Chemotherapy: safe use of cytotoxic drugs in practice

Author : Linda Roberts

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Linda Roberts VTS (Oncology), DipAVN (Medical), RVN, offers guidelines for the safe handling and administration of chemotherapy drugs

CANCER is widely considered to be the one of the most common causes of death in older dogs and cats. Despite this, a number of treatments are available to offer pets a good quality of life, including chemotherapy. Advances in veterinary oncology have increased owner awareness and the readiness of many veterinary practitioners to treat cancer patients, meaning that more pets with cancer are being managed long term.

Chemotherapy is used in veterinary patients to treat systemic cancer or as an adjunct to surgery or radiation for treating microscopic disease. It may be used with curative or palliative intent – the goal of all therapy being maintenance of optimum quality of life. This article aims to provide some background information and guidance for nursing staff on the safe use of cytotoxic drugs in veterinary practice.

Chemotherapy

In human cancer therapy, chemotherapy is often aggressive, with severe debilitating side effects, including immune suppression, vomiting and diarrhoea, weight loss and total hair loss. Therefore, many owners' initial reaction to chemotherapy is: "I don't want to put my pet through that." In veterinary oncology, quality of life is paramount, and chemotherapy protocols are less aggressive than those used for humans. Doses are generally onethird of those used in human treatment protocols, with lesser intensity (weekly treatments, rather than daily). The payback is often limited life expectancy. Time should be spent counselling owners on what to expect during their pet's

chemotherapy, the anticipated chances and duration of remission, potential side effects and estimated cost of treatment, to enable them to make an informed decision.

Basic concepts

The goal of chemotherapy is to inhibit the growth of cancer cells with minimum effect on normal cells. Most chemotherapeutic agents either bind directly to genetic material in the cell nucleus or affect a cell's ability to synthesise protein. This may also damage growth and reproduction of the patient's normal cells, as both healthy cells and cancer cells go through the same cell division cycle.

Treatment doses and schedules are determined according to the type of cancer and chemotherapy method employed. In some cases, periodic chemotherapy will be necessary to control the cancer for the rest of the pet's life. Combining cytotoxic drugs is an effective strategy in chemotherapy, designed to target different parts of the cell cycle to increase the proportion of total tumour cells killed during any one treatment. Combinations of drugs are beneficial as often they enhance the activities of each other. Drugs are also combined to minimise their dose-limiting toxicities and help reduce the development of tumour resistance – cells resistant to one drug may be sensitive to another within that regimen.

Of the cytotoxic chemotherapeutics used in small animal oncology, none are licensed for veterinary use. Until the recent availability of the tyrosine kinase inhibitors, there were no alternatives.

Potential hazards

Cytotoxic drugs may be life-saving for patients with cancer, but they pose a risk to patients and staff members who handle and administer them. The drugs are cytotoxic and potentially carcinogenic, mutagenic and teratogenic. They are irritant to the skin and mucous membranes. It is important that written safety protocols are established and followed in any veterinary clinic administering chemotherapy, and that cytotoxic drugs are handled with extreme caution and awareness of their potential danger. Exposure to cytotoxic drugs can occur through:

• skin exposure – direct or indirect contact;

• ingestion;

• aerosolisation;

• accidental inoculation; and

• exposure to metabolites – present in patients' excreta for 48 hours to one week after administration, depending on the drug.

Rules and regulations

Guidelines exist on the safe use of cytotoxics in the workplace. These are defined by the Control of Substances Hazardous to Health Regulations (COSHH) 2002. Drugs considered carcinogenic are subject to Appendix 1 of the COSHH Approved

Code of Practice. Further information can be found at www.hse.gov.uk/coshh

Preparation and administration

Before giving chemotherapy, both the nurse and the veterinary surgeon should review the patient's file and chemotherapy protocol. Double-check dose calculations of the cytotoxic. It is advisable to use flow sheets to track a patient through the process, as below.

• Each treatment: blood sample ATTcaractere ? results back ATTcaractere ? OK to proceed ATTcaractere ? catheter ATTcaractere ? drug dose ATTcaractere ? checked twice ATTcaractere.

• The overall course of chemotherapy: this consolidates pertinent information from each visit into a single chart for easy reference.

Preparation, storage and disposal

• Keep cytotoxics locked in a designated cupboard or fridge.

