Chemotherapy Extravasations: Prevention, Identification, Management, and Documentation

Tulia Gonzalez, RN, OCN®

The nurses’ role in safe and effective practice of chemotherapy administration is paramount. The purpose of this article is to present nurses administering chemotherapy with evidence-based information useful in eliminating or reducing the severity of an injury from a chemotherapy extravasation. Nurse education is essential to prevent, recognize, manage, and document chemotherapy extravasations. The classification of the cytotoxic drug and its mechanism of action is useful when selecting the IV access device and also will direct the nurse’s intervention to manage the injury. The Oncology Nursing Society’s Chemotherapy and Biotherapy Guidelines and Recommendations for Practice and the drug manufacturer are the best sources offering pharmacologic and nonpharmacologic recommendations. The nurse’s best ally in the prevention, prompt recognition, and management of an extravasation is the educated patient. Documenting chemotherapy extravasation is another important step to guide the treatment plan; therefore, the document must provide complete details and the extent of the event.

A 67-year-old male with non-small cell lung cancer receiving docetaxel via peripheral infusion in the outpatient clinic suffered an extravasation. The nurse caring for him noticed inflammation around the peripheral site, prompting her to stop the infusion and notify the advanced registered nurse practitioner (ARNP). The IV catheter from the peripheral site was removed and cool packs were applied to the site. The patient was discharged from the clinic with instructions from the ARNP to apply cool compresses for 15–20 minutes four times daily for the next 48–72 hours. By the third day, the patient’s hand had become erythematous with a burning-stabbing pain of 7 on a 0–10 scale. The ARNP in collaboration with the oncologist prescribed Vicodin® (hydrocodone and acetaminophen) for pain and Silvadene cream (silver sulfadiazine) applied over the affected area to prevent infection. Weekly appointments were arranged to follow-up, with specific instructions to call immediately if fever or skin changes occurred. The chemotherapy treatments were resumed four weeks later after the patient’s complete recovery.

Chemotherapy extravasation is the escape of antineoplastic fluid from the vessel into the surrounding tissue, increasing the patient’s risk for a cutaneous injury (Doellman et al., 2009). The severity of the injury depends on the noxious effect of the cytotoxic drug and its mechanism of action. Cytotoxic drugs are classified as irritants and vesicants. Irritants may cause inflammation, burning, or pain. They rarely cause tissue necrosis or ulceration unless large amounts or high concentration of the irritant is extravasated, in which case the injury can be compared to that of a vesicant (Schulmeister, 2011). In contrast, vesicants are capable of causing local blisters and extensive damage to the underlying tissues accompanied with pain, and can lead to tissue death and necrosis (Yarbro, Wujcik, & Gobel, 2011). However, the mechanism of action of the irritant or vesicant solution, which may be DNA binding or DNA nonbinding, must be taken into consideration to have an absolute stance of the potential damage to the patient’s surrounding tissue (Schulmeister, 2010) (see Figure 1). When a chemotherapy agent does not bind to DNA, the solution remains contained within the area of extravasation, which facilitates drug deactivation (Schulmeister, 2010). DNA binding agents, on the other hand, attach to nucleic acid in the cells’ DNA (Schulmeister, 2011). The contaminated cells exchange the caustic solution through the course of cellular ingestion. The result is an indolent and progressive destruction of soft tissue, causing the ulcer to become bigger, deeper, and more painful (Yu et al., 2011). An estimated 10%–25% of peripheral extravasations of this type require surgery (Kane, McGuinn, Dagher, Justice, & Pazdur, 2008).
Chemotherapy Extravasations

The incidence of chemotherapy extravasation of vesicants is 0.1%–6% from peripheral IV devices and 0.3%–4.7% from central venous access devices (CVAD) (Froiland, 2007). Those are relatively low incidences, yet the impact of an injury from a chemotherapy extravasation in an already-compromised patient with cancer can be devastating. Unfortunately, evidence-based research for antidotes to avoid pain and suffering from extravasations for patients is lacking (Doellman et al., 2009). Nonetheless, the lack of knowledge of the phenomenon is based on the low incidence of this type of event and the ethical concerns that would be raised by proposing human research for this kind of injury. Therefore, empirical treatment based on small, uncontrolled trials, case studies, and animal studies is the common approach to manage extravasations at this time.

