Taxol extravasation: A case report

By W.L. Bailey and R.M. Crump

Abstract
Taxol™ is a relatively new antineoplastic agent whose classification as either vesicant, non-vesicant, or irritant remains under debate. This case study is presented to follow a large-volume Taxol™ extravasation. The article illustrates assessment, follow-up, intervention and outcome of this situation. This case suggests the drug is a vesicant with the potential to cause moderate soft tissue injury.

Introduction
Taxol is a cell cycle phase specific (G2 or M phase) antimitotic agent presently utilized in the treatment of ovarian cancer and breast cancer. Currently it is also under study in a number of other disease sites.

The drug is highly lipophilic and insoluble in water (Bristol-Myers Squibb, 1994). The diluent Cremophor, with which the drug is mixed, is also thought to be responsible for the hypersensitivity reactions seen during administration in earlier Taxol studies. Due to the diluent requirement and other unique properties of the drug, numerous precautions such as pre-medication, use of non-PVC equipment, and use of in-line filters are required in the administration of this drug.

Taxol has been used in humans since 1983 when phase I clinical trials began (Dorr, 1994). Information is continually gathered on the incidence and management of side effects and toxicities. Similar to Adriamycin, Taxol has been reportedly associated with intravenous reaction. However, its classification as a vesicant, non-vesicant or irritant drug remains under debate to the present time.

The report below illustrates the case history of a woman treated with Taxol who suffered a large extravasation.

Case report
A 42-year-old woman was diagnosed in 1993 with stage IIIIC, well differentiated papillary serous carcinoma of the ovary. She was optimally debulked of her disease by a total abdominal hysterectomy, bilateral salpingo-oophorectomy, and omentectomy during a staging laparotomy. Initially she was treated with a combination of carboplatin and cyclophosphamide. The patient completed her treatment in January 1994 and unfortunately the tumour recurred in September 1994 with a large pelvic mass and two liver metastases. At this time the patient agreed to participate in a clinical trial of Taxol and Granulocyte Colony Stimulating Factor (GCSF) for platinum resistant ovarian cancer. The objectives of this phase III clinical trial were as follows:

- to determine if Taxol dose affects response rate, progression-free interval or survival
- to compare toxicities of the two regimens (Taxol 175 mg/m² v/s Taxol 250 mg/m²)
- to compare the efficacy and toxicity of two dose levels of GCSF 5 mcg/kg v/s 10 mcg/kg in the highest Taxol dose arm
- to determine the relationship between peak Taxol plasma concentration and toxicity/response.

The patient was randomized to receive Taxol 250 mg/m² (≤500 mg total dose) over 24 hours, and GCSF 10 mcg/kg s.q. daily from day 3 until the absolute neutrophil reached the level required in the protocol. (10.0) Near the completion of her ninth cycle of Taxol, the patient complained of pain at the intravenous site (left median cubital vein) and noted swelling at the site. The nurse assessed the site and noted good backflow of blood and consulted with a colleague who agreed with the assessment. Return bloodflow coupled with the patient’s reluctance for a site change led to their decision to leave the intravenous in situ and complete the Taxol infusion.

Upon completion of the Taxol infusion, the nurse clinician met with the patient to provide GCSF and supplies, and review the plan of care for home. An area of redness accompanied by inflammation was seen around the taped intravenous site. The intravenous, which was flushing with normal saline, was stopped and the tape was removed, exposing a 10 cm x 5 cm area of inflammation. This appeared to be a large extravasation of Taxol. A review of nursing notes revealed a four-hour time lapse between initial complaint of pain, site check by floor nurse, and completion of Taxol infusion, suggesting an extravasation of approximately 150 ml of Taxol solution. The medical oncologist and pharmacist were consulted before the intravenous was discontinued.

There is no known antidote to Taxol extravasation. The patient was discharged home with instructions to use alternating hot and cold compresses for 10 minutes every two to three hours, followed by room temperature exposure while awake, and to keep her arm elevated. A return clinic appointment was given for one week and the patient instructed to call should her skin blister, break down, change colour, or should any other concerns arise.

On return to the clinic (day 8 post extravasation) the patient reported mild discomfort with certain movements, such as bending or rotating the arm. The total area of skin changes measured 15 x 8 cm. There was a central area of redness which was raised, tender and warm to the touch, measuring 6 x 4 cm at the site of cannula entry and surrounding tissue.

The patient was prescribed oral Clocaxillin 500 mg q 6 h x 14 days for cellulitis. She was instructed to use cool compresses pm for comfort and again instructed to call with any signs of skin breakdown, worsening of cellulitis symptoms, or any other concerns.

