

Opioid-Induced Pruritus: A Case Series on Novel Uses of Nalbuphine in the Emergency Department

Christopher Fernandes, MD *; Aurelio Muzaurieta, MD, MBA *; Yoseph Semma, MD *; Shawna Greenleaf, MD *, Joshua Park PharmD *; Terence Ahern, MD *; Jon B. Lee, MD * †

*Stanford University Department of Emergency Medicine, 900 Welch Road, Suite 350, Palo Alto, CA 94304

†Stanford University Department of Anesthesiology, Perioperative and Pain Medicine, 300 Pasteur Drive, Room H3580 MC 5640



Abstract

Opioid-induced pruritus (OIP) is a common side effect of mu-opioid receptor (MOR) agonists and is often unresponsive to antihistamines.

Nalbuphine is a mixed kappa-opioid receptor (KOR) agonist and MOR antagonist that provides analgesia and prevents pruritus.

Two emergency department (ED) cases:

Case 1: 2.5 mg IV nalbuphine + hydromorphone prevented itching.

Case 2: 10 mg IV nalbuphine used as primary analgesic.

Both patients experienced pain relief without pruritus or sedation.

Highlights nalbuphine’s safety and potential role in acute care.

Introduction

Nalbuphine is a **synthetic opioid**: KOR agonist + MOR antagonist.

Benefits:

Provides analgesia while minimizing side effects (pruritus, respiratory depression, nausea).

FDA-approved since 1979 for moderate to severe pain (IV, IM, SC).

Mechanism:

KOR activation → spinal/supraspinal analgesia.

MOR antagonism → reduces side effects without reversing analgesia.

Typical dosing:

Analgesia: 10 mg IV/IM q3–6h (max 20 mg/dose, ceiling ~30 mg).

OIP treatment: 2.5–5 mg IV.

Evidence:

Effective in preventing/treating OIP in perioperative settings.

Reduces OIP incidence without reducing analgesia.

Shown to be **as effective as morphine** but with fewer side effects.

OIP pathophysiology:

Mostly **centrally mediated** via MOR activation → itch independent of histamine.

Explains why **antihistamines** (e.g., diphenhydramine) have limited effect.

Peripheral histamine-mediated itch less common.

Nalbuphine may be safer than morphine—less respiratory depression, less itching.

Cases

CASE 1

- 51-year-old woman with small bowel obstruction (SBO)
- History: severe OIP from hydromorphone (non-allergic, centrally mediated)

