

Eliminating Extravasation Events: A Multidisciplinary Approach

ABSTRACT

Administration of chemotherapy agents can give rise to many safety issues. Extravasation of a vesicant agent causes tissue blistering and necrosis. This complication of chemotherapy administration causes additional pain and suffering in patients who are already suffering with a diagnosis of cancer. Nurses hold key responsibilities for educating patients about administration issues and following practice standards to minimize the risk of extravasation. Defining a path of shared responsibilities among team members is a critical step in assuring the safe administration of drugs classified as vesicants. This article describes a clinical practice change that is used at a large midwestern academic medical cancer center. This practice and policy change has resulted in a 90% reduction in the administration of vesicant agents peripherally, with no occurrence of extravasations in the first 6 months of implementation.

Key words: care team, chemotherapy agents, communication, irritants, patient education, practice change, safety, vesicants

More than 1 million intravenous (IV) chemotherapy infusions are given worldwide each day.¹ Nurses and other health care professionals strive to make their administration safe to minimize adverse events. The administration of vesicant agents is a function of oncology nursing that may cause anxiety and fear. Specific institutional direction must be in place regarding the type of vascular access device to be used and how to monitor for the safest complication-free infusion. Ambiguities exist in the literature and guidelines. A change in practice must be based on evidence. Some evidence regarding safe administration of vesicants is available. To be meaningful, however, practice change must address questions about problematic situations presented by staff nurses. Appropriate venous access needs to be considered when the course of treatment is determined, rather than when the patient arrives for treatment. The care team must be proactive rather than reactive, and patients must present for chemotherapy with prior knowledge of the characteristics of the agent to be administered and indications for vascular access.

BACKGROUND

The infusion nurse may be faced with a patient expecting to receive the first cycle of treatment who presents

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with poor veins and orders that do not consider the risks of vesicant(s). Staff nurses have verbalized critical situations in which patients presented for vesicant chemotherapy without adequate peripheral veins or a central vascular access device (CVAD) in place. As a result, the patients' chemotherapy was held. These types of delays brought about frustration and concern for both nurses and patients. These far-from-desirable situations led to the development of an institution-specific practice change for the administration of chemotherapy in a midwestern academic medical cancer center.

CURRENT PRACTICE

As in many practice settings, policies and procedures for chemotherapy can be vague and fail to address all situations encountered. This was the case at the cancer center where the policy was often carried out. The policy lacked guidance for vascular access choices based on the prescribed treatment. In addition, vascular access typically was not discussed with the patient by the physician and providers when the treatment decision was made.

As a result, many patients arrived in the infusion clinic for treatment with the expectation that the nurse would initiate a peripheral IV and that agent(s) would be delivered. Anticipation of venous access problems were not assessed before the first day of treatment. It was found that some physicians and providers had little understanding of the advantages, disadvantages, and potential complications associated with CVADs. In addition, there was a lack of knowledge about the effects of certain agents on the veins when given peripherally and how the effects alter veins over time.

Delays in treatment, extended treatment appointments, increased patient wait times, multiple phone calls to the physician, and explanations and excuses to the patient resulted. These outcomes were considered unacceptable for cancer patients requiring treatment with chemotherapy. A process change was needed.

In collaborating with inpatient staff at this institution, it was found that their concerns about the policy and procedure related to vesicant administration matched those of the outpatient cancer center.

CLASSIFICATIONS OF CHEMOTHERAPY AGENTS

IV agents used for chemotherapy are classified as vesicants, irritants, or "other." Vesicants have the potential to cause serious tissue damage when leaked outside of the vein. Irritants have the potential to aggravate the vein, sometimes causing burning or pain during infusion. The category of "other" refers to medications that are not classified as irritants or vesicants.

These classifications have implications for nursing practice (Box 1). Awareness of drug classifications, delivery standards, and individual patient factors has an impact on nursing practice. To make the best decision for delivering chemotherapy, the care team and the patient need guidelines to substantiate a plan for the administration of chemotherapy agents.

