

Management of Cytotoxic Drugs And Related Wastes Disposal

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Abstract

Cytotoxic drugs are intended primarily for the treatment of cancer. They are known to be highly toxic to cells, mainly through their action on cell reproduction. Many have proved to be carcinogens, mutagens or teratogens. Patients receiving therapeutic doses of these drugs have exhibited many adverse effects, including cancers. All people who came in contact with cytotoxic drugs and related wastes are also at risk of exposure and possible adverse effects. In this study procedures are defined on how to prevent or minimise the risk of exposure to cytotoxic drugs and related wastes, Use of cytotoxic drugs includes preparation, handling, storage, transport and disposal of these products. The Bio -Medical Waste Management Rules,2016 have to be followed for the safe disposal of cytotoxic drugs and related wastes.

Keywords: Cytotoxic drugs, carcinogenic, mutagenic, cytotoxic waste, incineration.

Introduction

Cytotoxic drugs are also known as antineoplastic drugs and are used as anticancer drugs because they kill or slow down the growth of the living cells. They are used to treat cancer and other medical conditions such as rheumatoid arthritis and multiple sclerosis. Cytotoxic drugs are highly toxic to non target cells through their action on cell reproduction. Some are shown to be mutagenic or teratogenic in various experimental systems. Cytotoxic drugs and related waste can present significant risks to those who handle them. When control measures are inadequate, occupational exposure may occur through skin contact, skin absorption, inhalation of aerosols and drug particles, ingestion and needle stick injuries, during preparation of Cytotoxic drugs, administration of Cytotoxic drugs, transportation and cytotoxic waste disposal. Pharmacists ,pharmacy technicians, medical and nursing staff, laboratory staff, of hospitals and manufacturing chemists, research scientists of pharmaceutical industries who handle cytotoxic drugs and related waste are at a risk of exposure. Measures to control exposure should be applied in the following order: (a) Staff handling cytotoxic drugs and related wastes should be provided training on the risks and the precautions to be taken. (b) use of enclosed systems where reasonably practicable.(c) Adequate extraction systems should be used to control exposure at source.(d) Ensuring safe handling, storage and transport of cytotoxic drugs and related wastes. Personal protective equipment (PPE) should be provided to the employees and used by them where risks cannot be adequately controlled in other ways. Selection of the PPE should be done on the basis or the risk assessment of the area. PPE offers adequate protection for its intended use. Employees must be trained in the use of PPE and it must be properly maintained and stored. Procedures for dealing with spillage and contamination of the cytotoxic drugs and related wastes should be provided to the persons who are handling it. They should be familiar with the methods for dealing with spillages or contamination of people or work surfaces. Any spillages that do occur should be dealt with promptly. Disposal of cytotoxic drugs and related waste should be done as per The Bio Medical Waste Management Rules,2016.[1.2.3]

Aim of the Study

The aim of study is to identify, and minimise occupational exposure to cytotoxic drugs and related wastes in health care establishments, manufacturing units and research centers. People involved in the use, handling or disposal of cytotoxic drugs and related wastes should be made aware of associated matters relating to the safe handling or disposal of cytotoxic drugs and related waste.

The study of Sources of Cytotoxic Waste, Cytotoxic Waste hazards ,Preparation and Administration of Cytotoxic drugs, Minimization of Cytotoxic Waste, Techniques of Cytotoxic Waste Disposal, Handling, storage, labeling, packaging and transportation, spills and contamination, cytotoxic waste disposal and training are carried out for the proper Management of cytotoxic drugs and related waste disposal

Mridula Verma
Associate Professor,
Dept. of Chemistry
M.M.H College,
Ghaziabad, U.P., India

