

Hazards of Cytotoxic Drugs

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Abstract

Cytotoxic drugs include any drug that inhibits or prevents the function of cells. Cytotoxic drugs are increasingly being used in a variety of healthcare settings, laboratories and veterinary clinics for the treatment of cancer and other medical conditions such as rheumatoid arthritis, multiple sclerosis and auto-immune disorders. Occupational exposure to hazardous drugs and the resulting potential health risk to healthcare workers first became a recognized safety concern in the 1970s. Published data related to the issue of occupational exposure prompted the Occupational Safety and Health Administration (OSHA) to issue guidelines in 1986 for the handling of antineoplastic and other hazardous agents by healthcare personnel. Handling of cytotoxic drugs provides useful information for pharmacists, pharmacy technicians, medical and nursing staff, veterinary practitioners and others involved in handling these drugs, including people who clean up any spills. The guidance contains simple information on the potential health hazards and health surveillance, legal framework and the duties of employers and employees. It also gives useful tips on ways of controlling and monitoring exposure and appropriate waste disposal. Appropriate training, utilization of effective equipment and supplies, and strict compliance with detailed policies and procedures provide the best approach to reducing the potential health risks of occupational exposure to hazardous drugs.

Key words: Cytotoxic drugs, Handling of antineoplastic agents, Occupational exposure

The treatment of cancer involving the chemotherapy makes use of highly toxic drugs. These drugs act mainly by suppressing the multiplication of malignant cells. Alternatively they also inhibit all growing cells, and this includes the healthy cells as well. This might affect the cells of the healthy people who handle these drugs.

In the early 1980's, there was concern about the environmental contamination when handling cytotoxics. The mutagenic and allergic property of these drugs that were manifested in the personnel handling of drugs were of concern for the health care providers.

The first procedural manual, that provided assistance in the formulation of guidelines for handling of cytotoxics in hospitals, was released by American Society of Hospital Pharmacist in 1985. Surveys in the United States have shown that there exists a lack of standardized procedural manuals or guidelines for handling of the cytotoxic drugs or to deal with their spillage in hospitals¹

What are cytotoxic drugs?

Cytotoxic drugs are therapeutic agents intended for, but not limited to, the treatment of cancer. These drugs are known to be highly toxic to cells, mainly through their action on cell

reproduction. Many have proved to be carcinogens, mutagens or teratogens. Cytotoxic drugs are increasingly being used in a variety of healthcare settings, laboratories and veterinary clinics for the treatment of cancer and other medical conditions such as rheumatoid arthritis, multiple sclerosis and auto-immune disorders²

Potential health effect of cytotoxic drugs

Current statistics show that one in three people have a life-long risk of developing cancer. There is little scientific evidence currently available relating to whether working with cytotoxic drugs actually increases the risk of developing cancer or not. However, in the absence of such data, a strategy of prudent avoidance is recommended. In the workplace, occupational exposure may occur where control measures fail or are not in place. Exposure may be through skin contact, skin absorption, inhalation of aerosols and drug particles, ingestion and needle stick injuries resulting from the following activities:

- ♦ Drug preparation
- ♦ Drug administration
- ♦ Handling patient waste
- ♦ Transport and waste disposal or Spills.

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- ◆ Personnel likely to be involved in these activities include:
- ◆ Nurses and Medical officers
- ◆ Pharmacists
- ◆ Laboratory staff, and
- ◆ Cleaning, maintenance and waste disposal staff.

Where control measures are not adequate, adverse health effects may result from occupational exposure. Health effects attributed to cytotoxic drugs exposure amongst people preparing and administering cytotoxic drugs include:

- ◆ Abnormal formation of cells and mutagenic activity
- ◆ Alterations to normal blood cell count
- ◆ Fetal loss in pregnant women and malformations in the offspring of pregnant women
- ◆ Abdominal pain, hair loss, nasal sores and vomiting
- ◆ Liver damage, and
- ◆ Contact dermatitis, local toxic or allergic reaction, which may result from direct contact with skin or mucous membranes.

