European Journal of Oncology Nursing 16 (2012) 528–534

Contents lists available at SciVerse ScienceDirect

European Journal of Oncology Nursing

journal homepage: www.elsevier.com/locate/ejon

Management of chemotherapy extravasation: ESMO–EONS clinical practice guidelines☆

J.A. Pérez Fidalgo, MD[a], L. García Fabregat, RN[a], A. Cervantes, MD[a], A. Margulies, RN[b], C. Vidall, RN[c], F. Roila, MD[d,*] on behalf of the ESMO Guidelines Working Group

[a] Department of Hematology and Medical Oncology, Institute of Health Research INCLIVA, University of Valencia, Valencia, Spain
[b] European Oncology Nursing Society, Zurich, Switzerland
[c] Healthcare at Home Ltd, Staffordshire, UK
[d] Department of Medical Oncology, S. Maria Hospital, Terni, Italy

Definitions

Extravasation is the process by which any liquid (fluid or drug) accidentally leaks into the surrounding tissue. In terms of cancer therapy, extravasation refers to the inadvertent infiltration of chemotherapy into the subcutaneous or subdermal tissues surrounding the intravenous or intra-arterial administration site.

Extravasated drugs are classified according to their potential for causing damage as 'vesicant', 'irritant' and 'nonvesicant' (Table 1).

Some vesicant drugs are further classified into two groups: DNA binding and non-DNA binding. Allwood et al. (2002) divided the drugs into vesicants, exfoliants, irritants, inflammitants and neutrals.

Incidence

Data on the incidence of either extravasation or infiltration are scant due to the absence of a centralized register of chemotherapy extravasation events. Incidence rates vary greatly. Estimates between 0.01% and 7% are noted in various publications (Larson, 1982; Bertelli et al., 1995; Mader et al., 2009; Schulmeister, 2011a,b; European Oncology Nursing Society (EONS), 2007). Some data suggest that the incidence is decreasing probably due to improvements in the infusion procedure, early recognition of drug leakage and training in management techniques. A single-institution retrospective study confirmed that the overall incidence was 10 times less frequent in 2002 than 15 years earlier (0.01% versus 0.1%; $P = 0.001$) (Langstein et al., 2002). Data regarding extravasation from central venous access devices (CVAD) are limited.

Risk factors for extravasation

Adequate identification of the potential factors for extravasation is important to minimize the risk in some patients. In case of an increased risk of extravasation, preventive measures should be encouraged or in some cases, insertion of a CVAD should be considered. These factors can be classified under patient-associated and procedure-related risk factors (Mader et al., 2009; European Oncology Nursing Society (EONS), 2007; WOSCAN Cancer Nursing and Pharmacy Group, 2009). The most relevant risk factors for chemotherapy extravasation are shown in Table 2.

Prevention

Most extravasations can be prevented with the systematic implementation of careful, standardized, evidence-based administration techniques. Some preventive strategies recommended in relation to site of insertion, type of cannula and procedure protocols are listed in Table 3.

In order to minimize the risk of extravasation, the staff involved in the infusion and management of cytotoxic drugs must be trained to implement several preventive protocols (Mader et al., 2009; European Oncology Nursing Society (EONS), 2007; WOSCAN Cancer Nursing and Pharmacy Group, 2009).

Should an extravasation occur, it is important to remember that the degree of damage is dependent on the type of drug, the drug concentration, the localization of the extravasation and the length of time a drug develops its potential for damage.

Diagnosis

Patients must be informed to report any changes in sensation, signs or symptoms during the i.v. administration of any chemotherapy drug and to alert the healthcare professional to early signs of extravasation. Particular information must be given when a vesicant drug is administered.

Extravasation must be suspected if any of the specific signs or symptoms are present. Initially, among the most common symptoms are feelings of tingling, burning, discomfort/pain or swelling,

☆ Approved by the ESMO Guidelines Working Group: July 2012. These guidelines were developed by ESMO and EONS and are published simultaneously in Annals of Oncology (volume 23, supplement 7) and the European Journal of Oncology Nursing (volume 16, issue 5).

* Correspondence to: ESMO Guidelines Working Group, ESMO Head Office, Via L. Taddei 4, CH-6962 Viganello-Lugano, Switzerland. E-mail: clinicalguidelines@esmo.org and EONS: European Oncology Nursing Society, Avenue E. Mounier 83, B-1200 Brussels, Belgium. E-mail: eons.secretariat@cancernurse.eu.

1462-3889/$ – see front matter
http://dx.doi.org/10.1016/j.ejon.2012.09.004

Table 1
Classification of chemotherapy drugs according to their ability to cause local damage after extravasation.

