LETTERS TO THE EDITOR

Article on Mitoxantrone-Induced Extravasation Raised Useful Questions

The case study on mitoxantrone-induced extravasation presented in the “Clinical Challenges” column (Vol. 32, pp. 27–29) is a valuable addition to the scant published documentation of these types of injuries. I applaud the case study author for sharing her observations and photographic documentation of mitoxantrone-induced tissue necrosis and taking action to review the literature and change nursing practice at her institution.

The authors of the column raised intriguing questions about mitoxantrone classification and administration. At the case study author’s institution, mitoxantrone was added to the institution’s vesicant list. The reclassification appears to be based on the author’s experience of personally observing a mitoxantrone extravasation injury and the classification of mitoxantrone as a vesicant by the Oncology Nursing Society and authors of two journal articles.

Mitoxantrone-induced tissue necrosis has been documented in case reports (Levin, Caravone, & Geiser, 1996; Peters, Beijnen, & ten Bokkel Huinink, 1987) and research studies (Bertelli et al., 1995 [13 cases]; Tsavaris et al., 1990 [7 cases]), so additional evidence indicates that mitoxantrone has vesicant properties. As noted in the column, the manufacturer of mitoxantrone does not explicitly state that mitoxantrone is a vesicant; however, it advises that “care should be taken to avoid extravasation” and that “signs or symptoms of extravasation” include “burning, pain, pruritus, erythema, swelling, blue discoloration, or ulceration” (Serono, Inc., 2003).

Mitoxantrone is classified as an antecedrinel and has a mechanism of action that is similar to the action of the anthracylines, such as doxorubicin and daunorubicin, which are known vesicants. Mitoxantrone intercalates into DNA through hydrogen bonding, which causes crosslinks and DNA strand breaks. It also interferes with RNA synthesis and is an inhibitor of topoisomerase II (an enzyme responsible for uncoiling and repairing damaged DNA). The mean alpha half-life of mitoxantrone is 6–12 minutes; therefore, it is rapidly tissue bound if it inadvertently extravasates from a vein (Fox & Smith, 1990; Serono, Inc., 2003).

The collective documented evidence of 23 mitoxantrone extravasation injuries, manufacturer’s recommendations, and pharmacology of the drug suggest that mitoxantrone is indeed a vesicant and should be classified as such. The author notified her institution’s pharmacy and the U.S. Food and Drug Administration of the mitoxantrone extravasation injury. In addition, nurses who observe tissue injury secondary to extravasation of drugs classified by their manufacturers as nonvesicants, irritants, or exfoliants (a term commonly used in the United Kingdom) also should notify the drug’s manufacturer and perhaps advocate for revision of package insert information. (I sent a copy of the article to Serono, Inc., along with a copy of this letter, and have asked for a response.)

Whenever it is suggested that oncology drugs are reclassified, an important question needs to be asked, and that is how will a change in drug classification affect clinical practice? In the case of mitoxantrone, reclassification as a vesicant would warrant implementation of vesicant precautions when administering the drug. Quite simply, nurses would use greater care when administering mitoxantrone.

Nurses would inform patients about the risk for extravasation-induced tissue injury, instruct patients to report pain or any unusual sensations at the infusion site, and advise patients to refrain from movement during vesicant administration. Nurses would insert a new IV catheter using a “clean stick” (nonprobing) technique and administer the mitoxantrone in accordance with vesicant administration guidelines, which include verifying a blood return prior to and every 2–3 ml during an IV bolus (push) or monitoring an infusion approximately every five minutes (Brown et al., 2001). Also, as noted in the column, veins in the forearm as opposed to the hand are preferred for vesicant administration because the dorsum of the hand has little subcutaneous tissue and vesicant extravasation injuries in this area often are severe.

Mitoxantrone is used as a treatment for multiple sclerosis and, depending on the setting, is administered by oncology or nononcology nurses. Changing the classification of mitoxantrone to vesicant may have practice implications in settings where policies dictate that vesicants must be administered by chemotherapy-certified nurses.

Although it may be tempting to conclude that the patient’s extravasation injury would not have occurred if mitoxantrone had been classified as a vesicant, vesicant extravasation injuries still can occur even when vesicant administration precautions are utilized. Several factors that increase the risk for vesicant extravasation were described in the column. An additional factor, patient movement, merits mention. Movement of arms and hands may increase the risk for peripheral vesicant extravasation, and arm and shoulder movement may increase the risk of vesicant extravasation from an implanted port. Advising patients to refrain from movement during vesicant administration may help decrease the risk for extravasation.

Suspected vesicant extravasations must be assessed and managed promptly. If a mitoxantrone extravasation is known or suspected, elevation and ice packs are recommended by the manufacturer. The manufacturer further states that “because of the progressive nature of extravasation reactions, the area of injection should be frequently examined and surgery consultation obtained early if there is any sign of a local reaction” (Serono, Inc., 2003, p. 33).

Tsavaris et al. (1990) conservatively treated seven mitoxantrone extravasation injuries with hydrocortisone and antibiotic ointment. Time to recovery ranged from 6–48 days, and none of the patients required surgery. Bertelli et al. (1995) treated 13 mitoxantrone extravasations with topical dimethylsulfoxide (DMSO) (99% solution, with four drops applied per 10 cm2 of skin surface every eight hours for one week) and observed that 11 of the 12 evaluable patients had complete recovery within one week and one experienced residual hyperpigmentation. Mitoxantrone extravasation details, including drug concentration, estimated amount extravasated, location of extravasation, and photographs, were not included in the study report. Further evaluation of DMSO treatment of vesicant extravasations is needed before it can be advocated as a mitoxantrone extravasation treatment. Also, medical grade 99% DMSO solutions are not available in the United States but are available in other countries.

In addition to changing the classification of mitoxantrone at the author’s institution, another change was to begin administering it as an IV push through a free-flowing IV line rather than as an infusion. The manufacturer states that doses of mitoxantrone should be diluted to at least 50 ml with either normal saline (NS) or dextrose 5% (D5W). It may be further diluted with NS, D5W, or D5W with NS. The diluted solution is administered into