Extravasation

Management of haematology emergencies

28th meeting of the EBMT NG

Tuesday, 3rd April 2012

Thorunn Saevarsdottir
Topic

- Background
  - Definition, prevalence, pathophysiology
- Risk factors
  - Related to the antineoplastics, the patients and the clinician
- Prevention
  - Staff, patient and administration technique
- Management
  - General instructions and tools
Extravasation: Definitions

- The inadvertent instillation or leakage of vesicant material into the perivascular and subcutaneous spaces during medication administration (Infusion nursing society, oncology nursing society, 2006)

- *Extravasation*: Passage or escape into tissue of antineoplastic drugs. Tissue slough and necrosis may occur if the condition is severe (Mosby’s. 2002, p.648)

- The inappropriate or accidental infiltration of chemotherapy into the subcutaneous tissue or subdermal tissues surrounding the administration site (Chemotherapy extravasation guideline; WOSCAN Cancer Nursing and Pharmacy Group, 2009)
Prevalence

• Peripheral infusions
  • 0.1% to 6%

• Implanted venous access port infusions
  • 0% to 4.7%

Pathophysiology: Tissue damage secondary to drug infiltration occurs as a result of one of two major mechanisms

• The drug is absorbed by local cells in the tissue and binds to critical structures (e.g. DNA, microtubules), causing cell death. It then is released into the surrounding tissue. Healing is inhibited because the process is repeated as the drug is taken up by other cells

• The drug does not bind to cellular DNA. Local tissue damage is caused by the solvents used in the drug formulations and is more readily neutralized

(Albanell & Baselga, 2000; Dorr, 1994)
Risk factors for peripheral extravasation include the following: (Kassner, 2000; Langhorne & Barton-Burke, 2001; Steele, 2001)

- Small, fragile veins
- Poor vascular integrity or history of vascular or circulatory disease
- History of diabetes, other medical conditions, or previous chemotherapies leading to peripheral neuropathy
- Previous multiple venipunctures and IV medications causing decreased vascular integrity
- Limited vein selection because of lymph node dissection or limb removal
- Superior vena cava syndrome or other medical conditions causing peripheral edema
- Use of medications that produce somnolence, altered mental status, excessive movement, vomiting, or coughing
- Venipuncture technique
- Drug administration technique
- Site of venous access
- Device selection

Chemotherapy and Biotherapy Guidelines and Recommendation for Practice, Second Edition

Thorunn Saevarsdottir

3.4.2012
Extent of tissue damage:

- Factors that affect the amount of tissue damage include (Clamon, 2001):
  - the site of infiltration
  - the amount of drug infiltrate
  - the concentration of the agent
  - the vesicant nature of the agent
  - the management of the extravasation by the nurse or physician
### Appendix 1. List of drugs: vesicants, irritants and non-vesicants

<table>
<thead>
<tr>
<th>Vesicants</th>
<th>Irritants</th>
<th>Non-vesicants¹</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DNA-binding</strong></td>
<td>Carmustine</td>
<td>Asparaginase</td>
</tr>
<tr>
<td><strong>Alkylating agents</strong></td>
<td>Cyclophosphamide</td>
<td>Bleomycin</td>
</tr>
<tr>
<td>Mechlorethamine (Nitrogen mustard)</td>
<td>Dacarbazine</td>
<td>Bortezomib</td>
</tr>
<tr>
<td>Anthracyclines</td>
<td>Etoposide</td>
<td>Cladribine</td>
</tr>
<tr>
<td>Daunorubicin</td>
<td>Fluorouracil</td>
<td>Cytarabine</td>
</tr>
<tr>
<td>Doxorubicin</td>
<td>Ifosfamide</td>
<td>Etoposide phosphate</td>
</tr>
<tr>
<td>Epirubicin</td>
<td>Mephalan</td>
<td>Gemcitabine</td>
</tr>
<tr>
<td>Idarubicin</td>
<td>Mitoxantrone</td>
<td>Interferons</td>
</tr>
<tr>
<td><strong>Others</strong></td>
<td>Streptozocin</td>
<td>Interleukin-2</td>
</tr>
<tr>
<td>Dactinomycin</td>
<td>Possible irritants²</td>
<td>Methotrexate</td>
</tr>
<tr>
<td>Mitomycin C</td>
<td>Carboplatin</td>
<td>Monoclonal antibodies</td>
</tr>
<tr>
<td><strong>Non-DNA-binding</strong></td>
<td>Cisplatin</td>
<td>Pemetrexed</td>
</tr>
<tr>
<td>Vinca alkaloids</td>
<td>Docetaxel</td>
<td>Raltitrexed</td>
</tr>
<tr>
<td>Vinblastine</td>
<td>Irinotecan</td>
<td>Thiothepa</td>
</tr>
<tr>
<td>Vincristine</td>
<td>Oxaliplatin</td>
<td></td>
</tr>
<tr>
<td>Vindesine</td>
<td>Paclitaxel</td>
<td></td>
</tr>
<tr>
<td>Vinorelbine</td>
<td>Topotecan</td>
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</tr>
</tbody>
</table>