Nurses’ inability to recognize the noxious effect of each cytotoxic drug and its mechanism of action can interfere with their ability to identify and respond to the imminent danger patients may be facing and increase the incidences and severity of chemotherapy extravasation (Schulmeister, 2010). A patient inadequately instructed regarding the signs and symptoms that must be reported at once during a chemotherapy infusion is unable to assist and prevent an accident of this nature. In addition, a deficient baseline assessment to examine patients’ physical factors and comorbidities can add to the number of chemotherapy extravasations. Fragile veins and delicate skin in the very young and in the very old, obesity, and disseminated skin diseases (e.g., eczema, psoriasis) pose a risk for this type of injury (Froiland, 2007). In addition, circulatory and neurologic diseases may cause sensory deficits, depriving the patient from perceiving symptoms of extravasation.

Prevention

When the focus is on prevention, the nurses’ assessment skills and knowledge of cytotoxic solutions to select the appropriate IV access device and patient education are the most important aspects of injury deterrence. Thus, the requirement of chemotherapy certification and familiarity with the Oncology Nursing Society (ONS) Chemotherapy and Biotherapy Guidelines and Recommendations for Practice (Polovich, Whitford, & Olsen, 2009) are necessary for nurses working in this setting (Schulmeister, 2010).

Selection of IV access device: Critical assessment includes the patient’s medical history to identify comorbidities such as stroke, sensory deficit, paralysis, or lymphedema affecting the chemotherapy infusion; evaluating the patient’s vein, distinguishing the mechanism of action and types of cytotoxic drugs, and determining the duration of treatment all are necessary (Schulmeister, 2010). Those steps should yield adequate information to determine the safest vascular access device (Sauerland, Engeling, Wickham, & Corbi, 2006).

For peripheral access, a small-gauge plastic cannula is more suitable to achieve a clean venipuncture. Less trauma occurs during the introduction of the IV catheter, and the chance for puncturing through the back of the vein is reduced as well. In addition, alternating the IV site from one arm to the other preserves veins from the low pH and caustic effects of chemotherapy (Schulmeister, 2011). The forearm is the preferable site for peripheral access, away from flexible areas or joints. The cannula can be easily bent or displaced with movement at the joint, resulting in damage to tendons, ligaments, and nerves. Strict adherence to the distal-to-proximal technique for peripheral access is essential for decreasing the possibility of vesicant seepage below the site of recent venipuncture (Sauerland et al., 2006).

Continuous infusions and vesicants are safer when administered through CVADs (Schulmeister, 2011). Although CVADs are safe, nurse vigilance is paramount because the risk of extravasation cannot be totally eliminated (Schulmeister, 2008; Sauerland et al., 2006). During a vesicant infusion, the nurse should follow the institution’s guidelines to periodically check the patient’s condition, observe the site, ensure drug containment, and check blood return. Another good rule of thumb is to check blood prior to and after each drug infusion. Relying on a pump to signal an obstruction during the administration of vesicants should be avoided (Schulmeister, 2010). In many occasions, the pump may continue to deliver the vesicant without setting off a warning sign because infiltrations do not exert sufficient pressure to trigger the alarm from the pump until it is too late.

Regarding implanted ports, nurses should note that patients with large amounts of subcutaneous fat need longer needles to avoid needle dislodgement and subsequent subcutaneous extravasations (Sauerland et al., 2006). Many times, patients will request an anesthetic prior to vascular access. Only topical anesthetics with short duration are recommended, such as EMLA™ cream (Schulmeister, 2010). Long-acting anesthetics mask symptoms of vesicant extravasations, such as pressure or burning. Once the needle is secure, a transparent dressing should be applied because it allows easy viewing of the infusion site (Sauerland et al., 2006).

To verify needle placement, the site should be flushed only with normal saline and blood return attained after aspiration (Schulmeister, 2010). A peripheral line that does not provide a blood return should be discontinued. Another attempt should be made proximal to the most recent venipuncture. If blood return is not obtained from a CVAD, repositioning the patient

FIGURE 1. Cytotoxic Drug Classification: DNA Binding and Nonbinding


DNA Binding Irritants
Bendamustine* Dactinomycin Daunorubicin Doxorubicin Epirubicin Idarubicin Mechlorethamine Mitomycin

DNA Nonbinding Vesicants
Amsacrine Paclitaxel Vinblastine Vincristine Vinbeside Vinorelbine

*Treat like vesicants when extravasated in large amounts or high concentrations.
and gently flushing normal saline with a 10 cc or 20 cc syringe has been effective in attaining blood return. Failure to successfully obtain blood return from a CVAD will require verification of placement and patency. CVADs can become occluded with microscopic matter (Karamanoglu et al., 2003). Therefore, a dye study should be ordered to assess placement and patency of the CVAD (Sauerland et al., 2006).