TREATMENT

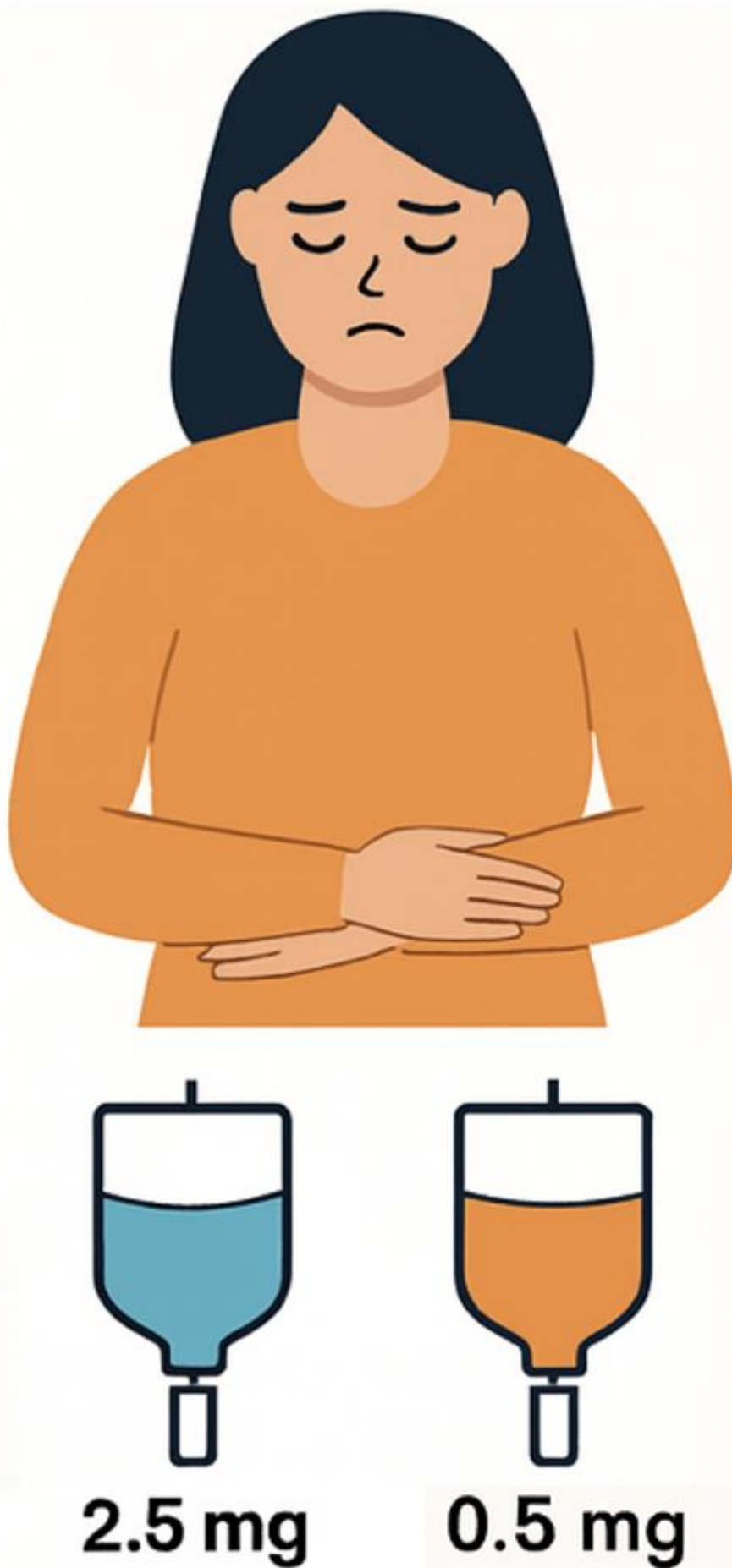
- 2.5 mg IV nalbuphine + 0.5 mg IV hydromorphone
- Continued nalbuphine 2.5 mg IV q4h PRN

POST-OP

- PCA hydromorphone + nalbuphine prophylaxis 5 mg IV q 3h) Maintained pain control

OUTCOME

- Tolerated the regimen well + discharged on hospital day 10



CASE 2

- 63-year-old man with gout, CAD, diabetes, OSA, and prior OIP history
- Presented with right knee pain

TREATMENT

- 10 mg IV nalbuphine → significant pain relief without itching
- Discharged with prednisone

FOLLOW-UP

- Returned 3 weeks later with gout flare → treated with nalbuphine 10 mg IV again
- Continued good pain relief, no itching or sedation

OUTCOME

- Nalbuphine well tolerated
- Discharged on hospital day 7 after improvement



Discussion

Nalbuphine is well-suited for managing **opioid-induced side effects**.

Mechanism-based benefits:

MOR antagonism → blocks central OIP mechanism.

KOR agonism → maintains analgesia with low respiratory risk.

Ceiling effect (~30 mg) limits use in severe pain but ideal for moderate pain.

Compared to diphenhydramine:

Antihistamines ineffective for central OIP.

Diphenhydramine causes sedation, cognitive side effects, misuse potential.

Advantages of nalbuphine:

True antipruritic effect (not just sedative).

Low abuse risk.

Minimal sedation.

Effective as both prophylactic and therapeutic option.

Caution: May precipitate withdrawal in chronic opioid users → monitor closely.

Barriers: Limited ED data, lack of formulary inclusion, prescriber unfamiliarity.