Extravasation is a serious complication of vesicant chemotherapy administration. It is imperative that potential side effects of extravasation are known not only by the nurse administering the agent but also by the patient.^{2,3} Although the incidence of extravasation is not common, the aftermath can be devastating to the patient. Vesicants have caused extravasation in 0.1% to 6% of patients with peripheral IV access and 0.3% to 4.7% of patients with CVADs.⁴ Long-term side effects of an extravasation can include tissue necrosis, tendon damage, pain, permanent disability, and disfigurement.² Although the incidence of extravasation is relatively low, many patients are at risk. Moreover, extravasation events have led patients to seek compensation for side effects through litigation.⁵

DRUG CHARACTERISTICS

Two drug characteristics to take into consideration when determining safe administration are the potential hydrogen (pH) and the osmolarity of the drug.⁶ The normal pH of body fluids is 7.35 to 7.45. An agent

BOX 1 Definitions

Infiltration

The inadvertent administration of a nonvesicant solution or medication into surrounding tissue due to the catheter puncturing the vein or vein rupture. Signs and symptoms include swelling at and/or above the insertion site, cool skin temperature at the site, leaking of fluid from insertion site, skin tightness, and pain.

Extravasation

The inadvertent administration of a vesicant solution or medication into surrounding tissue. Signs and symptoms include pain, burning, redness, swelling at and/or around the catheter insertion site and absence of a blood return during or after administration.

Vesicant

A drug or solution that can cause tissue necrosis or blistering when it accidentally infuses into tissue outside of a vein.

Irritant

A drug or solution that causes pain or discomfort in the vein during administration.

Source: *Infusion Nurses Society. Infusion nursing standards of practice. J Infus Nurs. 2011;34(1 suppl).*

with a low or high pH irritates the tunica intima—the smooth, thin lining of the vein—potentiating an inflammatory response of the endothelial cells.⁷ This reaction can lead to the agent leaking out of the vein into surrounding tissue, causing phlebitis, infiltration, or, potentially, an extravasation. An example of an agent with a low pH is gemcitabine (Gemzar, Eli Lilly, pH 2.7-3.3). An example of an agent with a high pH is sulfamethoxazole/trimethoprim (Bactrim, AR Scientific, pH 10). According to the Infusion Nurses Society (INS) *Infusion Nursing Standards of Practice*, infusates with a pH below 5 or above 9 should be infused through a CVAD.⁸

Osmolarity refers to the concentration of particles in a solution—the more particles, the higher the osmolarity. Isotonic solutions have the same osmolarity as body fluids (250-375 mOsm/L). Hypotonic solutions have fewer particles than isotonic solutions with an osmolarity below 250 mOsm/L. Hypertonic solutions have an osmolarity above 375 mOsm/L. When hypertonic infusates are administered into a peripheral vein, osmotic pressure moves from the endothelial lining into the vessel, causing the cells to shrink. In this way, cells lining the vein are damaged, possibly leading to leakage of the infusate out of the vein into the surrounding tissue. The INS *Standards of Practice* state that infusates with an osmolarity > 600 mOsm/L are to be infused through a CVAD.⁵ An example of a hyperosmolar solution is parenteral nutrition.

The administration of a drug with a high or low pH or high osmolarity can also cause venospasm, consequently constricting the vein, leading to back pressure at the peripheral IV catheter site. Venospasm can result in an expansion at the puncture site of the vein, allowing infusates to leak out of the vein into surrounding tissue, leading to infiltration or extravasation.⁹ The delivery of chemotherapy has inherent risks because of the chemical characteristics of the agents. Awareness of these characteristics can help the care team educate the patient. Together, a decision can be made regarding the most appropriate vascular access device for the patient's treatment.

DEVELOPMENT OF THE PRACTICE CHANGE

Development of a Vesicant List

The movement toward a practice change highlighted the fact that there was no consensus on which chemotherapy agents were classified as vesicants. Several lists existed from multiple sources, and there were contradictions on the classification of some of the drugs. With the help of the organization's Pharmacy, Nutrition, and Therapeutics Committee, a list of vesicants was created and agreed on by physicians, pharmacists, and nursing staff (Table 1).