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On day 22 post extravasation the patient returned for cycle 10 of Taxol. The Clexacillin was renewed. At the extravasation site there was a hard, red, raised, indurated and tender area measuring approximately 4.5 cm x 3 cm with no evidence of skin breakdown. It was elected to delay the patient's treatment for one week to allow for further resolution of the skin reaction. Meehan and Sporn (1994) reported on a large volume Taxol extravasation via peripheral vein that developed pain, erythema and induration with peeling and blistering of the skin and no ulcer formation. This reaction resolved without intervention. The subsequent chemotherapy treatment was administered via central line. The authors noted the development of a painful, erythematous indurated nodule at the previous Taxol injection site. The nodule developed in two days after subsequent treatment and included an area of yellow necrosis at the previous needle site. This recall reaction resolved without intervention in approximately eight days.

On day 28 post extravasation the patient received the tenth cycle of Taxol. The infusion was given in the opposite arm with no recall reaction. Subsequent Taxol treatments were administered with no recall reaction or worsening of the prior extravasation. The site continued to improve slowly. On day 49 post extravasation the site remained 4 x 2 cm, reddish brown in hue, hard to touch but not raised. At the time of the twelfth Taxol treatment (day 70 post extravasation) the changes to the site had completely resolved.

**Discussion**

There is very limited information in the literature regarding extravasation of Taxol. Further, it is unclear if the subsequent skin reaction is caused by the Taxol, or the Taxol/Cremophor® combination. Enquiries to the supplier of Taxol, Bristol-Myers Squibb, as to the availability of animal studies which may assist in the treatment of Taxol extravasation revealed a published study in mice. This study suggests that intradermal injection of Taxol does produce skin ulceration, which heals well with no treatment (Dorr, 1994).

An extravasation of this magnitude could have resulted in significant skin breakdown. The observed course of this extravasation is in keeping with the data in mice (Dorr, 1994), and consistent with moderate soft tissue injury described in literature review (Ajani, 1994; Meehan & Sporn, 1994; Bicher et al., 1995; Dorr, 1994).

We conclude that Taxol should be considered a vesicant agent due to the reported and observed potential to cause moderate soft tissue injury. Not all vesicants cause tissue necrosis upon extravasation. It is important to note that 89% of all extravasations do not progress beyond a mild reaction (Birdsall & Naleboff, 1988). Until a consensus is reached as to this drug's status as a vesicant, irritant, or non-vesicant agent, all extravasations should be reported, documented and followed with serial photography.

It is important for all intravenous nurses to be aware of the potential sequelae from extravasation of anti-neoplastic drugs. Extravasation of a vesicant agent is a medical emergency in the oncology setting. Extravasation of non-vesicant agents, while not as urgent, is not to be dismissed lightly. It also requires documentation, advice to the patient on care of the site, and appropriate monitoring and follow-up. Prevention of extravasation is the role of the oncology nurse. The old adage "when in doubt... resist" remains an intravenous nurse's rule of thumb when dealing with chemotherapy administration.

<table>
<thead>
<tr>
<th>Process of extravasation</th>
<th>Days Post Extravasation</th>
<th>Size</th>
<th>Appearance</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>10 x 15 cm (total area)</td>
<td>tender to touch, red &amp; inflamed, obvious extravasation of fluid</td>
<td>observation, application heat/cold</td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>15 x 8 cm (total area)</td>
<td>skin hue changes, tender to touch, raised, angry, warm to touch, cellulitis</td>
<td>Cloxacillin 500 mg q6h x 14 days, cool compresses, observation</td>
</tr>
<tr>
<td></td>
<td>22</td>
<td>4.5 x 3 cm cannula site</td>
<td>area of hyperpigmentation surrounding cannula site, hard, red, raised, indurated, tender</td>
<td>repeat antibiotics, delay chemotherapy</td>
</tr>
<tr>
<td></td>
<td>28</td>
<td>4 x 2 cm cannula site</td>
<td>area of hyperpigmentation surrounding cannula site, red and raised</td>
<td>chemo given in unaffected limb, no further Rx for extravasation site</td>
</tr>
<tr>
<td></td>
<td>49</td>
<td>4 x 2 cm</td>
<td>reddish brown area, hard to touch</td>
<td>Nil</td>
</tr>
<tr>
<td></td>
<td>70</td>
<td>0</td>
<td>resolved</td>
<td>Nil</td>
</tr>
</tbody>
</table>

**References**