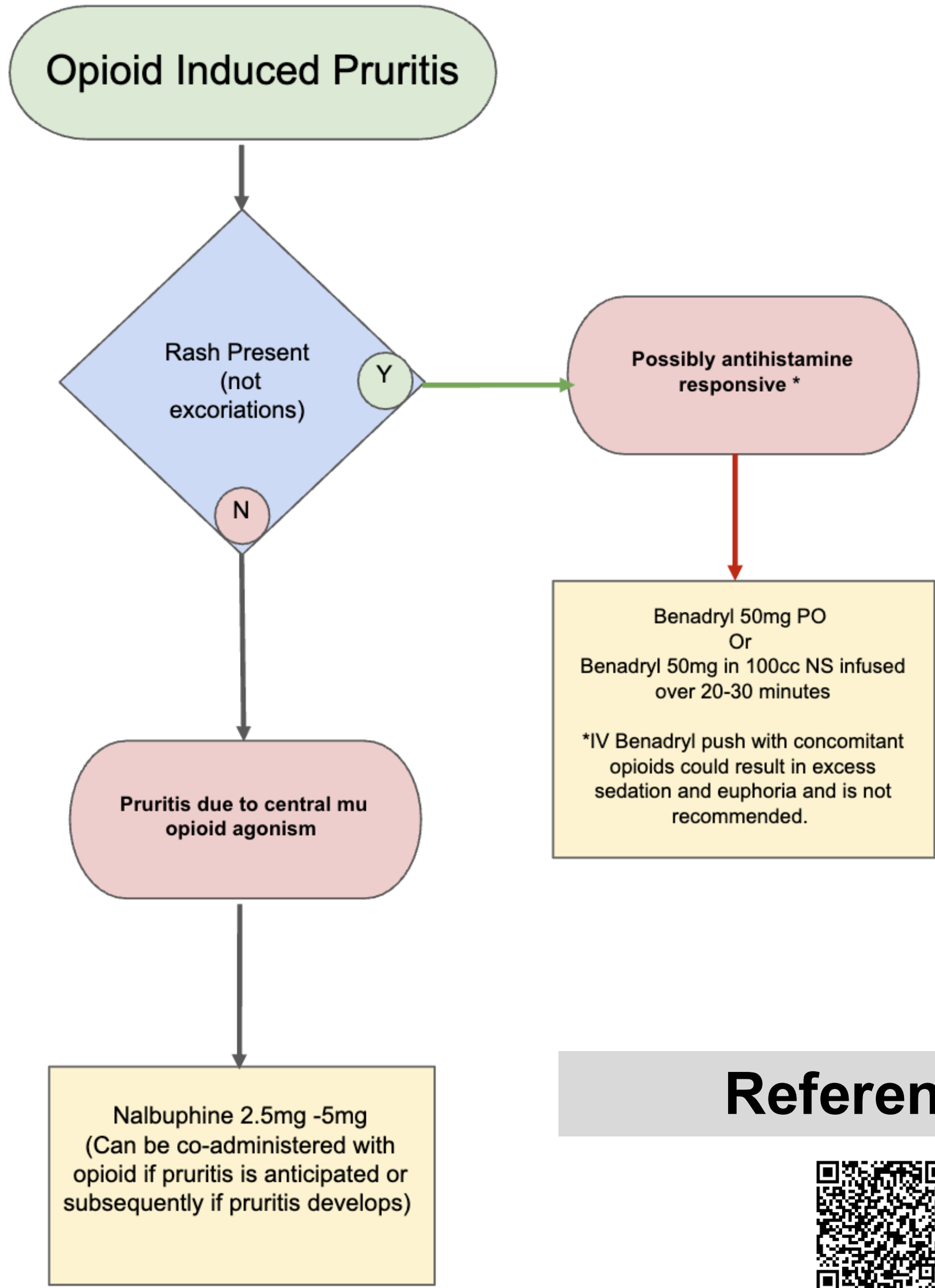
Conclusion: Nalbuphine could fill a critical gap as a **safe, mechanism-based option** for OIP and pain in the ED.

Conclusion

These two cases demonstrate the safe and effective use of nalbuphine in the ED, both as a prophylactic adjunct to prevent OIP and as a standalone analgesic. Nalbuphine’s dual receptor action provides targeted control of both pain and pruritus, reducing the need for sedating antihistamines and offering an alternative to conventional mu-agonist opioids. Its favorable safety profile and low abuse potential support further study and integration into emergency pain management protocols.

Next Steps

We are aiming at instituting the following protocol in our Emergency Department:



References

