Evaluation of Environmental Cytotoxic Drug Contamination in a Clinical Setting

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ABSTRACT

The use of cytotoxic drugs to treat neoplastic conditions is increasing in veterinary practices. Many agents have the potential to be genotoxic and evidence of exposure to cytotoxic drugs has been found in healthcare workers handling these pharmaceuticals. To date, limited contamination evaluations have been performed in veterinary practices. Evaluation for carboplatin contamination was performed at a veterinary teaching hospital involving twelve areas in the dispensary and treatment room. Detectable levels of platinum were found on the surface of the biological safety cabinet where drugs are transferred from vial to administration device. Results indicate contamination did occur and care must be taken during all phases of cytotoxic drug preparation and administration; precautionary procedures must be in place to limit the spread of surface contamination and personnel exposure. (J Am Anim Hosp Assoc 2017; 53:32–37. DOI 10.5326/JAAHA-MS-6471)

Introduction

Exposure to cytotoxic agents is documented in human healthcare personnel and has been evaluated by a variety of methods including urine mutagenicity assays; evaluation for chromosomal aberrations, DNA damage, and urinary metabolite levels of cytotoxic agents in healthcare personnel; and evidence of environmental contamination with various drugs.1–8 Many cytotoxic agents are known genotoxic agents with reports of acute symptoms such as vomiting, headaches, and dizziness; liver damage; reproductive deficits; and chromosomal aberrations.4,9–15 Lawson et al. recently reported a two-fold increased risk of spontaneous abortion before the twelfth week of gestation in nurses handling antineoplastic drugs.15 Aberrations in chromosomes 5, 7, and 11 were found in oncology nurses handling both alkylation and nonalkylating cytotoxic agents.3 The documented aberrations are consistent with those in individuals who develop acute myelogenous leukemia secondary to previous treatment with cytotoxic agents.4

Exposure routes of healthcare personnel include inhalation, dermal absorption, ingestion of contaminated food, mouth contact with contaminated hands, and accidental injection.16,17 Dermal absorption is the most likely route of exposure based on findings from previous studies.18,19 Guidelines to decrease personnel exposure to hazardous drugs have been developed by the National Institute for Occupational Safety and Health (NIOSH), the American Society of Health-System Pharmacists, and also the European College of Veterinary Internal Medicine of Companion Animals with the intent of minimizing occupational and environmental exposure to hazardous drugs.16,17,20 Additionally, in 2010, NIOSH released a Workplace Solutions document entitled “Safe Handling of Hazardous Drugs for Veterinary Healthcare Workers” to increase awareness of occupational risk associated with handling of hazardous drugs in veterinary medicine.21 Guidelines include the use of appropriate personal protective equipment (PPE) (such as protective gowns, double gloves, goggles,

BSC (biological safety cabinet); CSTD (closed system drug transfer device); HCl (hydrochloric acid); ICP-MS (inductively coupled plasma mass spectrometry); KSU VHC (Kansas State University Veterinary Health Center); NIOSH (National Institute for Occupational Safety and Health); PPE (personal protective equipment)

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and respirator masks), the use of a biological safety cabinet (BSC) designed to prevent hazardous drugs from being released into the work environment, and also the use of a closed system drug transfer device (CSTD) designed to limit the potential for generating aerosols and exposing personnel to needles when transferring hazardous drugs.16,17,20

The aim of this study was to evaluate environmental contamination in a veterinary teaching hospital setting where cytotoxic agents are used on a regular basis. Based on frequency of use amongst cytotoxic drugs at the Kansas State University Veterinary Health Center (KSU VHC) and practicality in measurement, carboplatin was chosen to assess for environmental contamination.

Materials and Methods
Cytotoxic drug preparation was performed in a clinically dedicated, class II, type B2 BSC, which has 100% venting outside of the building. Additionally, a drug transfer device was in use for administration of chemotherapy doses. Personal protective equipment used included a nonpermeable gown and two pairs of specified chemotherapy gloves for the dispensary personnel and a nonpermeable gown, single layer pair of chemotherapy gloves, and protective eyewear for administration personnel. Once the cytotoxic drug was transferred into the appropriate syringe for administration within the BSC, the transfer device for administration was attached to the syringe and the syringe placed into a small sealable bag. The outer gloves were removed by pharmacy personnel and the small bag was placed into a larger sealable bag outside of the BSC for transport to the chemotherapy administration area. Following administration, all disposables used for administration were packaged into the large outer transport bag for disposal, sealed, and placed in appropriate disposal containers.

For surface evaluation, wipe samples were obtained using the standardized sample kits. Two sample kits were obtained, each with material for six samples. Each kit contained 12 tissues (2 per site), 6 droppers with 17 mL 0.5 M hydrochloric acid (HCl) solution, 6 containers with labels and plastic mini bags for shipping, and 6 pairs of gloves. Twelve locations in the KSU VHC were assessed for platinum contamination: five locations within the dispensary and seven locations within the chemotherapy treatment area. The sizes of each location were measured and the areas were calculated in cm². Samples were acquired according to manufacturer’s instructions (Figure 1). In short, 17 mL of 0.5 M HCl solution was supplied in bottles with a dropper applicator for each sampling site. The entire 17 mL volume of HCl was applied to each designated surface using the dropper applicator. The solution was...
spread over the surface by the supplied tissue. This tissue was then placed in a container labeled with a description of the surface sampled. A second supplied tissue was then used to wipe the defined surface until dry and placed in the same container as the first. This procedure was performed for each designated surface. All samples were frozen after sampling and during transport until sample preparation and analysis. Platinum ions were measured instead of the platinum-containing drugs themselves. Platinum analysis was performed with stripping voltammetry according to standard procedures previously described.22 Samples were analyzed in duplicate and mean values were reported. Contamination was calculated in ng/cm². Due to background levels of platinum, quantification limits were set at 0.50 ng/mL HCl.

