
6. Protus, B. M., Kimbrel, J. M., & Grauer, P. A. (2015). *Palliative care consultant: Guidelines for Effective Management of Symptoms*. Hospiscript Services.