Safe handling of cytotoxics

Cytotoxic medicines safety implies the safe management of the dispensing, reconstitution (if it is done in the pharmacy), transportation, administration of the cytotoxics and the final disposal of the used dosage form. It also implies the safety procedures be formulated in dealing with the management of the spillage. The personnel who are in daily contact with the cytotoxic drugs have a high chance being front of the cabinet produces an air curtain, exposed to these agents and becoming contaminated.

The adverse effects of the cytotoxic drugs make it highly imperative to be careful in the handling of these cytotoxic drugs. Some of the measures in the safe handling of the cytotoxic drugs must include;

- Categorizing and separating these drugs to a specialized unit in the pharmacy, where adequate protective measures are taken like aprons, masks and glasses for the protection of the body and eyes
- Training and educating the pharmacists handling these agents about the risk involved and the protection to be taken while handling them.
- Educating the pharmacist involved on the measures to be taken in case of spillage of these drugs or while the transferring of these drugs into smaller packages for the use by the patients.
- Providing written procedural manual to deal with situations when spillage of cytotoxic occurs
- Special labeling of the containers should be instituted to ensure proper handling and disposal.
- Pregnant staff should never be allowed to handle

cytotoxics.²

Facilities to be provided where cytotoxic are handled and prepared

The risk associated in the handling and administration of the cytotoxic drugs have resulted in the widespread use of safety cabinets for the preparation and dispensing of these products. The facility provided should be such that it serves the need of protection against the prepared cytotoxic drugs for the person handling it and the quality of the product is not affected which intern may affect the therapeutic efficacy for the patient.

Vertical Laminar Flow Cabinet (VLFC), Isolators (Totally Enclosed Glove Boxes) may be used. Vertical laminar flow cabinet has the characteristic that the entire contaminated zone is under negative pressure. The operating principle is that air filtered through HEPA filter is passes over work surface. This air then passes through vents at the back and white front of the cabinet and is recirculated. Some of the air is exhausted and to compensate this more air is taken in through the front opening this creates a negative pressure in the cabinet. The balance between the cabinet down flow and the air drawn in at the which provides the basis for the product and personnel protection.

Isolators are totally enclosed workstations with filtered air. Work can be done through glove ports or a half suit arrangement to access the working areas. Materials are introduced through a air lock or using an access port and docking device. At work the system is totally air sealed from the outside.

The minimum requirements to protect staff when handling cytotoxic drugs at these different stages are outlined below

- Preparation of the dosage form in a controlled environment requires gown gloves of a suitable quality. Here there is no need of the protection for the eyes as the agents are handled in the negative pressure conditions of the controlled environment, which provides the protection for the personal. For preparation of the dosage form in the uncontrolled environment requires a gown, gloves, glasses for eye protection and a dust mask.
- For staff checking the prepared dosage form requires a long sleeved uniform and gloves.
- While transportation of the prepared dosage form to the ward no special requirement is needed, if they are transported in a suitable container, and the messenger is aware of the hazards
- While dealing with spills the protective measures required are a nonabsorbable overall with a plastic apron, a heavy-duty gloves, suitable eye protection and a respiratory mask.
- After the dosage has been administered the person handling the waste, should be dressed in long sleeved

uniform, plastic apron, gloves of suitable quality, a suitable eye protection and a respiratory mask. Care should be taken that the waste are not discarded into drainage as this sewage may be recycled and reach the system, as the recycled sewage may be used for many general purpose like irrigating fields (as this recycled sewage may have a natural fertilizer quality). The toxic qualities of the discarded cytotoxics may reenter the cycle again, where the humans are at risk of being contamination. Here the risk is of higher magnitude as the volume of the people involved is greater.

The methods of disposal of the commonly used drugs are discussed later and care should be taken to ensure the strict adherence to the procedure of disposal of the wastes to avoid contamination.