 TABLE 1 Chemotherapy Vesicant List	
amsacrine (Amsidine)	
dactinomycin (Cosmegen)	
daunorubicin (Cerubidine)	
docetaxel (Taxotere)	
doxorubicin (Doxil)	
epirubicin (Ellence)	
idarubicin (Idamycin)	
mechlorethamine (Mustargen)	
mitomycin (Mitosol)	
mitoxantrone (Novantrone)	
oxaliplatin (Eloxatin)	
paclitaxel (Taxol)	
streptozocin (Zanosar)	
trabectedin (ET-743, Yondelis)	
vinblastine (Velban)	
vincristine (Oncovin)	
vindesine (Eldisine)	
vinorelbine (Navelbine)	

Risk Reduction Strategies

The organization's risk management department and medication safety officer partnered with nursing leadership and staff to develop standards of practice for vesicant administration. Options to reduce the risk of extravasations were discussed and considered. It was considered imperative that the practice change would allow for the following:

- Patients who were to receive a drug classified as a vesicant or an irritant would have to be told in the educational session before treatment, and the potential risks would have to be verbalized by the patient and documented.
- The care team—including the physician, advanced practice nurse, clinic nurse, and infusion nurse—would all have ownership and responsibility for educating patients about the definition of a vesicant, the risks of administration associated with infusing a vesicant/irritant, and the options available to decrease the risk of extravasation.
- The process to determine the safest way to administer chemotherapy had to be a joint decision of the patient and the care team.

An expert on IV administration was consulted for assistance in formalizing the principles. A draft guideline was completed by the consultant. Nursing staff and leadership reviewed the draft, which was forwarded to the institution's Nursing Practice Council and finally to the physician leadership group for final input and approval.

Literature Search and Review of Guidelines


The second step was to complete a literature search. Databases such as CINAHL, PubMed, Google Scholar, Ebscohost, Ovid, and others were used. In addition, several institutions were contacted to find out which guidelines they used, if any. The institutions were asked about CVAD placement for vesicant administration and how their staff dealt with situations in which a CVAD might cause a greater risk than peripheral access (eg, in malignant hematologic patients), as well as other perplexing issues.

The Oncology Nursing Society's (ONS) *Chemotherapy and Biotherapy Guidelines and Recommendations for Practice* (2009) and INS' *Infusion Nursing Standards of Practice* (2011) were used as professional references. The ONS guidelines for IV vesicant chemotherapy are listed as piggyback or short-term infusions, continuous, and IV push. "Short-term" infusions are implied to infuse less than 30 minutes. For these piggyback or short-term infusions through a peripheral access device, the guideline states that a nurse should stay with the patient, monitor the site, and verify positive blood return every 5 to 10 minutes.¹⁰ It also states that infusion of vesicants over more than 30 to 60 minutes should be avoided.¹⁰ In addition, the guideline indicates that a peripheral IV site should not be used for continuous vesicant administration, and blood return should be checked according to institutional policy.¹⁰ It was assumed that "continuous" is an IV method infusing over more than 30 minutes. Frequently used vesicant agents that infuse over more than 30 minutes are paclitaxel (Taxol) and docetaxel (Taxotere).

INS' *Standards of Practice* state that continuous infusions of vesicants are not to be administered through a peripheral access device.¹¹ The standard leaves room for interpretation because the term *continuous* is not defined. There are clear guidelines for the administration of IV push vesicants in the ONS guidelines for monitoring the site: a blood return is to be verified every 2 to 5 mL infused. For this practice change, the cancer center defined continuous as an infusion to be delivered over more than 30 minutes.

