

Preventing Serious Tissue Injury with Intravenous Promethazine (Phenergan)

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PROBLEM: Promethazine (Phenergan, Wyeth) is a commonly used injectable product that possesses antihistamine, sedative, anti-motion sickness, and anti-emetic effects. The drug is also a known vesicant that is highly caustic to the intima of blood vessels and surrounding tissue. Formulated with phenol, promethazine has a pH between 4 and 5.5. Although deep intramuscular (IM) injection into a large muscle is the preferred parenteral route of administration, the product's labeling states that the drug may be given by slow IV push, the method typically used in most hospitals. However, because of the frequency of serious, tragic, local injuries after infiltration or inadvertent intra-arterial injection, the Institute for Safe Medication Practices (ISMP) recommends that the FDA re-examine the product labeling and consider eliminating the intravenous (IV) route of administration.

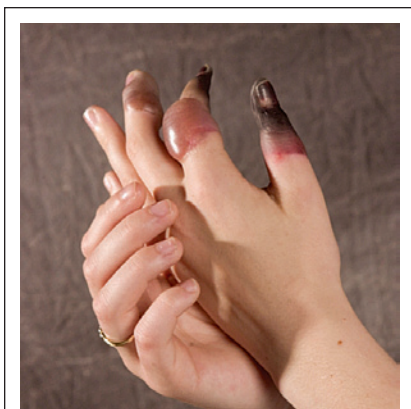


Figure 1 The fingers of a patient who received promethazine have shriveled and turned black. The patient's thumb, index finger, and top of her middle finger had to be amputated.

Severe tissue damage can occur regardless of the route of parenteral administration, although IV and inadvertent intra-arterial or subcutaneous (SQ) administration results in more significant complications, including burning, erythema, pain, swelling, severe spasm of vessels, thrombophlebitis, venous thrombosis, phlebitis, nerve damage, paralysis, abscess, tissue necrosis, and gangrene. Sometimes a surgical intervention, such as fasciotomy, skin graft, and even amputation, has been required.

The true extent of the problem may be unknown, but it appears that patients are being harmed more often than is commonly recognized. Scores of reports have been submitted to the ISMP, the U.S. Pharmacopeia, and the Pennsylvania Patient Safety Reporting System. Articles in professional literature; news of lawsuits in the media; and communications on various Internet listservs and message boards (ISMP, the National Patient Safety Foundation, <http://allnurses.com>, and others) have also been prevalent.

The following scenarios were brought to our attention at the ISMP:

- A 19-year-old woman arrived in the emergency department (ED) with flu-like symptoms. She received IV promethazine.¹ During the injection, she yelled out in pain and was tempted to pull out her IV line. Afterward, she told the nurse that her arm was still in pain and that she felt "something was wrong." The nurse reassured the patient and left the room. The patient's arm and fingers became purple and blotchy. The patient remained in the hospital for 30 days, during which time she watched her previously healthy fingers turn black and shrivel (Figure 1). Her thumb, index finger, and top of her middle finger had to be amputated.
- A patient received 12.5 mg of promethazine into an IV site in the hand. The patient complained of extreme burning, during the injection, but the nurse con-

tinued administering the agent. An area of necrosis developed on the patient's hand, and skin grafting and physical rehabilitation were eventually needed.

- A professional guitar player, Diana Levine from Vermont, was awarded \$2.4 million for past and future medical expenses and \$5 million for pain and suffering after she endured two amputations following accidental arterial administration of the branded drug, Phenergan.² Because of a migraine, the patient had gone to the ED, where she received Phenergan, intended for IV administration. She experienced circulatory problems and then progressive gangrene, which led to amputation of her arm in stages. Her case eventually reached the Supreme Court.

SAFE PRACTICE RECOMMENDATION: The package insert for Phenergan states: "Proper IV administration of this product is well tolerated, but use of this route is not without some hazards." To reduce the risk of these hazards, the manufacturer recommends giving the drug in concentrations no greater than 25 mg/mL and no faster than a rate of 25 mg/minute. The drug should be injected through the tubing of an infusion set that is running and known to be functioning satisfactorily, and the injection should be stopped immediately if the patient reports burning in order to evaluate possible arterial placement or perivascular extravasation. Nonetheless, the ISMP believes that health care providers, the FDA, and promethazine manufacturers must take further action to prevent these long-standing hazards.