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- Sources of Cytotoxic Waste** The main sources of cytotoxic wastes are health care facilities, manufacturing facilities and research centers. Cytotoxic waste includes materials that have been contaminated from drug preparation and administration (expired cytotoxic drugs, left-over cytotoxic drugs, returned drugs, syringes, needles, gauzes, vials, packaging; patients samples). personal protective equipment (PPE) such as gowns and gloves. Contaminated with cytotoxic drugs are also considered as a cytotoxic waste.[4]
- Cytotoxic Waste Hazards** Cytotoxic drugs and related wastes are hazardous to human health. While little is known of the specific long term effects of occupational exposure to cytotoxic drugs and related wastes, there is sufficient evidence to indicate that they may cause adverse health effects such as abdominal pain, liver damage, leukemia, infertility, birth defects, skin rashes, vomiting and hair loss. Many cytotoxic drugs are shown to be carcinogenic and mutagenic.in various experimental systems. The severity of the hazards for health-care facilities, manufacturing units and research centers workers responsible for the handling or disposal of cytotoxic drugs and related waste is mainly attributed to its toxicity and the extent and duration of exposure. There is no workplace exposure limit set for cytotoxic drugs. Medical opinion suggests that even low level exposure to cytotoxic drugs should be avoided. All healthcare facilities, manufacturing units and research centers that work with cytotoxic drugs and related waste must implement effective control measures to protect workers and other people.[4,5,6]
- Preparation of Cytotoxic drugs** Preparation of cytotoxic drugs should be in compliance with standard guidelines.[4,6 ,7 ,8] Handling of cytotoxic drugs should be done by properly trained personnel only. Professionals, technical and housekeeping personnel who may come in contact with these drugs should be given training for the Safe handling of cytotoxic drugs. Recommended Practices for preparing Cytotoxic Drugs should be followed.
1. Cytotoxic drug preparation must be performed in a Class II Type A2, B1, or B2, or Class III biological safety cabinet exhausted outside the building.
 2. Personnel preparing the drugs should wear Nitrile gloves and a disposable gown with elastic or knit cuffs. Gloves should be changed regularly and immediately when contaminated, torn, or punctured. Contaminated gowns require immediate removal and replacement. Thoroughly wash the affected area with soap and water, in case of skin contact with any cytotoxic drug, In case of the eye contact of cytotoxic drug, flush the affected eyes with copious amounts of water for at least 15 minutes. Then seek medical evaluation by a doctor.
 3. Drugs Vials to be reconstituted should be vented to reduce internal pressure. This can be done by using a 0.22-micron hydrophobic filter or a chemotherapy dispensing pin. This reduces spraying and spilling of the cytotoxic drug..
 4. When chemotherapy pin is not used, a sterile alcohol pad should be placed around the needle and vial top during withdrawal from the septum..
 5. .When opening the glass ampule, wrap it and then snap it at the break point using an alcohol pad to reduce the possibility of injury and to contain the aerosol produced. When removing the drug solution, we should use a 5 micron filter needle or straw.
 6. V bottles and Syringes containing cytotoxic drugs must be labeled and dated unless they are being used immediately.
 7. The external surfaces contaminated with a cytotoxic drug should be cleaned with 2% sodium hypochlorite solution before transfer or transport.
 8. When the cytotoxic drug preparation is complete, cleaning of the interior of the safety cabinet should be done by 2% sodium hypochlorite solution using disposable towel. All wastes are considered contaminated and must be disposed of properly.
- Administration of Cytotoxic drugs**
1. Cytotoxic drugs may be administered by different routes: (i) Orally,(ii)Subcutaneous or intramuscular injection,(iii) Subcutaneous infusion,(iv) Intravenous injection or infusion,(v) Topical administration.
 2. Nitrile or other chemotherapy gloves should be worn. Gloves should be changed regularly and immediately when contaminated, torn, or punctured. Hands must be thoroughly washed before gloves are donned and after gloves are removed.

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3. Disposable closed-front gowns with elastic cuffs should be worn. Gowns should be made of polyethylene-coated polypropylene material
4. When bubbles are removed from IV tubing, or syringes an alcohol pad should be placed over the tip in order to collect any of the cytotoxic drugs that may be inadvertently discharged. Discard gloves after each use and wash hands.[2,4]

Minimisation of Cytotoxic Waste

Cytotoxic waste can be minimised by careful segregation and purchasing of drug quantities as per requirement, proper clean-up procedures and spill containment methods are employed for the minimisation of Cytotoxic waste. If possible substituting environmentally persistent drugs with degradable drugs will minimise the cytotoxic waste.

