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Safe Handling of Hazardous Drugs

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Firstly What are Cytotoxic Drugs and What do We Use Them For?

Cytotoxic drugs are drugs that kill cells. They are mainly used to treat cancer but can be used for other therapeutic indications e.g. rheumatoid arthritis, multiple sclerosis. Cytotoxic drugs mainly kill cells through their action on cell reproduction, affecting cell DNA division. They are indiscriminate in their effect and will kill any type cell that commences cell division to reproduce. Most cancers, especially in the early stages of the disease, are dividing rapidly and thus are the main target for cell kill. However, some cells within the human body also divide more often than others and it is these cells that are also affected by cytotoxic cells e.g. blood cells, the entire lining of the gastro-intestinal tract and skin and hair cells. Thus the most common toxicities we see in patients being treated with cytotoxic drugs are due to the death of non cancer cells. Low white blood counts leading to increased susceptibility to develop infections and less ability to fight infections, low platelets leading to less ability for blood to clot and an increased risk of bleeding and low red blood cells leading to anaemia and a need for blood transfusions.

What Sort of Danger do They Pose for Staff and Patients?

As well as the general toxicities noted above, cytotoxic drugs have unique toxicities of their own. They may be carcinogenic, mutagenic and/or teratogenic. Thus patients receiving cytotoxic drug therapy have developed second cancers from their treatment (carcinogenic), have changes to their genetic DNA that increase their risk of developing cancer (mutagenic) and have increased foetal deaths and birth abnormalities (teratogenic). Second cancers do not appear for many years after treatment has ceased. These second cancers are not secondary cancer or metastases but totally new cancers. In the past, many patients did not live long enough after treatment to see the development of these second cancers but this is not the case today.

In addition to the direct toxicity of the drug, the administration of the drug can also pose a risk. Many cytotoxic drugs can damage/kill tissue if they are mistakenly injected into the tissue surrounding the vein instead of into the vein. Today's patients are advised of the possible toxicities of their treatments but as they expect to gain from the treatment (after all they have cancer) and their treatment is limited to a specific number of different drugs and to a certain time frame, the possible benefits outweigh the possible risks.

For staff it is a different matter. They can expect no benefit from being exposed to cytotoxic drugs. They handle many more drugs than a patient would receive and they do this over long periods of time, not a set course of treatment. So while a patient receives much higher doses, staff handling cytotoxic drugs may be exposed to low levels of many different drugs over a long period of time. Exposure may be via skin contact, inhalation of aerosols/drug particles or needle stick injuries. Adverse effects seen from this exposure include increase in mutagenicity, change in blood counts, foetal loss, foetal malformation and contact dermatitis. The main concern is the possibility of development of a cancer. It is impossible to quantify this risk, especially as there is rarely an immediate effect seen, but it is essential to minimise exposure. After all, employees are entitled to a risk free environment in which to work. Employers may have scoffed once at the possible toxic effects of asbestos exposure, again a problem with a long lag time and we do not want this delayed adverse outcome to happen with exposure to cytotoxic drugs. Evidently the handling of these drugs is a huge safety issue for both pharmaceutical companies and also hospitals and healthcare institutions.

Could You Tell Us About the Main Safety Precautions?

Pharmaceutical company employees have the biggest risk as they deal in very large volumes of drugs during the manufacturing process. However, they also have the best possible resources to ensure employees do not come into contact with the drug and require the use of 'space-suits' with external respiratory devices. Staff manipulating the drugs to create an individual dose are most at risk. Due to the requirement to individualise doses (based on patient parameters on the day of treatment) and the short expiry date of prepared doses, cytotoxic drug doses must generally be prepared on the day of treatment at the site of administration of the treatment. Many are provided as powders and must be reconstituted to be given as injections and even those provided as liquids must be handled to withdraw the correct dose and place it into an appropriate administrative format (e.g. into an IV infusion bag or a syringe or an ambulatory delivery device). Those administering the dose are also at risk although this risk is less as no actual manipulation of drug is required and the drug is often well diluted. Disposal of drug is also vital. All equipment such as used/partially used drug vials, used syringes, needles, empty IV infusion bags and IV giving sets, dressings and bandages must be appropriately segregated and stored prior to disposal. Waste must be identified as cytotoxic and

transported and disposed of in a way to protect the environment from contamination. Incineration at over 1000°C is recommended.