¹ Any agent extravasated in high enough concentration may be an irritant.

² There have been few reports of these agents acting as irritants, but there is no clear evidence for this.

**NOTE:** For those medications that are not considered a vesicant but cause prolonged patient discomfort at the infusion site, it is strongly recommended that a central line be placed.
Prevention of extravasation: Staff

- Proper staff training and competency.
- Training in measures to prevent extravasation.
- Training in management of an extravasation incident.

(Chemotherapy extravasation guideline; WOSCAN Cancer Nursing and Pharmacy Group, 2009)
Prevention of extravasation: Patient

- Patient education and co-operation
- Patients at risk of extravasation

(Chemotherapy extravasation guideline; WOSCAN Cancer Nursing and Pharmacy Group, 2009)
Prevention of extravasation: cannulation site

- Selection of a new and appropriate cannulation site

(Chemotherapy extravasation guideline; WOSCAN Cancer Nursing and Pharmacy Group, 2009)
Prevention of extravasation: Administration via peripheral lines

- Verify the patency of the intravenous site, check for blood return.
- Inform the patient to report any sensation of burning or pain at the infusion site.
- Vesicant drugs should be given first and by slow IV push via the side-arm port of a fast running infusion.
- Irritant drugs should be sufficiently diluted.

(Chemotherapy extravasation guideline; WOSCAN Cancer Nursing and Pharmacy Group, 2009)
Prevention of extravasation: Administration via central lines

- Central line or PICC should be used for slow infusion of high-risk drugs
- Extravasation can also occur with central venous catheters
- Prior to administration of chemotherapy, blood return should be ensured

(Chemotherapy extravasation guideline; WOSCAN Cancer Nursing and Pharmacy Group, 2009)
Signs, symptoms and consequences of extravasation. (Langhorne & Barton-Burke, 2001; Otto, 2001)

- Swelling
- Stinging, burning, or pain at the injection site
- IV flow rate that slows or stops or the infusion is not flowing freely
- Leaking around catheter or implanted port needle
- Lack of blood return
- Erythema, inflammation, or blanching at the injection site
- Induration
- Vesicle formation
- Ulceration
- Necrosis
- Sloughing
- Damage to tendons, nerves and joints

Chemotherapy and Biotherapy Guidelines and Recommendation for Practice, Second Edition; WOSCAN Cancer Nursing and Pharmacy Group, 2009
General treatment instructions

- Stop infusion immediately. DO NOT remove the cannula
- Disconnect the infusion (not the cannula/needle)
- Leave the cannula/needle in place and try to aspirate as much of the drug as possible from the cannula with a 10 ml syringe.
- Mark the affected area and take digital images of the site
- Remove the cannula/needle
- Collect the extravasation kit, notify the physician and seek advice from the chemotherapy team
- Elevate limb and administer pain relief if required
- Give patient information sheet and arrange follow up and documentation

