In This Issue

From the Department of Pharmacy
Drug Information Service
(216) 444-6456, option #1

Clinical Rx Forum
Cleveland Clinic

Comprehensive information about medications, biologics, nutrients, and drug therapy

Cleveland Clinic
Clinical Rx Forum
From the Department of Pharmacy

September/October Issue **2025 Volume 13 Issue 5**

Can Posaconazole DR Tablets Be Administered Through a Feeding Tube?

By: Joseph Cherian, Pharm.D.

Introduction: Posaconazole is an antifungal agent that is approved by the Food and Drug Administration (FDA) for various indications including prophylaxis and treatment of certain invasive fungal infections. It is available in a variety of dosage forms, including a 100 mg delayed-release (DR) tablet, 300 mg DR suspension, 40 mg/mL immediate-release suspension, and an intravenous (IV) formulation. The oral suspension is associated with erratic absorption, requiring divided dosing and administration with food or acidic beverages to optimize bioavailability; this can be challenging in patients unable to tolerate oral intake or those with enteral feeding tubes. Unlike the suspension, the oral DR tablets do not need to be administered with food and may be given once daily. Furthermore, the DR tablet formulation provides more predictable pharmacokinetics and higher plasma concentrations than the oral suspension. However, one potential drawback of the DR tablet is that its FDA labeling specifically states it should be swallowed whole and not crushed, divided, or chewed.

Rationale for Crushing Posaconazole DR Tablets: Most DR tablets contain a special coating or matrix that allows for a gradual, controlled release of the medication. Delayed-release tablets should generally be swallowed whole since crushing could disrupt their DR mechanism, resulting in dose dumping and an increased risk of drug toxicity. However, posaconazole DR tablets are unique compared with other DR products. The polymer powder matrix of the tablet is designed to dissolve at the alkaline pH of the small intestine. Crushing the posaconazole DR tablet does not interfere with the polymer powder matrix's pH-sensitive release mechanism.

Factors Supporting Feeding Tube Administration: Crushed posaconazole DR tablets have been considered for administration via a feeding tube in patients unable to swallow, particularly when the oral suspension is unavailable or may be ineffective due to variable absorption. Therapeutic drug monitoring (TDM) can be used to adjust dosing to achieve target plasma concentrations and has been proposed as a strategy to ensure adequate drug exposure and improve clinical outcomes. Although target levels are still debated, clinical studies suggest that trough concentrations >0.7 mg/L are appropriate for prophylaxis, while levels >1.0–1.25 mg/L are recommended for treatment. Routine measurement of posaconazole levels may not always be needed due to the improved pharmacokinetics of the DR tablets.

Clinical Studies: Several case series and retrospective studies support crushing the DR tablets and administering them via a feeding tube. Dieringer and colleagues found that 71.5% of patients (n=14) receiving crushed posaconazole via an enteral feeding tube achieved target plasma levels on first assessment (mean

(Continued on page 2)

(Continued from page 1)

1.61 ± 0.77 mg/L), for those with subtherapeutic initial levels. Most patients received standard maintenance dosing, and no breakthrough invasive fungal infections were reported during monitoring. Furthermore, dosing posaconazole via a feeding tube was estimated to spare 526 days of IV therapy, facilitating earlier hospital discharge and reducing overall healthcare costs. Additionally, Manesh and colleagues reported that all patients (n=19) who received crushed DR posaconazole tablets via a nasogastric tube reached therapeutic levels and had favorable outcomes.

Final Considerations: Coadministration of posaconazole DR tablets with a proton pump inhibitor or any other agent that raises gastric pH can cause the drug to be released in the stomach rather than the small intestine resulting in subtherapeutic levels. A potential advantage of administering crushed posaconazole DR tablets through a feeding tube is the ability to discontinue the IV formulation earlier, resulting in lower drug costs. Cleveland Clinic restriction criteria state that posaconazole DR tablets may be crushed and administered via an enteral feeding tube with dosage adjustments made based on TDM. When used for the initial treatment of fungal infections, transition to crushed posaconazole tablets should be done in consultation with the Department of Infectious Diseases. Of note, posaconazole is not listed by the National Institute for Occupational Safety and Health as a hazardous drug, so it may be crushed on the nursing units.

References:

1. Posaconazole delayed-release tablets [package insert]. Congers, NY: Chartwell RX, LLC.; August 2025.
2. Krishna G, Ma L, Martinho M, O'Mara E. Single-dose phase I study to evaluate the pharmacokinetics of posaconazole in new tablet and capsule formulations relative to oral suspension. Antimicrob Agents Chemother. 2012;56(8):4196-201.
3. Dieringer TD, Schaenman JM, Davis MR. Enteral feeding tube administration with therapeutic drug monitoring of crushed posaconazole tablets and opened isavuconazonium sulfate capsules. J Antimicrob Chemother. 2022;77(5):1417-23.
4. Mason MJ, McDaneld PM, Musick WL et al. Serum levels of crushed posaconazole delayed-release tablets. Antimicrob Agents Chemother. 2019; 63(5):e02688-18.
5. Dekkers BGJ, Bakker M, van der Elst KCM et al. Therapeutic drug monitoring of posaconazole: an update. Curr Fungal Infect Rep. 2016;10:51-61.
6. Manesh A, Devasagayam E, Bhanuprasad K, et al. Efficacy of crushed delayed-release posaconazole tablets in rhino-orbito-cerebral mucormycosis. Antimicrob Agents Chemother. 2022; 2066(12):e0108522.
7. Störzinger D, Borghorst S, Hofer S et al. Plasma concentrations of posaconazole administered via nasogastric tube in patients in a surgical intensive care unit. Antimicrob Agents Chemother. 2012;56(8):4468-70.
8. Prayag PS, Panchakshari SP, Mahalle NP, et al. Factors associated with subtherapeutic levels of oral posaconazole tablet: a detailed analysis from a tertiary care center in India. Int J Infect Dis. 2022;124:76-80.
9. Wiederhold NP. Pharmacokinetics and safety of posaconazole delayed-release tablets for invasive fungal infections. Clin Pharmacol. 2015;2:8:1-8.