THE PRACTICE CHANGE

A thorough review of the plan of treatment and goals of care, and an assessment of the patient's veins, along with a history of the patient's prior venous access, was

 TABLE 2 Peripheral Arm Assessment	
Patient has small, fragile veins	Yes or No
Consider age, diabetic, long-term steroid use	
Patient has sustained many previous venipunctures	Yes or No
Consider recent hospitalization, ecchymotic arms, frequent labs or intravenous (IV) medications, history of IV drug abuse	
Patient has limited extremity vein selection	Yes or No
Consider history of axillary lymph node dissection, sentinel lymph node biopsy, lymphedema, cerebrovascular accident, amputation, dialysis fistula	
Patient has decreased sensation and/or circulatory impairments	Yes or No
Consider stroke, previous surgeries, infection, or neuropathy	
Patient has altered mental status/impaired cognition	Yes or No
Patient has 2 or more palpable or visible veins are absent in medial aspect of lower arm when manual blood pressure cuff is applied with compression	Yes or No
<i>If any of these assessment items result in a yes response, further intervention and follow-up are required.</i>	

agreed on as an initial step. The assessment includes a medical history, current physical status, and the long-term projected plan of care (see Table 2). If the patient's venous assessment indicates a potential issue with access, a discussion with the physician and nurse ensues to determine a course of action. Along with the assessment, the patient receives information on the drugs planned, classification, duration of therapy, and risks related to administration. It was acknowledged that this educational process had to be repeated and reinforced over time, and the care team needed to be involved in providing consistent information, education, and reinforcement.

Vascular Access Considerations

If vesicants or irritants are given peripherally, the arm veins may become sclerosed or damaged over time and, as a result, may increase the risk of extravasation. The use of CVADs can decrease this risk.

The most commonly placed CVAD for chemotherapy administration is the implanted port or a peripherally inserted central catheter (PICC). The advantages of an implanted port for a patient with cancer are that it provides reliable access and reduces/eliminates the need for needlesticks in the arms for blood draws, treatment, and some radiographic tests. The only visible sign that a port is present typically is a small bump under the skin. The patient can swim and shower without concern.

A dressing is not required when the port is not accessed, and the port usually needs to be flushed only once a month. The negative aspects of an implanted port are that the patient still needs to endure a needlestick for access, must undergo a surgical procedure for placement and removal, and may have concerns about body-image alterations.

The other most frequent choice for a CVAD is a PICC. PICCs are often chosen for patients who are averse to needlesticks, do not want to undergo a surgical procedure, or are not candidates for a port placement. PICCs typically are not the first choice for vascular access because they are visible, extending out of the arm, and require frequent flushing and weekly dressing changes, usually by a health care professional.

For a number of reasons, CVADs are not always placed in patients who will receive vesicants. Barriers to placement of a CVAD in patients who will receive vesicant agents must be acknowledged and discussed among care team members. Patients may refuse to submit to another procedure for placement of a device. There also may be physical reasons that a CVAD cannot be placed, such as a tumor impinging on a large central vein. Cost may be a factor with patients who have no insurance or poor reimbursement. Sometimes there is resistance at the physician level because of a lack of education, previous experience, and/or awareness of the potential complications.

Components of the Practice Change

Key components of the practice change include:

- An initial assessment tool completed and documented when chemotherapy is planned and before the start of treatment. The tool, which is completed by the oncologist's RN in the electronic health care record (EHR), documents whether chemotherapy is planned, if a planned chemotherapy includes a vesicant, and the vein assessment (Table 2). If there are any positive responses on the vein assessment tool, consideration is given to the placement of a CVAD.
- Documentation of interventions implemented as a result of assessment findings in the EHR. This includes determination of the appropriate vascular access device for the patient and scheduling placement of a CVAD with interventional radiology. The infusion area's clinical nurse specialist (CNS) is notified when a patient is to receive a vesicant peripherally in order to review the assessment to ensure that the prescribed agent can be given safely, notify the infusion staff, and make sure patient teaching has been completed.
- Standardized patient education regarding the risks of chemotherapy administration. Documentation of the discussion with the patient about the

characteristics of the agents and the risks involved with both peripheral and CVAD access is carried out, and printed patient education regarding vesicant chemotherapy with signs of extravasation is provided for reinforcement. The education is repeated each day of treatment.