**Patient education:** Patient education empowers the patients, allowing them to become active participants in their care (Hartkopf, 2009). Explaining the risks of dislodgment by disturbing the IV site and teaching them to notify the nurse immediately if swelling, redness, burning, or pain is observed during the chemotherapy infusion is helpful for earlier identification of chemotherapy extravasations (Hartkopf, 2009; Sauerland et al., 2006; Schulmeister, 2010). Patients with CVAD need to be counseled on the manifestations of intrathoracic extravasations, fever, cough, chest pain, or pleuritic pain.

The goals of therapy, the type of chemotherapy with possible short- and long-term effects, the schedule for therapy, the plan for monitoring, and follow-up should be discussed with the patient. Signs and symptoms that should prompt a phone call must be included with a phone number to contact the triage nurse. Patient education material written for the patient’s reading level and patient and caregiver understanding also may be useful (American Society of Clinical Oncology [ASCO] & ONS, 2012).

### Recognition

After prevention, prompt recognition is the next best measure in caring for chemotherapy extravasations (Schulmeister, 2008). Responding without delay and with the appropriate intervention will reduce patient distress and severity of the injury (Chanes, da Luz Goncalves Pedreira, & de Gutiérrez, 2012). Uncertainty in the type of pain the patient is describing and sudden loss of blood return from an IV site needs to be treated as an extravasation and the infusion must be stopped. Immediate assessment of the site must follow. Next, the doctor should be notified and treatment ought to start as established by the institution’s guidelines or the recommendations of the drug manufacturer. The Court of Appeals in Mississippi held an oncology clinic responsible for the actions of a nurse working for the practice, who for two hours neglected to respond to a man’s plea to check his brother’s arm, which began to swell 45 minutes into the paclitaxel infusion (Chemotherapy: Nurse Ruled Negligent, 2008).

### Management

When extravasations occur, the infusion must be stopped immediately (Polovich et al., 2009). The tubing containing the vesicant must be disconnected without removing the needle from the peripheral site or implanted port. Using a 1–3 cc syringe, the nurse must withdraw as much of the vesicant solution from

### TABLE 1. Vesicant Extravasation Management Guidelines

<table>
<thead>
<tr>
<th>Drug Classification</th>
<th>Medication</th>
<th>Topical Therapy</th>
<th>Antidote or Treatment</th>
<th>Antidote or Treatment Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alkylation</td>
<td>Mechloretamine</td>
<td>Apply ice for 6–12 hours following sodium thiosulfate injection.</td>
<td>Sodium thiosulfate</td>
<td>Inject 2 ml of sodium thiosulfate for each milligram of mechloretamine extravasated. Inject subcutaneously into extravasation site using a 25 gauge or smaller needle (change needle with each injection). Monitor extravasation site according to the institution’s policies and procedures.</td>
</tr>
<tr>
<td></td>
<td>Oxaliplatin</td>
<td>Apply warm compresses.</td>
<td>Dexamethasone 8 mg twice daily for 14 days</td>
<td></td>
</tr>
</tbody>
</table>
| Anthracyclines | Daunorubicin, doxorubicin, epirubicin, idarubicin | Apply ice pack (remove 15 minutes prior to Totect® treatment). | Totect | Infusion should be initiated within six hours of extravasation. Infused over 1–2 hours for three days in an area other than the extravasation site. The dose recommended is based on the patients’ body surface area.  
  - Day 1: 1,000 mg/m²  
  - Day 2: 1,000 mg/m²  
  - Day 3: 500 mg/m² |
| Antibiotics | Mitomycin, dactinomycin | Apply ice pack for 15–20 minutes four times daily the first 24 hours. | No known antidote or treatment | Monitor extravasation site according to the institution’s policies and procedures. |
| Plant alkaloid | Vinblastine, vincristine, vindesine, vinorelbine | Apply warm pack for 15–20 minutes four times daily the next 24–48 hours and keep extremity elevated. | Hyaluronidase | Administer 1 ml of hyaluronidase subcutaneously in five separate injections, each containing 0.2 ml of the solution using a 25 gauge or smaller needle. |
| Taxanes | Docetaxel, paclitaxel | Apply ice pack for 15–20 minutes four times daily the first 24 hours. | No known antidote | Monitor extravasation site according to the institution’s policies and procedures. |