The Risk Management Approach

The aim of a risk management approach (outlined in Table 1) is to eliminate or reduce the risk of illness or injury associated with work. This generally involves a process of:

- ✓ Hazard identification
- ✓ Risk assessment
- ✓ Risk control, and
- ✓ Evaluation of control measures.

Effective management of health and safety also involves:

- ✓ Consultation
- ✓ Personnel management
- ✓ Training
- ✓ Documentation of activities, and
- ✓ Regular review of the management system.

Management of cytotoxic spills

▶ Restrict the movement of all the personnel to and from the area until decontamination is done.

▶ The person doing the decontamination should wear proper dressing with gloves, mask and eyeglasses of proper quality.

▶ The spilled material should be placed in a rigid container, if the spillage is a liquid, cover it with an absorbent cloth, leaving it there for sufficient time for the liquid to be absorbed. If the spilled material is powder, it should be covered with a wet cloth, and additional water added as required.

▶ All the absorbent material and spillage are transferred to a separate bag.

▶ All the surface contamination is washed with water and detergent by several rising with clean water. Absorbent clothes should not be used for this procedure.

▶ All potentially exposed skin surface should be washed with water and soap.

Conclusions

Exposure to the cytotoxins, though in small quantities over a long period of time is harmful to the human body. The exposure to these drugs increases the allergenic reaction in the personnel handling these drugs in the hospital. The above discussion attempts to discuss the hazards involved in the exposure of cytotoxic drugs. It also tries to outline the importance of maintaining a procedural manual in handling, dealing of spillage of cytotoxics and facilities needed in the disposal of cytotoxic drugs.

Procedures for destruction or disposal of some commonly use cytotoxic drugs.

The spillage that has been carefully collected using the proper protection and in the proper container are mainly destroyed by incineration at the very high temperature or by chemical degradation. The incinerating temperature and the chemical reagents used for denaturation of certain very commonly used cytotoxic drugs are outlined below.

Table 1

Name	Physically	Chemically
Asparaginase	Destruction is by incineration at 800°C.	Chemically destroyed by denaturation with strong acid or alkali.
Bleomycin	Destruction is by incineration at 1000°C.	Chemically destroyed by 5% Sodiumhydroxide, 10% Hypochlorite solution for 24 Hrs or alkaline potassium permanganate.
Carboplatin	Destruction is by incineration at 1000°C	Diluted with large volume of water and allowed to stand for 4/8 Hrs. On contact with skin should wash with water.
Cisplatin	Destruction is incineration at 1000°C.	Chemically destroyed by diluting with large volume of water or a 12% alkaline sodium borohydride. On contact with skin it may be washed with large volume of water. A cream may be added if a stinging sensation is experienced.

Name	Physically	Chemically
Cyclophosphamide	Destruction is by incineration at 900°C	Chemically destroyed by denaturation with 5% sodiumhydroxide or with 0.2M potassiumhydroxide in methanol for 24 hrs. On contact with skin wash well with water or soap. If eyes are contaminated, immediately irrigate with normal saline.
Cytarabine	Destruction is by incineration at 1000°C.	Chemically destroyed by treating with 5% hydrochloric acid. On contact with skin it may be washed with large volume of water. If eyes are contaminated, immediately irrigate with normal saline.
Dacarbazine	Destruction is by incineration at 500°C	Chemically destroyed by treating with 5% hydrochloric acid at pH 2 for 24 hrs or 10% sulphuric acid for 24hrs. On contact with skin it may be washed with large volume of water. If eyes are contaminated, immediately irrigate with normal saline.
Doxorubicin	Destruction is by incineration at 700°C.	Chemically destroyed by treating with 10% sodium hypochlorite soaked for 24hrs. on contact with skin it may be washed with large volume of water or sodium bicarbonate solution. If eyes are contaminated, immediately irrigate with normal saline.
Epirubicin	Destruction is by incineration at 1000°C	Chemically destroyed by treating with 10% sodium hypochlorite soaked for 24hrs. On contact with skin it may be washed with large volume of water or sodium bicarbonate solution. If eyes are contaminated, immediately irrigate with normal saline.
Etoposide	Destruction is by incineration at 1000°C	Chemically destroyed by treating with alkaline potassium permanganate or 10% sodium hypochlorite soaked for 24 hrs. On contact with skin it may be washed with large volume of water. If eyes are contaminated, immediately irrigate with normal saline.
5 Fluro Uracil	Destruction is by incineration at 700°C	Chemically destroyed by treating with 5% sodium hydroxide or 10% sodium hypochlorite soaked for 24hrs. On contact with skin it may be washed with large volume of water or sodium bicarbonate solution. If eyes are contaminated, immediately irrigate with normal saline.