- Determination that any vesicant administration that requires an infusion time of 60 minutes or more would require a CVAD to decrease the risk of peripheral extravasation.
- Establishment of an interval assessment for blood return monitoring during infusion of a vesicant. For vesicant agents given peripherally over less than 15 minutes, an RN needs to stay with the patient and check for a blood return every 2 to 5 mL or every 5 minutes until completion. For vesicants given peripherally over 15 minutes and up to 60 minutes, an RN checks blood return before the infusion, after 30 minutes, and at the end. (A short-term trial was instituted in which RNs administering vesicants, even those infusing over 3 hours, were required to stay with the patient and assess for a blood return every 5 minutes. In a busy cancer center this proved to be an unrealistic expectation. One-on-one nursing was unachievable.) As previously stated, no infusion of vesicants over more than 60 minutes is done without a CVAD.
- Building of a daily EMR report, which provides a list of patients scheduled to receive vesicant chemotherapy and the type of venous access present. This information is sent every day to the manager of nursing practice and the CNS and serves as a second check in identifying patients who do not have a CVAD before their first chemotherapy treatment.

Nursing Education

There were many different steps in implementing the practice change. The objectives for staff education were to provide definitions and rationale, state the role of the nurse, review the tools available, and discuss any barriers the nursing staff perceived with implementation. These topics were presented in a lecture and discussion format for groups of 8 to 10 staff nurses. It was explained that the primary reason for implementing this guideline was to promote safe administration of vesicants and that becoming proactive instead of reactive was paramount.¹² It was crucial that the nurses understood that the decision-making process within the guideline would be shared among the health care team and the patient.¹³ Definitions of vesicants and irritants and a list of each as defined by our facility were made available electronically and also printed on laminated pocket cards. These tools are used to ensure that all staff,

including providers, know which medications are classified as vesicants by our institution and, therefore, fall under the guideline. Although the practice change primarily addressed the risk of extravasations with peripheral access devices, education also was provided about the risk associated with CVAD infusions. The most common “vesicants” administered in our outpatient center are paclitaxel (Taxol; Bristol-Myers Squibb), doxorubicin (Adriamycin; Pfizer), vincristine sulfate (Vincristine; BDI Pharma), and eloxatin (Oxaliplatin; Sanofi).

Instruction was provided on how to use the assessment tool. The prewritten assessment is embedded in the electronic medical record within the chemotherapy patient education documentation. Once the assessment is complete, the nurse discusses the findings with the patient and the other members of the care team to make a joint decision and recommendation on what would be the safest vascular access plan for the patient.

In relation to the barriers of implementation, some of the nurses expressed concern about getting buy-in from the provider if they were to recommend a CVAD for chemotherapy administration. During the education session, it was stressed that the final decision would be shared by the care team. In addition, some of the staff brought up the fact that patients sometimes refuse to have a catheter placed. It was reinforced that the patient was to be made aware of the potential risks involved in order to make an educated decision and, most important, that appropriate documentation of the conversation with the patient is required should this situation arise. All of these factors were considered to be barriers by the nursing staff.

In the event that a patient does not have a CVAD placed, interval assessments are required. Patients receiving vesicants peripherally would be evaluated at the beginning of each cycle or once a month, whichever comes first. In this assessment, the patient is asked the following questions:

- Have there been issues with starting a peripheral IV since treatment began?
- Were more than 2 attempts required by the staff to start a peripheral IV?
- Did IV placement require the use of the venous access team?
- Have you had any complications with previous IV sites?

All of the previously mentioned factors were considered in the decision to recommend/implement CVAD placement and the need for ongoing education with the patient.

Patient Education

The patient and caregiver must be informed about the risks related to the infusion of vesicants and irritants

into peripheral veins.¹⁴ In a busy oncology clinic setting, the completion of patient education before the first treatment can be challenging. Patients must be ready to hear in order to comprehend. New patient teaching about the diagnosis, the treatment plan, and the side effects of chemotherapy agents usually occurs at diagnosis. Information overload and the emotional aspects related to a cancer diagnosis frequently prevent the patient from hearing and understanding everything that is presented in a brief period of time (see Box 2).

The concept of a CVAD may be difficult to understand in terms of function, placement, and daily living issues. The use of a manikin or other visual teaching aids can assist in clarifying vague concepts and can ease the decision-making process. A description of the risk of tissue damage also must be explained. The teaching must be reinforced with materials written at a sixth-grade reading level.¹⁵ If the patient chooses peripheral access over a CVAD after the teaching, the patient needs to be reminded of the risks related to peripheral administration before every dose of the vesicant.¹³ Detailed



BOX 2

Patients' Frequently Asked Questions About Vesicant Drugs

What is a vesicant?