the peripheral device or CVAD as possible. With an indelible pen, the nurse should mark the affected area and take a photograph as soon as possible. Notify the physician or ARNP and remove the needle from the peripheral site or implanted port. To ensure faster intervention, extravasation orders and antidotes including Totect™ for anthracyclines should be available in the institution’s pharmacy (Tyson & Gay, 2010).

The reviewed literature offers pharmacologic and nonpharmacologic measures to manage extravasations presented in Table 1 (Polovich et al., 2009; Schulmeister, 2011). The recommended measures from the manufacturers of vinblastine and vincristine (DNA nonbinding) propose local injection of hyaluronidase and topical warming with warm compresses to minimize discomfort in cases of extravasation (Schulmeister, 2008). Their synergistic effect promotes absorption of the drug and speedy dispersion (Schulmeister, 2011). The evidence-based recommendations for taxanes, which are also DNA nonbinding, are topical cooling with ice packs and close monitoring of the extravasation site (Schulmeister, 2011). When mechlorethamine extravasates, the manufacturer’s recommendation is to inject the affected area with sodium thiosulfate (Polovich et al., 2009; Schulmeister, 2009), which reduces free radicals and forms the same nontoxic thioesters excreted in urine (Schulmeister, 2011). Following the injections, placing an ice pack to the injured site is advised to alleviate pain by blocking nerve conduction (Schulmeister, 2008). For years, healthcare providers erroneously assumed that local cooling prevented the spread of vesicant solution to surrounding tissue by causing constriction of blood vessels; however, studies have proven that incorrect (Schulmeister, 2011).

Dexrazoxane has demonstrated 98% efficacy in the treatment of anthracycline extravasations with minimum toxicities (Mouridsen et al., 2007). It has been approved by the U.S. Food and Drug Administration for the treatment of anthracycline extravasation (Polovich et al., 2009). The medication has the ability to bind to iron and topoisomerase II, slowing the destructive trajectory of anthracyclines at a cellular level (Schulmeister, 2011). Applying ice over the tissue extravasated with an anthracycline is the initial recommendation (Polovich et al., 2009). However, the ice must be removed 15 minutes prior the initiation of the dexrazoxane treatment to allow sufficient blood flow to carry the infusion of dexrazoxane to the area of extravasation.

No antidote is known for irritants. In general, cold compresses are recommended for extravasation with an irritant agent. Patients should be instructed to apply an ice pack or cold compress for 15–20 minutes four times daily for the first 24 hours. Patients suffering an oxaliplatin extravasation initially should be treated with warm compresses and prescribed dexamethasone tablets, 8 mg daily for 14 days. Applying a warm compress is the only suggestion for irritants.

Patients suspected of having suffered an extravasation should receive a follow-up phone call within 1–3 days of the incidence (British Columbia Cancer Agency, 2012). Based on the patient’s report at the time of the phone call, the patient may be brought to the clinic for a closer assessment. For patients with a known extravasation, follow-up appointments ought to be arranged to assess the site on days 2, 5, 7, 14, and continue until the patient has fully recovered (Surrey, West Sussex and Hampshire Cancer Network, 2009).
Documentation

A form tailored for chemotherapy extravasation and specific to the workplace (see Figure 2) is an ideal tool for documentation (Schulmeister, 2008). The document should be structured in a manner that begins at the starting point of the event, followed by actions taken, plus a complete assessment and description of the affected area with a photograph of the site. The document should include a patient teaching section or checklist to confirm that the patient was instructed to call immediately for skin and temperature changes and for the onset of pain to the affected area. A segment for follow-up recommendations also should be included in this document (see Figure 3).