• No eating or drinking and no through traffic allowed in the area.

• Avoid disruption by keeping the door closed and display a warning sign.

• Protective clothing must be worn when handling, preparing or administering chemotherapy drugs – by the person handling the drug and any assistants (Figure 1). This consists of a minimum of two pairs of powder-free latex gloves and full-length, longsleeved impermeable gown, mask and goggles. Gloves should be worn even to handle unopened or packaged cytotoxic drugs.

• Drugs should ideally be prepared in a fume hood (Figure 2). If this is not possible, a vented dispensing pin or a closed drug transfer system is recommended, which improve staff safety when used as instructed (Figure 3).

• Drugs should be prepared on a plastic-backed, absorbent pad.

• Use screw-on Luer-Lok syringes and T-connectors/giving sets.

• When reconstituting powder, tap the vial gently to loosen impactions. This prevents the need for

vigorous shaking.

• Prevention of aerosolisation is vital. Do not allow pressure to build up in vials – never push air or drug back into a vial (or allow it into the environment), and wrap a swab around the junction of needle and vial (Figure 4).

• Do not re-cap needles.

• Label syringes with drug and patient name – keep in the fume hood or a locked cupboard until administration.

• Never split tablets or capsules – it poses a safety risk and accurate dosing cannot be guaranteed.

• If spillage or personal contamination occurs, soak up with paper towels, incontinence pads or cat litter and spray the area with copious amounts of water or disinfectant, and clean with paper towels.

• All contaminated waste should be disposed of in a designated sharps bin or clinical waste bin. Protective clothing should be worn to handle waste. Cytotoxic waste should be placed in a solid container, clearly labelled and sealed, ready for collection.

• Keep a chemotherapy spill kit close to hand. This should contain latex gloves, gown, mask and eye protection, incontinence pads, cat litter and a large zip-lock bag for disposal.

• When dispensing tablets or capsules to owners, label them “Cytotoxic – wear gloves” and give written information on safe administration.

Owners must be given clear instructions for at-home administration, handling the drugs, and for dealing with drugcontaminated urine and faeces. While it is important to point out potential hazards associated with human exposure to metabolites of these drugs, it is equally important not to frighten people. Chemotherapy patients’ excretions may be hazardous, but the pet is safe to be around all family members.

If chemotherapy patients remain hospitalised, it is important to clearly label the kennels of treated patients and ensure that all ward staff are aware of safety protocols for dealing with the patient and handling waste products.

Adverse effects

Although serious adverse effects can occur following chemotherapy, fewer than five per cent of patients require hospitalisation. It is important to help owners feel in control by providing information and advice on how to nurse their pet at home and when to contact the practice.

Potential side effects of cytotoxic drugs include the following:

• **“Off days”** – this is the most common side effect reported, and it usually resolves spontaneously after a short time. Owners should be advised to have water available at all times and to contact the clinic if they have concerns, including refusal of food or water, or repeated vomiting and/or diarrhoea, for 24 hours or more, if there is blood in the faeces, urine or vomit, noticeably increased PU/PD, changes in behaviour and lethargy, or manifestation of pain.

• **Gastrointestinal signs** – for example anorexia, vomiting and/or diarrhoea – are usually not severe or prolonged, but patients may experience some form of stomach or intestinal discomfort, two to seven days after chemotherapy. Analgesic or antispasmodic medication may be prescribed for administration at home. Anti-emetics may be prescribed. Food may be withheld for up to 12 hours, as long as the patient is otherwise well. When feeding is reinstated, small, bland meals should be offered frequently, instead of one large meal. In the case of anorexia, owners should be provided with practical advice on encouraging patients to eat. Appetite stimulants may be tried, but are not usually successful long term and may have adverse effects. If patients experience diarrhoea, but are bright and happy, symptomatic treatment can be given and a normal routine followed. However, if it is persistent, the patient is dull and/or there is melaena, fresh blood or concurrent pain and/or nausea, the patient should be re-examined. If side effects are prolonged or severe, hospitalisation may be required.