What Are Some Therapeutic Alternatives to Meperidine for Shivering/Rigors?

By: Marianne Said, Pharm.D.

Introduction: Shivering is a physiological response involving repeated skeletal muscle contractions to generate heat when exposed to cold temperatures; rigors is a more intense form of shivering. The American Society of Anesthesiology guidelines had previously recommended meperidine as the first-line treatment for shivering during emergence and recovery after anesthesia. Due to a shortage of this medication, alternative therapeutic options should be considered for the treatment of shivering/rigors for various indications.

Morphine and Monoclonal Antibody-Related Infusion Reactions: Morphine primarily reduces shivering by binding to mu-opioid receptors which regulate body temperature. Meperidine's anti-shivering effect is due to its action on the kappa-opioid receptor and the alpha2b adrenergic receptor subtype. A 2024 retrospective cohort study conducted by Yakubi and associates compared the effectiveness of meperidine 25 mg to morphine 2 mg for treating monoclonal antibody infusion-associated rigors. This study reported 153 rigor events, with approximately 80% of participants requiring only one dose of either medication to alleviate rigors. From the results of this study, investigators concluded that morphine was a suitable alternative to meperidine for antibody-related infusion reactions.

Dexmedetomidine and Caesarean Delivery Induced Shivering: Dexmedetomidine is used to treat shivering by inhibiting the sympathetic response through its action as a selective alpha2 receptor agonist. Given its potential adverse effects on the cardiovascular and nervous systems, dexmedetomidine should be administered in an intensive care unit with continuous monitoring. A 2019 prospective, double-blind, randomized clinical study by Yu and associates compared dexmedetomidine (0.5 μg/kg) to meperidine (0.5 mg/kg) for shivering after caesarean delivery. This study included 100 participants, with 50 assigned to each of the two treatment groups. There was no difference in efficacy between the two treatments, and both induced a response within 15 minutes of administration.

Ketamine and Postanesthetic Shivering: Ketamine has a thermoregulatory effect primarily due to its noncompetitive N-methyl-D-aspartate receptor antagonist activity. A meta-analysis by Zhou and associates evaluated the role of ketamine compared to placebo and other pharmacological agents, such as tramadol and ondansetron, in post-anesthesia shivering. Ketamine was shown to be superior to placebo in reducing postanesthetic shivering, but demonstrated no significant difference in efficacy compared to other anti-shivering agents such as tramadol and ondansetron.

Buspirone and Therapeutic Temperature Modulation: Buspirone acts on the 5-HT1A serotonin receptors to reduce the threshold for shivering. It is used off-label as part of a multimodal anti-shivering protocol in the critical care settings. A 2007 study by Lenhardt and associates investigated the role of buspirone 60 mg orally with or without dexmedetomidine (target plasma concentration of 0.6 ng/mL) in reducing shivering in eight healthy patients. Buspirone alone was able to lower the shivering threshold by 0.7°C, while the combination of buspirone and dexmedetomidine produced an additional decrease of 1.8°C, suggesting a synergistic effect.

Final Considerations: Some alternative treatments to meperidine for shivering/rigors include morphine, dexmedetomidine, ketamine, and buspirone. It is important to note that there are other pharmacologic options. The choice of therapy would depend on the indication and the patient's clinical status.

References:

1. Apfelbaum JL, Sliverstein JH, Chung FF, et al. Practice guidelines for postanesthetic care: an updated report by the American Society of Anesthesiologists Task Force on Post anesthetic Care. Anesthesiology. 2013;118(2):291-307.
2. Amsalu H, Zemedun A, Regasa, et al. Evidence-based guideline on prevention and management of shivering after spinal anesthesia in resource-limited settings: Review Article. Int J Gen Med. 2022;15: 6985-98.
3. Yakubi H, Steele AP, Tsao M. Meperidine compared to morphine for rigors associated with monoclonal antibody-related infusion reactions. J Oncol Pharm Pract. 2025;31(5):775-9.
4. Yu G, Jin S, Chen J, et al. The effects of novel α_2-adrenoreceptor agonist dexmedetomidine on shivering in patients underwent caesarean section. Biosci Rep. 2019; 39(2):BSR20181847.
5. Zhou Y, Mannan A, Han Y, et al. Efficacy and safety of prophylactic use of ketamine for prevention of postanesthetic shivering a systematic review and meta analysis. BMC Anesthesiol. 2019;19(1):245.
6. Lenhardt R, Orhan-Sungur M, Komatsu R, et al. Suppression of shivering during hypothermia using a novel drug combination in healthy volunteers. Anesthesiology. 2009;111(1):110-5.