Thorough documentation demonstrating that nursing care met the standard of practice is the best defense to potential litigation (Sauerland et al., 2006). The outstanding documentation of a team of nurses reflecting periodic communication with the physicians and continuous assessment of their patient permitted the California Court of Appeals a full analysis of the events in a 2011 lawsuit for extravasation against the nursing staff. As a result, the court was unable to find nursing negligence and dismissed the lawsuit (Chemotherapy Nurses Ruled Not Liable for Extravasations, 2011).

Implications for Nursing

The unfavorable signs and symptoms of extravasations affect patients’ physiologic, psychological, and situational dynamics, diminishing their quality of life (Verity, Wiseman, Ream, Teasdale, & Richardson, 2008). The injury becomes a source of anxiety, and the severity of the injury dictates patients’ increased risk for infection, pain, and functional impairment. Subsequently, the patient’s inability to function as desired may result in role changes and provide grounds for disability (de Oliveira Gozzo, Sanches Panobianco, Clapis, & de Almeida, 2010). An understanding of the patient’s level of distress and physical problem must be addressed to avoid reluctance to continue treatment and to regain functioning ability (Cox & Fallowfield, 2007). Therefore, an injury placing a patient at increased risk for infection, pain, and functional impairment would require a consultation with the surgeon.

Therefore, nurses, in collaboration with the oncologist and pharmacist, should incorporate procedures and policies to minimize chemotherapy extravasation (Chanes et al., 2012).

Implications for Practice

- Physiologic, psychological, and situational dynamics that diminish quality of life must be addressed to increase patients’ quality of life and avoid reluctance to continue treatment.
- Yearly educational programs explaining the potential for vesicants to cause harm, as well as the signs and symptoms to readily identify extravasations, build confidence among nurses, and improve their knowledge and patient care.
- The development of algorithms for the infusion of vesicants and for interventions after extravasations have occurred has promoted uniformity, resulting in fewer injuries requiring surgery.

For Patient: Care of Site

To minimize discomfort, follow instructions checked below.

- Apply cool compress to affected area for 15–20 minutes for the next 24–48 hours.
- Apply warm compress to affected area for 15–20 minutes for the next 24–48 hours.
- Elevate affected arm on a pillow whenever possible.
- Apply a thin layer of hydrocortisone cream 1% twice daily until redness resolves; discontinue if it blisters and call physician immediately.
- Do not apply any other lotions, creams, or ointments.
- After shower, pat dry; do not rub; if tub bath, cover affected area with watertight dressing or barrier.
- Gently exercise the affected arm or hand.
- Take pain medicine prescribed as needed.
- Do not expose affected area to strong sunlight.
- Avoid wearing tight clothing around the affected area.

Once a day, check the affected area. If yes to any of the problems below, you must contact your physician immediately.

- Skin color changes or increased redness
- Area blistering, peeling, or flaking
- Area becoming more uncomfortable
- Pain interfering with exercise of the arm or hand

Contact telephone number:

Leape et al. (2000) conducted a 15-month study in 1996 in which they demonstrated that using empirical evidence to create protocols and standardizing the care of patients receiving chemotherapy reduced the incidence of serious events by 50%. Yearly educational programs intended to study the potential for vesicants to cause harm, as well as the signs and symptoms to readily identify extravasations, have been shown to build confidence among nurses and improve their knowledge and patient care (Gibson, Sander, Whelman, & Bolton, 2009). In addition, the development of algorithms for the infusion of vesicants and for interventions after extravasations have occurred has promoted uniformity, resulting in fewer injuries requiring surgery (Chanes et al., 2012).

Conclusion

Extravasation is a phenomenon with diverse symptom patterns (Sauerland et al., 2006). Its degrees of physical distress can range from mild to severe (Cox & Fallowfield, 2007). Emotional distress and alteration in functional capabilities and social role are among the ailments encountered by patients with cancer suffering an injury of this magnitude. For these reasons, nurses need to have a comprehensive clinical knowledge of extravasations to eliminate or mitigate the potential harm for this population (Schulmeister, 2010). Research supporting evidence-based
interventions is scarce for this clinical problem (Doellman et al., 2009). ONS is the only organization that has created guidelines and recommendations for practice for chemotherapy and biotherapy (Polovich et al., 2009). ASCO and ONS (2012) suggested that the management of extravasations follow current literature. Therefore, nurses must review literature periodically, seek educational programs addressing management of chemotherapy extravasations, encourage their institution to establish guidelines supported by current evidence, and propose antidotes accessible to the organization.

References


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