



## PALLIATIVE CARE CASE OF THE MONTH

### “Scratching the Surface of the Treatment of Pruritus in Palliative Care”

by

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Volume 15, No. 49

June 2015

**Case(s):** Over the course of a month, three patients demonstrated the challenges of treating pruritus in the palliative care setting. Mrs. M is a 79-year-old woman with cutaneous T-cell Non-Hodgkin lymphoma with hypercalcemia and diffuse itching. She was treated with topical emollients (Aquaphor) and menthol creams (Sarna), which helped minimally, and hydroxyzine which caused delirium without improving itching. Mr. R is a 57-year-old gentleman with hepatocellular carcinoma, acute kidney injury and diffuse itching coincident with progression of his malignancy. He was started on hydroxyzine with subsequent worsening of his mental status. Mrs. L is a 66-year-old woman with metastatic appendiceal cancer, status post debulking surgery with acute, diffuse itching post-operatively who became sedated after treatment with diphenhydramine.

**Clinical Question:** Are anti-histamines effective in treating pruritus caused by medical illness? Are there medications other than less deliriogenic medications than anti-histamines that can be used to treat pruritus?

**Discussion:** *Pruritus related to renal dysfunction*

Uremic pruritus is one of the most common symptoms for patients with chronic kidney disease (CKD),<sup>i</sup> affecting up to 44% of patients undergoing dialysis.<sup>ii</sup> The pathophysiology of uremic pruritus is poorly understood, although hypotheses implicating immunologic and opioidergic systems have been proposed.<sup>iii</sup> These hypotheses guide management and treatment of this symptom. The initial therapy includes ensuring adequate dialysis and encouraging phosphate binders. Pruritus can be treated with gabapentin, pregabalin and sertraline. The initial dose of gabapentin is 100mg after each dialysis session which can be gradually increased to a maximum dose of 300mg after each session.<sup>iv</sup> Pregabalin can be used if gabapentin is ineffective,<sup>v</sup> and should be initiated at 25mg/day. Pregabalin doses greater than 75mg/day are not recommended in dialysis patients. If gabapentin or pregabalin is used, the patient should be monitored closely for adverse drug reactions such as dizziness and somnolence. Sertraline may also be an effective treatment option. In one uncontrolled study among 20 non-dialysis dependent CKD patients with severe pruritus refractory to antihistamines, 17 responded to sertraline (mean dose: 35mg/day) after a mean duration of 5.1 weeks.<sup>vi</sup> There is also a small amount of evidence and support for topical capsaicin, ondansetron, and naltrexone.<sup>vii</sup> Caution should be paid to the use of naltrexone as reversal of opioids being used for pain may be a side effect.

*Pruritus related to liver dysfunction*

Cholestatic pruritus is due to the impaired secretion of bile. The purported mechanism of action involves elevated plasma opioid levels and the enzyme autotaxin and its substrate lysophosphatidic acid.<sup>viii ix</sup> Other evidence-based therapies include: cholestyramine, colestipol, rifampin, naltrexone and sertraline.<sup>x</sup> The bile acid sequestrants (cholestyramine and colestipol) are effective first-line agents based on their favorable safety profile and tolerability. Effective dose ranges are 4-16g/day. Medication adherence can be a challenge with these as they are unpalatable, induce constipation and can interfere with the absorption of other medications. Rifampin may also be used to treat pruritus at doses of 150-300mg twice daily with consideration given to the risk of medication-induced hepatotoxicity.<sup>xi</sup> Sertraline at doses of 75-100mg/daily may be beneficial. Opioid antagonists may also be used.

*Pruritus due to malignancy*

Pruritus associated with malignancy may be due to cutaneous manifestation of malignancy as in mycosis fungoides or via a paraneoplastic process.<sup>xii</sup> Paroxetine has been shown to relieve itching from various malignant causes;<sup>xiii</sup> however, paroxetine induced nausea and vomiting can be limiting. Studies suggest starting low doses of 5-10mg/day to limit these effects. Relief of pruritus can be seen within 24-48 hours.<sup>xiv</sup>

*Pruritus due to opioids*

Opioid-induced pruritus occurs in 2-10% of patients receiving chronic opioid therapy. The mechanism of this is not known but appears to be mediated by  $\mu$ -opioid receptors, inhibited by  $k$ -opioid receptors and related to both histamine and serotonin pathways.<sup>xv</sup> There are no prospective studies on the treatment of opioid-induced pruritus. Treatment may include opioid rotation; however, cross-reactivity between all opioids is suspected.<sup>xvi</sup> Small amounts of evidence exist to support the use of paroxetine,<sup>xvii</sup> opioid-antagonists, NSAIDs, ondansetron, mirtazapine and gabapentin to relieve opioid induced pruritus. The strongest evidence available supports the use of ondansetron to treat opioid-induced pruritus, specifically pruritus from neuraxial opioids.<sup>xviii</sup>

*Personal details in the case published have been altered to protect patient privacy.*

For palliative care consultations please contact the Palliative Care Program at PUH/MUH, 647-7243, beeper 8511, Shadyside Dept. of Medical Ethics and Palliative Care, beeper 412-647-7243 pager # 8513, Perioperative/ Trauma Pain 647-7243, beeper 7246, UPCI Cancer Pain Service, beeper 644-1724, Interventional Pain 784-4000, Magee Women's Hospital, beeper 412-647-7243 pager #: 8510, VA Palliative Care Program, 688-6178, beeper 296. Hillman Outpatient: 412-692-4724. For ethics consultations at UPMC Presbyterian-Montefiore and Children's page 958-3844. With comments about "Case of the Month" call Dr. Robert Arnold at (412) 692-4834.



**Back to Cases:** Identifying the origin of a patient's pruritus is the first step in treating itching. Treatment should be tailored to the causative pathway. Evidence does not support the use of anti-histamines to treat pruritus in palliative care patients. Topical agents, other than capsaicin in the setting of uremic pruritus, have not been sufficiently studied to guide evidence-based decision making. In order to relieve pruritus and maximize mental status, we suggested changes to each patient's medications. We stopped the anti-histamines for all three patients. Mrs. M was started on paroxetine to treat itching related to malignancy. Mr. R was started on cholestyramine to treat itching related to hyperbilirubinemia. Mrs. L was started on nalbuphine, a mixed opioid agonist-antagonist, with improvement in pruritus and mental status without compromise of pain control.

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