• **Alopecia** – pets rarely have dramatic hair loss, but many owners worry about it. Some undergo changes in coat condition, such as development of a soft, fluffy “puppy-coat”. This is due to the loss of guard hairs. Certain dog breeds, such as poodles, old English sheepdogs and other breeds whose hair grows continually, may have a greater degree of hair loss. Cats often lose their whiskers. Hair regrowth over clipped areas may be slower during treatment, but coat condition is normally restored at the end of chemotherapy treatment.

• **Myelosuppression** – many chemotherapeutic agents impair the bone marrow’s ability to produce cells. As a result, neutropenia may occur seven to 10 days after chemotherapy. Neutropenia alone is not dangerous to the patient, but the inability to fight infection is. A thrombocytopenic patient may lose normal clotting function, and bruising and bleeding may become evident. If significant myelosuppression occurs, chemotherapy may need to be delayed. If the effects are severe, antibiotics may be prescribed to reduce the patient’s risk of infection. Owners should be advised to keep their pets in their own environment as far as possible and avoid potential sources of infection. To monitor for this potential side effect, a full haematology screen should be performed immediately before, and seven to 10 days after, each dose of chemotherapy.

• **Tissue damage** – many cytotoxic drugs are vesicant and, if given perivascularly, severe tissue reactions can result (Figure 5), leading to non-healing wounds and limb amputations. Therefore, chemotherapy agents must be administered with the utmost care and only by trained staff. Always ensure adequate patient restraint during chemotherapy administration. An aseptically prepared

“clean-stick” intravenous catheter should be placed specifically for chemotherapy drugs (Figure 6). This should be checked for patency and flushed with copious amounts of sterile 0.9 per cent saline immediately before use – ensure blood is flowing back through the catheter (but do not apply excessive suction), palpate and observe area over the catheter for evidence of patient discomfort or “blowing” of the vein. If in doubt, do not give the drug and place a new catheter. Always have the catheter site in view. If it appears to “blow”, the animal shows signs of discomfort, or if irritation of the injection site develops, stop administration immediately. Apply gentle suction to withdraw the drug. When as much of the drug as possible has been removed, take out the catheter. When using vinca-alkaloids, the application of hot packs may help; for doxorubicin extravasation, cold packs may be applied. In all cases, cover the area with a light sterile dressing and instigate standard wound management protocols. Adequate analgesia is essential. Inform owners that a problem has occurred. Commonly used vesicant cytotoxics include vincristine, vinblastine and doxorubicin.

• **Allergic reactions** – these are rarely seen with chemotherapeutic agents. These reactions are generally acute and should be treated as any other allergic anaphylaxis. Doxorubicin and L-asparaginase are cited as being the most common drugs to cause anaphylaxis – signs include vomiting, tachycardia, tachypnoea, red mucous membranes, restlessness and/ or urticaria. At-risk patients should be closely monitored and “ABC” first aid employed if a problem develops. Dexamethasone and chlorphenamine may be used in conjunction with standard CPR.

• **Cardiotoxicity** – some chemotherapeutic agents, specifically doxorubicin, may irreversibly damage the heart muscle. Owners should be warned of the risk, and at-risk patients screened in advance. Fewer than 10 per cent of patients develop heart disease as a result of standard chemotherapy protocols, and the risk versus the benefit will be discussed with the owner. Texts suggest that levels of 180-240mg/m2 are not exceeded in a patient’s lifetime.

• **Sterile haemorrhagic cystitis** – this condition may occur with cyclophosphamide use. It is caused by excretion of irritant metabolites in the urine. Patients receiving this drug should have frequent urine sampling to monitor for blood. While administering cyclophosphamide, hydration should be maintained and diuresis encouraged.

Conclusions

Veterinary nurses have a vital role to play in the care of chemotherapy patients and in maintaining the health and safety of both patients and staff. Careful administration of cytotoxics and subsequent patient monitoring should avoid many potential complications of using these drugs. If guidelines are followed, the safe use of cytotoxic drugs should be possible for the majority of veterinary practices, with minimal risk to staff involved. Practices and personnel should not become complacent with cytotoxic drug use, and regular risk assessment and updates to local rules should be performed.

Further reading

- Dobson J and Lascelles D (2011). *BSAVA Manual of Canine and Feline Oncology* (3rd edn). BSAVA, Gloucester.
- Bexfield N (2006). The safe use of cytotoxic drugs in companion animal practice, *EJCAP* **16**(1): 51-62.