Techniques of Cytotoxic Waste Disposal

Cytotoxic waste is a hazardous substance and should never be land filled or discharged into the sewerage system. When disposal of cytotoxic drugs and related wastes by high temperature incineration or chemical degradation methods are not possible in a facility then encapsulation or alkaline hydrolysis methods can be considered. The recommended disposal options include: the following.[5,9,10.11.12.13]

1. Return to the original supplier: Outdated cytotoxic drugs and cytotoxic drugs that are no longer required should be returned to the supplier. Outdated drugs are considered as cytotoxic waste and its transportation must be done according to the provisions of the law.
2. Incineration at higher temperature: The complete destruction of cytotoxic drugs and related wastes require temperature up to 1200^o c .Double chamber incinerator which ensures a temperature of 1200^o c with a maximum gas residence time of 2 seconds in the secondary chamber is required for the incineration. The incinerator should be fitted with a gas clearing equipment and it should have an operating authority from a relevant government body for hazardous waste incineration including cytotoxic wastes..
3. Chemical degradation: Chemical degradation methods which convert cytotoxic compounds into non toxic compounds can be used for the drug residues. It is used for cleaning of contaminated urinals, spillages and protective clothing. Chemical degradation methods are safe, they include oxidation by Potassium permanganate or sulfuric acid, denitration by hydrobromic acid or reduction by nickel and aluminum..
4. Chemical neutralization: Chemical neutralization through oxidation using sodium hypochlorite is a new alternative method for treatment of cytotoxic drugs and related wastes.
5. Encapsulation: Encapsulation leaves cytotoxic waste materials unchanged but prevents them from seeping into the environment. Cytotoxic waste should be immobilized or encapsulated prior to disposal into landfill as per the following encapsulation methods:(i) If the cytotoxic waste is with their secondary packages, remove from their package but not from the primary packaging.(ii).plastic/steel drum should be filled up to 65% capacity with cytotoxic waste.(iii). Remaining space will be filled with the following at approximate ratios by weight: Cement 15%, Lime 15%,Water 5% to obtain required consistency.(iv)close the lid of the drum and place it at the base of the land fill and cover with soil.
6. Alkaline hydrolysis: sodium hydroxide or potassium hydroxide solutions or slurries are employed at high temperature for the alkaline hydrolysis of cytotoxic wastes. High PH(>10) aqueous solution or slurry breaks down the complex biological molecules. The caustic liquid and high temperature kill living organisms, including pathogens. bacteria are destroyed as are viruses, rickettsia and fungi.

Handling of Cytotoxic drugs and related wastes

The primary focus during the handling of cytotoxic drugs and related wastes must be on control of the working environment, safe work practices and education and training of the personnel. While working with cytotoxic drugs and related wastes, it is essential to minimize exposure wherever it is possible. Therefore, cytotoxic drugs in all forms should be handled by a limited number of persons in a manner which avoids skin contact, liberation of aerosols and cross-contamination with other drugs. For all aspects of handling of cytotoxic drugs and wastes , detailed written procedures and safe work practices have to be in place and must be followed. It has

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to be assured that personal protective equipment, facilities (e.g. biological safety cabinets, isolators etc.) and clothing for personnel working with cytotoxic drugs and wastes are provided and used correctly. The minimum requirements for protective clothing for people preparing cytotoxic drugs should include a protective gown, shoe or boot covers, headwear and mask. Gloves should be changed immediately in case of perforation or contamination. The use of PPE and gowning should depend on the different stages of the process. Protective clothing should not be worn outside the working area. The employer is responsible for the occupational safety of the personnel. He is obliged to evaluate the risk potential for employees handling cytotoxic drugs and arrange appropriate safety measures. All personnel handling cytotoxic drugs and related wastes should be examined regularly by a physician for medical check-up. Furthermore, performance of routine blood tests is recommended.[3]

Storage of Cytotoxic drugs and related wastes

Cytotoxic drugs and related wastes must be stored in appropriate containers ensuring prevention of unintended release in a secure area with adequately maintained environmental condition (e.g. no airflow), with access limited to specified authorized personnel. Warning labels should be applied to all cytotoxic drug containers and bins where these containers are stored.

