
Edward Scott Vokoun, MD

I thank SGM Bowling for his interest in my article. One of the advantages of intravenous (IV) acetaminophen (Orfirmev®; Mallinckrodt Pharmaceuticals, www.ofirmev.com) is the ability to reach peak plasma concentration and thus meaningful pain relief within 15 minutes of infusion.¹ No other route of administration will result in a pharmacokinetic profile as rapid and as consistent. However, I acknowledge that the ability to achieve IV access cannot be assumed in the field.

Oral administration is characterized by relatively high bioavailability (85–93%) but varying early plasma concentrations such that the concentration may remain subtherapeutic for as long as 60–80 minutes.¹ I do not have information on whether the rapid-release gel cap formulation described by SGM Bowling significantly decreases time to peak plasma concentration compared with a pill or capsule. However, it could be considered as an option for the field medic who cannot administer IV acetaminophen.

It should be noted that oral administration is subject to hepatic first-pass metabolism. Avoidance of the portal circulation and hepatic first-pass exposure is one of the major advantages of the IV route.² While there is scant evidence that acetaminophen toxicity occurs at therapeutic dosing, even in chronic liver disease, in overdose the mechanism of toxicity is the exhaustion of hepatic glutathione stores in the liver during first-pass metabolism.³ This highlights the importance of properly documenting the time and dose of acetaminophen, regardless of the administration route, before medical evacuation, in order to avoid inadvertent overdose due to subsequent administration of acetaminophen at higher echelons of medical care.

Another possibility for use of acetaminophen in a patient unable to take oral medication would be acetaminophen suppositories. This is a very common perioperative pain strategy in the pediatric population. Suppositories are small, lightweight, and easy to place. Unfortunately rectal administration requires 4 hours to achieve peak plasma concentration. Rectal formulations are associated

with lower bioavailability and wider variability in effect among patients compared with oral formulations due to the possibility of obtaining a subtherapeutic plasma concentration.¹

Theoretically, the intramuscular (IM) route would be advantageous to both preserve some of the physiologic advantages gained by IV acetaminophen and avoid the need for obtaining IV access or placing a nasal gastric tube. However, to make the IM route feasible, a more concentrated formulation would be required from the manufacturer, as the Orfirmev® concentration is 1g in a 100mL vial, which is too dilute for IM use. At this time, I am unaware of any data on the pharmacokinetics of the IM route. This is probably due to the lack of an IM formulation.

Disclaimer

The views expressed in this article are those of the author and do not necessarily reflect the official policy or position of the US Fleet Forces Command, the Department of the Navy, the Department of Defense, or the US Government.

References

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CDR Vokoun graduated from the University of Texas Southwestern Medical School. He is a board-certified anesthesiologist who has served as head anesthesiologist at a Role 2 in Afghanistan. He is currently the senior medical officer at Explosive Ordnance Group Two and a staff anesthesiologist at Naval Medical Center Portsmouth, Portsmouth, Virginia. He can be reached at Edward.vokoun1@navy.mil.