(WOSCAN Cancer Nursing and Pharmacy Group, 2009, EONS extravasation guidelines 2007)
Extravasation Kit

- Cold pack (instant or reusable)
- Hot pack (instant or reusable
- Antidotes according to local procedures
- 2 ml syringes
- 25 G needles
- Skin disinfectant as per local guidelines
- Indelible pen for marking the affected area
- Documentation forms
- Copy of extravasation management procedure
- Patient information leaflet

(EONS Extravasation guidelines 2007)
Heat

- This will cause vasodilation, increasing drug distribution and absorption and thus aiding in the dispersal of the drug from the injury site. Heat is used in non-DNA binding drug extravasations.

Cold

- Will cause vasoconstriction and minimize the spread of the drug from the initial injury allowing time for local vascular and lymphatic systems to disperse the agent. Cold is used in DNA binding drug extravasations.
## Use of Antidotes

<table>
<thead>
<tr>
<th>Extravasated Drug</th>
<th>Suggested Antidote</th>
<th>Level of Evidence</th>
<th>Advice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anthracyclines</td>
<td>Savene™ (dexamethasone)</td>
<td>Efficacy in biopsy-verified anthracycline extravasation has been confirmed in clinical trials</td>
<td>3 day course of Savene™ treatment: 1000 mg/m² IV as soon as possible (no later than 6 hours) after extravasation on day 1; 1000 mg/m² on day 2; and 500 mg/m² on day 3. See Appendix 4 for full details</td>
</tr>
<tr>
<td>Anthracyclines</td>
<td>Topical DMSO (99%)</td>
<td>Suggested as a possible antidote in many literature sources. Due to lack of evidence it is recommended that this is further studied</td>
<td>Apply locally as soon as possible. Repeat every 8 hours for 7 days. See Appendix 5 for full details</td>
</tr>
<tr>
<td>Mitomycin C</td>
<td>Topical DMSO (99%)</td>
<td>Suggested as a possible antidote in many literature sources. Due to lack of evidence it is recommended that this is further studied</td>
<td>Apply locally as soon as possible. Repeat every 8 hours for 7 days. See Appendix 5 for full details</td>
</tr>
<tr>
<td>Mechlorethamine (Nitrogen Mustard)</td>
<td>Sodium thiosulfate</td>
<td>Due to lack of evidence, this antidote is not recommended</td>
<td>2 mL of a solution made from 4 mL sodium thiosulfate + 6 mL sterile water for subcutaneous injection</td>
</tr>
<tr>
<td>Vinca Alkaloids</td>
<td>Hyaluronidase</td>
<td>Suggested as a possible antidote in many literature sources. Due to lack of evidence it is recommended that this is further studied</td>
<td>150–1500 IU subcutaneously around the area of extravasation. See Appendix 6 for full details</td>
</tr>
<tr>
<td>Taxanes</td>
<td>Hyaluronidase</td>
<td>Suggested as a possible antidote in many literature sources. Due to lack of evidence it is recommended that this is further studied</td>
<td>150–1500 IU subcutaneously around the area of extravasation. See Appendix 6 for full details</td>
</tr>
</tbody>
</table>

*For a detailed list of vesicants, please refer to Appendix 1*
# Extravasation of cytotoxic agents – Documentation (I)

<table>
<thead>
<tr>
<th>Cannula used:</th>
<th>○ Butterfly*</th>
<th>○ Venflon*</th>
<th>○ Other</th>
<th>.................................</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cannula fixated with:</td>
<td>.................................</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diameter</td>
<td>...............</td>
<td>G</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Site of puncture:**
- ○ Left arm
- ○ Right arm
- ○ Forearm
- ○ Antecubital fossa
- ○ Wrist
- ○ Dorsum of hand
- ○ Other | ................................. |

**Was it necessary to puncture the same limb more than once?**
- ○ Yes
- ○ No

**Where – in relation to the original puncture site – was the vein punctured?**
- ○ Proximal
- ○ Distal
- ○ Medial/lateral