Vesicants	Irritants	Nonvesicants
DNA-binding compounds	**Alkylating agents**	Arsenic trioxide
Alkylating agents	Carmustine	Asparaginase
Mechlorethamine	Ifosfamide	Bleomycin
Bendamustinea	Streptozocin	Bortezomib
Anthracyclines	Dacarbazine	Cladribine
Doxorubicin	Melphalan	Cytarabine
Daunorubicin	**Anthracyclines (other):**	Etoposide phosphate
Epirubicin	Liposomal doxorubicin	Gemcitabine
Idarubicin	Liposomal Daunorubicin	Fludarabine
Others (antibiotics)	Mitoxantrone	Interferons
Dactinomycin	**Topoisomerase II inhibitors**	Interleukin-2
Mitomycin C	Etoposide	Methotrexate
Mitoxantrone[a]	Teniposide	Monoclonal antibodies
Non-DNA-binding compounds	**Antimetabolites**	Pemetrexed
Vinka alkaloids	Fluorouracil	Raltitrexed
Vincristine	**Platin salts**	Temsirolimus
Vinblastine	Carboplatin	Thiothepa
Vindesine	Cisplatin	Cyclophosphamide
Vinorelbine	Oxaliplatin[a]	
Taxanes	**Topoisomerase I inhibitors**	
Docetaxel[a]	Irinotecan	
Paclitaxel	Topotecan	
Others	**Others**	
Trabectedin	Ixabepilone	

[a] Single case reports describe both irritant and vesicant properties.

and redness at the injection site. Later symptoms may include blistering, necrosis and ulceration.

Signs that frequently raise suspicion of an eventual extravasation are the absence of blood return, resistance on the plunger of the syringe during delivery of a bolus drug, or an interruption to the free flow of an infusion.

Table 2
Patient and procedure-associated risk factors.

Patient-related	Cannulation and infusion procedure-related (peripheral or port)
Small and fragile veins	Untrained or inexperienced staff
Hard and/or sclerosed veins as a consequence of multiple previous chemotherapy courses or drug abuse	Multiple attempts at cannulation
Prominent but mobile veins (e.g. elderly persons)	Unfavorable cannulation site
Known diseases or situations associated with an altered or impaired circulation like Raynaud syndrome, advanced diabetes, severe peripheral vascular disease, lymphedema or superior cava syndrome.	Bolus injections
Predisposition to bleeding, increased vascular permeability or those with coagulation abnormalities.	High flow pressure
Obesity in which peripheral venous access is more difficult.	Choice of equipment (peripheral catheter choice, size, steel 'Butterfly' needle)
Sensory deficits that impair the patient's ability to detect a change in sensation at the site of chemotherapy administration.	Inadequate dressings or poor cannula fixation
Communication difficulties or young children, which hinder the early reporting of the signs and symptoms allowing the identification of extravasation.	Poorly implanted CVAD (too deep for cannula, difficult to secure cannula)
Prolonged infusion	

Table 3
Preventive protocols to minimize the risk of extravasation.

'Site of insertion': Identification of the most appropriate cannulation site should be undertaken before insertion. If venous access continually proves difficult, placement of a central venous access device should be considered. The following are among the conditions of the cannulation site:
a) Large veins in the forearm are recommended for peripheral administration.
b) Cannulation should be avoided over joints.
c) The inner wrist and the lower extremities should not be used.
d) Veins in the anticubital fossa or on the dorsum of the hand, particularly for vesicant drugs, are not recommended.
e) Avoid cannulation where lymphedema is present.
f) Cannulation on the side of a mastectomy is still a matter of discussion.

'Cannula'. Preventive measures related to the type of cannula include:
a) Winged steel infusion devices ('butterfly' needles) must not be used for infusion of vesicant drugs as the needle can be easily displaced or puncture the venous wall.
b) Flexible cannulae should be used.
c) For infusion of vesicant drugs of longer duration (e.g. 12–24 h) the central venous access is highly recommended.

'Procedures':
a) After cannulation, check for blood flow. Then, flush with 10-ml normal saline and check for signs of extravasation.
b) Flushing with 10–20 ml of saline solution between different drug infusions is recommended.
c) A blood return (flashback) should always be obtained before drugs are administered and checked regularly throughout the bolus infusion.
d) Continue monitoring of the cannula insertion site and check regularly for the appearance of symptoms such as swelling, pain or redness sluggish infusion rate. This is highly recommended during infusion of all drugs.
e) Bolus dosages of vesicant drugs may be administered concurrently with a fast-running infusion of compatible i.v. fluid.

If an extravasation is suspected, the cannula should never be removed immediately and general and specific measures should be started.

Differential diagnosis

A differential diagnosis assessment should be carried out if an extravasation is suspected. Some chemotherapy drugs, even if correctly administered, can cause a local reaction which resembles an extravasation. This should not be confused with a true extravasation. Signs and symptoms of local nonextravasation reactions include erythema around the cannula site and along the accessed vein ('flare'), urticaria and local itching. Drugs that may cause these reactions are shown in Table 4.

Another potential differential diagnosis is chemical phlebitis. This vein inflammation, frequently followed by a thrombosis or sclerosis of the veins, may cause a burning sensation at the cannula site and cramping along the vein proximal to the cannula site. This chemical phlebitis can be caused by several drugs (see Table 4).

Table 4
Chemotherapy drugs possibly causing local reactions.

Local skin reactions	Chemical phlebitis
Asparaginase	Amsacrin
Cisplatin	Carmustine
Daunorubicin	Cisplatin
Doxorubicin	Dacarbazine
Epirubicin	Epirubicin
Fludarabine	5-Fluorouracil (as continual infusion in combination with cisplatin)
Mechlorethamine	Gemcitabine
Melphalan	Mechlorethamine
	Vinorelbine