Labeling, Packaging and Transportation of cytotoxic drugs and related wastes

All cytotoxic drugs and related wastes must be labeled clearly with detailed, accurate and legible information. Appropriate control measures must be in place to ensure that there is no cytotoxic residue contaminating the outside of the primary container or other packaging. Cytotoxic drugs and related wastes should be properly identified with the capital C symbol and under it, the word cytotoxic in capital letters. Cytotoxic drugs should be packaged and transported so as to provide adequate physical and chemical protection for the drug during storage and transport, and protection for people in the event of spillage. Transport containers should be labeled to allow easy identification of the contained substances. People involved in the transport of cytotoxic drugs and related wastes should be cautioned and trained in the necessary procedures should a spill occur, including sealing off the contaminated area and calling for assistance.[3]

Spills and Contamination of cytotoxic drugs and related wastes

Spills of cytotoxic drugs and related wastes must be dealt with immediately as they present a high risk of exposure to the personnel. Spills may occur in all areas where cytotoxic drugs and related wastes are handled, stored, transported and disposed. Spills and breakages must be cleaned up immediately by a properly protected person trained in the appropriate procedures. People in the direct vicinity of a cytotoxic spill should be alerted immediately that a spill has occurred and requested to keep away. A spill should be identified with a cytotoxic signage so that other persons in the area will not be affected. Spill kits containing neutralizing agents, absorbent materials, protective equipment and instructions for use must be stored in appropriate locations and should be labeled accordingly. Further, every workstation has to be equipped with an emergency plan containing the names and telephone numbers of the responsible persons. The circumstances and handling of all spillages have to be documented. After contamination of the skin with a cytotoxic product, first aid measures are to be taken depending upon the type of substance. In many cases, immediate thorough washing with water is recommended. In case of a large spillage or exposure to people and environment, it should be referred to the Material safety data sheet (MSDS) of the respective product. After removal of the spillage and decontamination, the affected area has to be tested for cytotoxic residues by swipec samples and must be released prior to resumption of work.[2]

Cytotoxic Waste Disposal

Disposal of Cytotoxic drugs and related wastes should be done as per the Bio-Medical Waste Management Rules 2016. The term cytotoxic waste includes any material that comes in contact with cytotoxic drugs during their handling, preparation, administration, storage and disposal. Cytotoxic waste should be packed in yellow coloured non chlorinated plastic bags or containers. It should be properly identified with the symbol of Cytotoxic hazard. Treatment and disposal options employed for the cytotoxic drugs and related wastes are as follows. Expired cytotoxic drugs and items contaminated with cytotoxic drugs to be returned back to the manufacturer or supplier for incineration at temperature > 1200°C or to common bio medical waste treatment facility or hazardous waste treatment, storage and

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disposal facility for incineration at 1200^oc or Encapsulation or Plasma pyrolysis at > 1200^oc.[1,3]

Training

All people involved in the preparation, storage, transport and disposal of cytotoxic drugs and related wastes must be trained in the handling of these products and in the necessary precautions to be taken if a spill occurs. It shall be ensured that appropriate working instructions are in place and all people handling cytotoxic drugs and related wastes have access to the relevant information. Training measures should be documented, continuously improved and updated.

Conclusion

In this study, the focus was on the management of cytotoxic drugs and related waste disposal. We have discussed the functional elements involved in cytotoxic drugs and related waste management(i.e. sources, hazards, preparation, administration, minimization, techniques, handling, storage, labeling, packaging, transportation, spills, contamination, waste disposal and training.). Subsequently we explained the techniques of cytotoxic waste disposal through the return to supplier, incineration, chemical degradation, chemical neutralisation and encapsulation methods to reduce their impact on public health and the environment. We then discussed some of the techniques for handling and cytotoxic waste minimisation. Provision of a cytotoxic waste management planning and monitoring system is a prerequisite issue for effective reduction of cytotoxic waste associated risks

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