**Has the patient any of the following symptoms:**
- → Upper blockage to inflow: ○ Yes ○ No
- → Lymphoedema (same arm): ○ Yes ○ No
- → Haematoma (same arm): ○ Yes ○ No

**Sequence of application:**

<table>
<thead>
<tr>
<th>Amount</th>
<th>Substance or trade name</th>
<th>Volume</th>
<th>Extravascular</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>mg</td>
<td>in</td>
<td>ml</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>○ extravascular</td>
</tr>
<tr>
<td>2.</td>
<td>mg</td>
<td>in</td>
<td>ml</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>○ extravascular</td>
</tr>
<tr>
<td>3.</td>
<td>mg</td>
<td>in</td>
<td>ml</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>○ extravascular</td>
</tr>
<tr>
<td>4.</td>
<td>mg</td>
<td>in</td>
<td>ml</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>○ extravascular</td>
</tr>
<tr>
<td>5.</td>
<td>mg</td>
<td>in</td>
<td>ml</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>○ extravascular</td>
</tr>
</tbody>
</table>

**Estimated volume of extravasated drug:** ........... ml

**Type of administration:**
- ○ i.v.
- ○ i.a.
- ○ Bolus
- ○ Infusion
- ○ Infusion pump

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3.4.2012
### Extravasation of cytotoxic agents – Documentation (II)

<table>
<thead>
<tr>
<th>Extravasation recognised:</th>
<th>Date (mm/dd/yyyy)</th>
<th>Time of day: ........</th>
</tr>
</thead>
<tbody>
<tr>
<td>○ During administration</td>
<td></td>
<td></td>
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<tr>
<td>○ Immediately after administration</td>
<td></td>
<td></td>
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<tr>
<td>○ . . . . hours after administration</td>
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<td></td>
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<tr>
<td>○ . . . . days after administration</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Measures: Aspiration of cytotoxic drug possible:</th>
<th>○ Yes</th>
<th>○ No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recommended general and substance specific measures taken:</td>
<td>○ Yes</td>
<td>○ No</td>
</tr>
<tr>
<td>Additional measures taken: ..........................................................</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Risk factors that may influence wound healing (for example, diabetes mellitus):</th>
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<thead>
<tr>
<th>Information for/ instructions to patient:</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Plastic) surgeon consulted:</td>
</tr>
<tr>
<td></td>
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<tr>
<td></td>
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<tr>
<td>Next control appointment:</td>
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| Documented by: | ..........................................................
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<td>Name in capital letters, please</td>
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| E-mail: | ..........................................................
| Affiliation: | .......................................................... |
### Extravasation of cytotoxic agents – Documentation (III)

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<td>Date</td>
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<tr>
<td>Paraphe of doctor</td>
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</tbody>
</table>

**Symptoms after extravasation:**

- Pain (burning, stinging)
- Oedema
- Erythema
- Blistering
- Discolouration
- Induration
- Functional impairment
- Ulceration
- Necrosis
- Denarcation
- Formation of eschar
- Infection
- Complete healing

**Extent of extravasation:**

- Two biggest diameters in cm

**Measures:**

- Conservative measures
- Surgical measures: Incision
- Transplantation

**Notes:**

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Thorunn Saevarsdottir  
3.4.2012
Conclusion

- The prevalence of chemotherapy extravasation is not high, however the consequences can be serious, cause the patient pain and discomfort and possibly cause delay in treatment and in some cases hospitalization.
- The avoidance and prevention of chemotherapy extravasation is the primary goal.
- By maintaining high standard of care in the delivery of IV chemotherapy and management of the extravasation incidences we go a long way.
References.

- ONS Chemotherapy and Biotherapy Guidelines and Recommendations for Practice. Sec. edit. 2005

- EONS Extravasation guidelines 2007
  Guidelines Implementation Toolkit

- Chemotherapy extravasation guideline. WOSCAN Cancer Nursing and Pharmacy Group. 2009.
  http://www.beatson.scot.nhs.uk/content/mediaassets/doc/Extravasation%20guidance.pdf
Thank you for your attention