2007

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http://hdl.handle.net/10026.1/3718

Hospital Pharmacy Europe

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Safe handling of cytotoxics

Despite the adoption of standard protective measures, healthcare workers are still exposed to cytotoxic drugs. The risks to the operator and the environment may be reduced by considering effective decontamination and intervention methods.

To protect the worker when handling cytotoxic drugs, more is needed than careful use of personal protective equipment and techniques. Despite the implementation of collective protective measures, many international studies have demonstrated levels of cytotoxic contamination in the surrounding environment and in the urine of operators. The risk posed by cytotoxic drugs to the operator and the environment may be reduced, if not eliminated, by considering additional approaches: firstly, the application of effective decontamination methods, and secondly, the use of intervention (i.e., a closed-system drug transfer device).

Routes of exposure
Cytotoxic contamination in the workplace and subsequent worker exposure may arise from several sources, even in the absence of manipulation errors. Figure 1 shows leakage onto the base of the isolator chamber which occurred when quinine sulphate was used as a fluorescent marker simulating cytotoxic manipulation in an isolator. The event occurred when withdrawing a syringe needle after addition to an infusion bag. Such surface contamination could be transferred to any surface coming into direct contact with it (e.g., contact with gloves could later result in dermal exposure through glove penetration, or in transfer of contamination to further surfaces). Successive use of the same syringe has also been implicated as a source of gloved contamination by cyclophosphamide and of potential dermal contact with cyclophosphamide.

If such surface contamination were not immediately removed, it could dry out, become airborne and contribute towards inhalation. It has been suggested that dried drug particles on surfaces or on the high-efficiency particulate air (HEPA) filter of the isolator or biological safety cabinet (BSC) may act as a reservoir, providing a source area from which molecules could slowly vapourise. Some drugs, such as cyclophosphamide, can vapourise at room temperature or higher – and certainly, temperatures higher than room temperature may be reached under normal conditions in which cytotoxic drugs are manipulated, with factors such as continual running of isolators and BSCs, and ongoing use of ancillary equipment such as lighting and pump motors.

Production of aerosols has also been demonstrated as a source of contamination when applying techniques used to reconstitute and dilute cytotoxic drugs. Oral ingestion or accidental dermal exposure from needlestick injuries, spillages or breaks could also occur. These events happen relatively less often, but can contribute to airborne and long-term workplace contamination.

Precontaminated sources taken into the environment before any manipulations are carried out will contaminate gloves and any surfaces subsequently touched. It has been demonstrated that the external surfaces of drug vials may be contaminated with the drug contained, which could also contaminate packaging. Levels found varied according to origin, indicating that precautionary measures taken are not standardised. Contamination on vials’ external surfaces may occur due to splashing, foaming or dusting during the filling process. This may be reduced by vial washing and subsequent application of protective sleeves.

In the UK and France, current practice in hospital pharmacies is to use negative-pressure isolators. Isolators offer containment, but there is no evidence for their superiority over BSCs. Isolators have their limitations and there is the potential for contamination to pass through hatches from the main chamber to the environment. Cytotoxic contamination has been reported on interior surfaces and on surfaces of the finished product in isolators and BSCs.

If vapourisation were a common occurrence, the HEPA filters of both isolators and BSCs would not be effective in retaining molecules of cytotoxic vapour smaller than the filter’s pore size. As a result, any cytotoxic aerosols generated would pass through the filter and be released into the environment. Therefore, whichever source is used, it is paramount to operator protection that the air be exhausted externally, away from the working environment.

Guidelines
Recommendations on good practice have been produced by the Occupational Health and Safety

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July/August 2007 Hospital Pharmacy Europe

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Decontamination methods

Agents chosen for decontamination in areas where cytotoxic drugs are compounded are mainly intended for biological decontamination. Decontamination protocols should be carefully designed and validated to confirm a biological “kill,” and likewise to confirm the removal or chemical degradation of cytotoxic drugs. Different biological agents have varying modes of action and efficacies against different microorganisms; the same applies to cytotoxic drugs, which represent a diverse range of chemical structures.

It is recommended that all surfaces be cleaned according to a protocol, which includes an appropriate deactivation agent to facilitate the removal and/or breakdown of biological and chemical contamination. Water-soluble cytotoxic drugs should be removed using wipes impregnated with an aqueous-based agent which binds the target drug, and the wipe should be disposed of afterwards. The drug would be more likely to be picked up by applying a detergent formulated at a pH at which the target drug is ionised. One should consider the possibility that surface contamination may take the form of multidrug chemical contamination, since cytotoxic drugs are frequently handled simultaneously; here, a combination of agents may be required. The chemistry of any breakdown products (which may retain cytotoxic activity) should also be considered alongside removal of the target drug. Wiping with industrial methylated spirit is common practice, but may also play a part in the removal of less water-soluble drugs and degradation products.

Intervention with closed-system containment device

The US National Institute for Occupational Safety and Health recommends the use of a closed-system drug transfer device to prepare cytotoxic drugs, and this has been acknowledged by the relevant European directive and by international guidelines.

Studies carried out at research centres worldwide, using the PhaSeal® closed-system drug transfer device have all demonstrated a significant reduction of contamination.

Preventing contamination at source is more effective than trying to remove the contamination once it has occurred. Eliminating the primary contamination event will also prevent secondary contamination of areas outside the immediate drug environment.

However, while closed-system devices may have a role in minimising staff exposure, one cannot recommend that they replace trained pharmacy staff using personal protective equipment and a pharmaceutical isolator. Containment by the device
References (continued)

Conclusions
Despite the adoption of standard protective measures, healthcare workers continue to be exposed to cytotoxic drugs. Targeting decontamination to the chemistry of the drugs used should be considered, as should the implementation of a closed-system device. Manufacturers should also be encouraged to improve their decontamination procedures and to guarantee the supply of vials free of cytotoxic contamination.

References

July/August 2007 Hospital Pharmacy Europe