Along with the manufacturer's recommendations, the following strategies should be considered to prevent or minimize tissue damage when patients receive IV promethazine:

1. **Limiting the concentration.** Because 25 mg/mL is the highest strength of promethazine that can be given intravenously, only this concentration (not

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50 mg/mL) should be stocked.

2. **Limiting the dose.** Promethazine 6.25 to 12.5 mg should be considered the starting IV dose, especially for elderly patients. These smaller doses have proved quite effective in hospitals.

3. **Diluting the drug.** Further dilution of the 25-mg/mL strength is required to reduce vesicant effects and to enable slow administration. For example, the drug can be diluted in 10 to 20 mL of normal saline if it is to be given via a running IV line. Alternatively, it can be prepared in mini-bags containing normal saline if the pharmacist has time to dispense them as needed for individual patients. Extravasation is also recognized more quickly when promethazine is diluted than when it is given in a smaller volume.

4. **Using large patent veins.** Promethazine should be administered only via a large-bore vein, preferably via a central venous access site, not by veins in the hand or wrist. The patency of the access site should be checked before administration. According to the package insert, aspiration of dark blood does not preclude intra-arterial placement of the needle because blood can become discolored upon contact with promethazine. The use of syringes with rigid plungers or small-bore needles might obscure typical arterial backflow if practitioners rely on this method alone. The medication should be injected through a running IV line at the port that is farthest from the patient's vein.

5. **Administering the drug slowly.** IV promethazine can be administered over 10 to 15 minutes.

6. **Revising order forms.** Preprinted order forms should be revised to ensure that the orders for promethazine reflect the safety measures listed previously.

7. **Educating patients.** Before administration, patients should be advised to let the practitioner know immediately whether burning or pain occurs during or after the injection.

8. **Creating alerts.** An alert should appear on computer-generated medication administration records (MARs), on electronic MARs, and on the screens of automated dispensing cabinets for nurses to view each time they access and administer a dose of promethazine. This approach can be an effective reminder that the drug is a vesicant and that it

should be diluted and should be administered slowly through a running IV tube.

9. **Treating the patient.** The manufacturer notes that no method has proved successful in managing unintentional intra-arterial injection or perivascular extravasation. However, sympathetic block and heparinization have been used during the acute management of promethazine extravasations.

10. **Trying alternative therapies.** Practitioners can consider safer alternatives to use for various conditions commonly treated with IV promethazine. As an example, 5-hydroxytryptamine type 3 (5-HT₃) receptor antagonists can be used for both prophylaxis and as a rescue antiemetic agent for postoperative nausea or vomiting (PONV). The package insert for ondansetron (Zofran, GlaxoSmith-Kline) states that patients not receiving prophylactic ondansetron who experience PONV may receive this agent to prevent further episodes. Appropriate surgical patients should receive 5-HT₃ for PONV, and patients should be well hydrated to reduce the risk of PONV and to reduce the need for a rescue antiemetic agent.

10. **Removing promethazine from the formulary.** Some hospitals that have continued to experience adverse outcomes despite safety measures have removed promethazine from the formulary or have banned its IV use.

REFERENCES

1. Friederich S. Malpractice allegations spotlight anti-nausea medication. *The Daily World*, Aberdeen, WA; December 7, 2005. Available at: www.thedailyworld.com/articles/2005/12/07/local_news/02news.txt. Accessed March 3, 2009.
2. Patrick J. Marshfield woman wins \$7.4 million jury award after she loses arm. *The Barre Montpelier Times Argus*; Barre, VT; March 19, 2004.

The reports described in this column were received through the ISMP Medication Errors Reporting Program (MERP). Errors, close calls, or hazardous conditions may be reported on the ISMP Web site (www.ismp.org) or communicated directly to ISMP by calling 1-800-FAILSAFE or via e-mail at ismpinfo@ismp.org ■