A vesicant is a chemical agent that can cause severe blistering of the skin or a mucosal area. If you are a cancer patient, some of the chemotherapy drugs that are given through your veins (through an IV) may be classified as vesicants and can cause severe damage to you if they escape to areas outside your vein.

How do I know if I am going to receive a vesicant?

Your doctor or nurse will tell you. Make sure you ask if they do not mention it.

If I am going to receive a vesicant, what do I need to know?

Ask your health care providers what they suggest is the best way for you to receive the medication. Ask if a central venous access device (CVAD)—also known as a “port,” Hickman catheter, or peripherally inserted central catheter (PICC)—is appropriate for you.

What changes should I report to the nurse when I am receiving chemotherapy?

If you notice any of these symptoms—pain, burning, tingling, itching, swelling, or redness—where the IV goes into your body, call the nurse immediately.

What is a central venous access device?

A central venous access device, or CVAD, is a broad term that includes many types of catheters (thin, flexible, hollow tubes) that are inserted into and positioned within a vein in the body to deliver chemotherapy, fluids, blood, or other drugs into the bloodstream, or to withdraw blood for testing. Your nurse can provide you with information about specific examples.

Can a vesicant be given safely through a regular IV in my arm?

In some cases a vesicant can be given safely through a regular IV in your arm. However, talk with your physician and nurse. It depends on your history, how long it will take to give the drug, and several other factors.

documentation of these conversations and teaching sessions is imperative.³ The use of a guideline for vesicant administration ensures that up-front assessments allow for a safe administration plan on day 1 of treatment. In addition, the use of an evidence-based practice change ensures that multiple providers and staff members approach a challenging question using “the best” approach known to care.

OUTCOMES

The practice and policy change has resulted in a 90% reduction in the administration of vesicant agents peripherally, with no occurrence of extravasations in the first 6 months of implementation. The infusion clinic treats about 120 patient visits a day.

Staff, including physicians, are mindful of the type of chemotherapy prescribed and assist in determining the safest method of administration. When the patient needs to receive a vesicant over 1 hour, the CNS is notified. When the patient presents for treatment, the CNS assists the RN with appropriate patient education and monitoring. It is a practice change that has benefited our patients, ensured standardized protocols, and increased patient and nursing satisfaction.

FUTURE IMPLICATIONS

The implementation of a practice change that affects health care teams and patients in a complex setting requires detailed follow-up to maintain the desired outcome. The enculturation of a guideline into practice requires frequent discussion focusing on the value of the action steps involved. When implementation steps are required of providers who do not work with one another regularly, acknowledging the impact of being proactive takes time to develop. Steps to ensure enculturation of the guideline and any needed modifications include audits by quality council representatives, refinements of the assessment tool as needed, monitoring of extravasation rates with ongoing review to determine trends, and follow-up with the care team when crucial steps in the guideline have been missed. The authors' institution has been working toward transitioning the guideline into a policy statement that standardizes chemotherapy administration across all practice settings.

As we look to improve compliance with the guideline, we continue to focus on how best to care for the patients who refuse CVAD placement, yet have assessment findings that may lead to potentially high-risk infusions. To date, patients in this situation are addressed with an individual plan of care. Patients require support and understanding of their individual values and needs.

However, the final decision regarding whether an agent can safely be administered rests with the infusion nurse. This guideline provides support for nurses to remain proactive in addressing critical safety issues.

SUMMARY

The administration of vesicant agents is a complex process, requiring education about not only the agent but also the safest method of administration for providers and staff at all levels. Establishing institutional standards helps ensure patient safety related to all aspects of administration.

Documentation of patient education related to vesicant agent administration must be precise, detailed, and complete. The existence of a guideline that follows evidence-based practices should direct the care team at all levels, with the intent that safe administration will be introduced to the patient as early in the process as possible. Adherence to a clinical practice guideline can maximize the best patient outcomes. The ultimate goal must be zero tolerance for extravasation events.

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