What Methods can Hospitals Use to Reduce Contamination as Much as Possible?

Institutions should review their need to create doses on site. If the use of cytotoxic drugs is limited, they should be purchased pre-prepared from an external source (such as a commercial company or a larger institution). If doses are required to be produced on site, their preparation should be centralised and done only by trained staff. Specific secure preparation areas are needed with clean rooms containing laminar flow cytotoxic drug safety cabinets or pharmaceutical isolators. Use of closed needleless systems further reduces possibility of exposure. Personal protective equipment is essential not only for those preparing the cytotoxic drug doses but also for those administering the doses, for staff unpacking purchased drug from suppliers (drug contamination has been found on the outside of newly purchased vials, glass vials may have broken) or for staff handling/moving waste. Other decisions can reduce the risk of exposure. Where there are choices always purchase vials not ampoules, liquids not powders, drugs packaged in plastic or plastic coated glass rather than glass alone. Staff transporting cytotoxic drugs must have training to ensure correct procedures are carried out should a spill occur. All of these require a substantial financial investment and ongoing financial commitment.

Risk Management for These Processes Must be Key. In General What Protocols and Processes are Put in Place by the Management?

Yes risk management is the key issue. If an institution is using cytotoxic drugs within its premises, such use crosses many departments and staff with different knowledge. Education is the key to risk minimisation. Written policies and procedures need to be developed, promulgated, implemented and evaluated throughout the institution. Effective planning and design of the workplace, 'best practice' control measures and specialised equipment, stringent safe handling procedures, training and education of employees (on commencement and at regular intervals), provision of personal protective equipment (and ensuring its use), instituting a staff health monitoring programme, ensuring specialised laundry of non-disposable equipment and arranging appropriate waste disposal of contaminated items are all vital. Clearly successful staff training is essential. In general how are staff trained and is this a continuous process? In general staff are trained on-the-job by experienced practitioners.

Many institutions have developed their own in-house training modules. At a minimum, staff preparing cytotoxic drugs must be validated in aseptic technique (using broth manipulations) and in the specialist requirements for handling cytotoxic drugs. Validation is recommended to be performed yearly. Prior to introducing any new techniques required for specific manipulations, time to provide full training to those handling the drugs must be available. Since staff preparing the cytotoxic doses are often 'isolated' in their secure cleanrooms, it is imperative that these training requirements are considered well in advance of the patient arriving at the hospital ready to receive their treatment. Communication is a key issue.

Many Healthcare Facilities are Introducing Robotics into the Process. Can This Really Help With Safety and Prevent Dosage Errors?

The use of robots in drug dose preparation does certainly reduce the opportunity for exposure but does not eliminate it. The robot still has to be loaded and the final products handled and transported. Not all drugs are able to be handled by a robot. Robots are best used when large preparation runs are planned rather than for individualised doses. In addition, robots are very expensive. Robots do not replace the need for experienced staff but they can supplement preparation activities. Robots can work non-stop but they cannot operate unsupervised and are best utilised in very large operations such as a major institution supplying surrounding smaller institutions or in commercial operations. I am not familiar enough with the use of robots to comment on their ability to prevent dosage errors – however, as humans have to programme the robot, I do not see how human error would be totally eliminated.

In Your Opinion What Does the Future Hold for the Safe Handling of Hazardous Drugs?

It is really pleasing that the current breakthroughs in cancer treatment are not reliant on cytotoxic drugs. Most new treatments involve targeted therapies, vaccines and monoclonal antibodies. The risks handling these drugs are much reduced compared to cytotoxic drugs. Even new forms of cytotoxic drugs such as liposomal forms are much less toxic to handle and administer BUT much more expensive to purchase and cannot be simply substituted for the parent drug. So while I think the percentage of patients requiring cytotoxic drugs is reducing, unfortunately the numbers of patients requiring treatment is increasing. Cytotoxic drugs are also becoming progressively cheaper compared to the newer treatments and they still remain the treatment of choice in many cancers. In the foreseeable future I do not see an elimination of the use of cytotoxic drugs and as such it behoves us to create as risk-free as possible an environment in which these drugs can be prepared, administered and the contaminated waste disposed.

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