Name	Physically	Chemically
Ifosphamide	Destruction is by incineration at 1000°C	Chemically destroyed by treating with 2N sodium hydroxide in dimethyl formamide soaked for 24 hrs. On contact with skin it may be washed with large volume of water or sodium bicarbonate solution. If eyes are contaminated, immediately irrigate with normal saline.
Dactinomycin	Destruction is by incineration at 1000°C	Chemically destroyed by treating with 5% trisodium phosphate or 20% sodium hydroxide soaked for 24 hrs. On contact with skin it may be washed with large volume of water or sodium bicarbonate solution. If eyes are contaminated, immediately irrigate with normal saline.
Danorubicin	Destruction is by incineration at 700°C	Chemically destroyed by treating with 10% sodium hypochlorite (1% available chlorine) soaked for 24 hrs. On contact with skin it may be washed with large volume of water or sodium bicarbonate solution. If eyes are contaminated, immediately irrigate with normal saline.
Idarubicin	Destruction is by incineration at 700°C	Chemically destroyed by treating with 10% sodium hypochlorite (1% available chlorine) soaked for 24 hrs. On contact with skin it may be washed with large volume of water or sodium bicarbonate solution. If eyes are contaminated, immediately irrigate with normal saline.
Melphalan	Destruction is by incineration at 500°C	Chemically destroyed by treating with 5% sodium thiosulphate in sodium hydroxide soaked for 24 hrs. On contact with skin it may be washed with large volume of water or sodium bicarbonate solution. If eyes are contaminated, immediately irrigate with normal saline.
Methotrexate	Destruction is by incineration at 1000°C	Chemically destroyed by treating with 1:1 mixture of 5% sodium hydroxide and sodium hypochlorite. On contact with skin it may be washed with large volume of water and apply any cream if any stinging is present. If eyes are contaminated, immediately irrigate with normal saline. If sufficient quantity is inhaled or injected calcium folinate cover has to be provided.
Mitomycin C	Destruction is by incineration at 1000°C	Chemically destroyed by treating with 2-5% sodium hydroxide or hydrochloric soaked for 12 hrs. On contact with skin it may be washed with large volume of water or sodium bicarbonate solution followed by soap and water. Avoid any hard creams. If eyes are contaminated, immediately irrigate with normal saline.

Name	Physically	Chemically
Vincristine	Destruction is by incineration at 1000°C	Chemically destroyed by treating with 5% sodium hydroxide or 10% sodium hypochlorite soaked for 24 hrs. On contact with skin it may be washed with large volume of water. If eyes are contaminated, immediately irrigate with normal saline.
Vinblastine	Destruction is by incineration at 1000°C	Chemically destroyed by treating with 5% sodium hydroxide or 10% sodium hypochlorite soaked for 24 hrs. On contact with skin it may be washed with large volume of water or sodium bicarbonate solution. If eyes are contaminated, immediately irrigate with normal saline.
Interferons	Destruction is by incineration at 1000°C	Chemically destroyed by treating with 5% sodium hydroxide or 10% sodium hypochlorite soaked for 24hrs. On contact with skin it may be washed with large volume of water. If eyes are contaminated, immediately irrigate with normal saline soap and water.

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