Results
In the 12 mo preceding evaluation, 73 doses (17,128mg total) of carboplatin had been prescribed and prepared by the KSU VHC dispensary (Figure 2). The areas sampled included five areas within the dispensary: (1) the surface of the BSC, (2) the floor in front of the BSC, (3) the drug storage container, (4) the refrigerator handle, and (5) the drug storage basin in the refrigerator where drugs are stored until they are ready for administration. Seven areas within the chemotherapy treatment room were sampled: (1) the door handle into the room, (2) the administration table, (3) the floor below the administration table, (4) the floor under the stand where syringes containing chemotherapy dosages are placed prior to administration and waste is packaged after administration, (5) the counter in the chemotherapy treatment room, (6) the door threshold into the secondary oncology room, and (7) the desk in the secondary oncology room. Results of wipe sample analysis are reported in Table 1. Assuming 100% recovery and wipe efficiency, all results are underestimates. Low-level contamination was found on the surface of the BSC. No other areas sampled showed evidence of platinum contamination.

Discussion
The results of this evaluation show platinum contamination on the drug preparation surface within the BSC. Although no evidence of platinum contamination was detected outside of the BSC, the significance of what was detected cannot be overlooked. Without strict guidelines for PPE and handling procedures in place, the contamination detected is a potential source for dissemination to other surfaces increasing the risk of exposure to veterinary personnel not properly protected. Cytotoxic drugs are prepared in many veterinary clinics on a daily basis without the use of a BSC, CSTD, or appropriate PPE. The use of such equipment, as outlined in the NIOSH guidelines, decreases the risk to personnel; however, if not used or if contaminated surfaces are used for other procedures, exposure to unprotected personnel is likely to occur. In the evaluation presented here, because strict handling guidelines were followed, the potential for dissemination of the contamination outside of the BSC was minimized as evidenced by the lack of platinum detected in other areas of the dispensary and chemotherapy administration room.

The amount of platinum detected in the current evaluation is comparable to what was detected in a previous veterinary study by Kandel-Tschiederer et al, but higher than a more recent evaluation by Janssens et al, although the amount of platinum handled was substantially higher in the current study than that by Janssens et al. and approximately 1.5 times that of Kandel-Tschiederer et al.23,24
In the study by Kandel-Tschiederer et al., a reduction in platinum contamination after the institution of the CSTD was detected. Even at the final evaluation, which was 9 mo after instituting the CSTD, however, contamination was still present on the surface of the BSC, but other areas with previous evidence of contamination showed no evidence of contamination at the 9 mo time frame. Janssens et al. also showed evidence of platinum contamination in six veterinary oncology centers and all of them had contamination on the surface of the workbench where drug was prepared, among other locations. In that study, surfaces were sampled at one time point and one of two types of drug transfer devices were used at the veterinary oncology centers, although information on which transfer device was used at the individual sites was not available. The specific PPE used in both of the aforementioned veterinary studies was not stated.

According to the 2004 NIOSH guidelines for handling hazardous drugs, a CSTD is “a drug transfer device that mechanically prohibits the transfer of environmental contaminants into the system and the escape of hazardous drug or vapor concentrations outside of the system.” Multiple devices are commercially available, however, only two systems fit the specific definition contained within the 2004 NIOSH guidelines. Both of these systems have dry connections and a mechanism by which they prevent air leakage into the environment during drug transfer. The drug transfer device used in the current study does not have a specific mechanism by which air leakage is prevented.

In the present study, we chose to evaluate for platinum contamination due to the frequency in which carboplatin was prescribed at our institution and also due to practicality in that evaluation for surface contamination of platinum was commercially available. The analytic method by which platinum was measured in the current study was stripping voltammetry. Other analytic methods described for measuring platinum include high-performance liquid chromatography and inductively coupled plasma mass spectrometry (ICP-MS). When considering the previously reported veterinary studies, stripping voltammetry and ICP-MS have been the methods used. Previously reported limit of quantification of platinum measurements for these two methods are 0.1 pg/cm² for voltammetry and 0.05 pg/cm² for ICP-MS. Given these two comparisons, the measurement in the present study may be an underestimation of actual contamination.

Evaluation for platinum contamination was measured at only one point in time in the present study. To the authors’ knowledge, duration of platinum contamination has not previously been determined. The BSC and areas evaluated in the current study are dedicated for clinical use. Platinum agents would not have been handled within the hood that were not administered to clinical patients and, therefore, accounted for in the overall carboplatin amount dispensed and then administered within the oncology treatment area. In the previous veterinary study using similar analytic methods, platinum contamination was measured before and 3, 6, and 9 mo after the institution of a CSTD. During this time period there was reduction in the amount of platinum contamination.
detected and two sites became negative for platinum contamination in the span of 3 mo suggesting that the duration of platinum contamination is less than 3 mo.23

Conclusion
Based on the evidence of contamination found in this evaluation and the two other veterinary studies, it is necessary that dedicated areas for cytotoxic drug preparation, preferably in a class II, Type B2 BSC, be available in veterinary clinics providing chemotherapy services. Additionally, PPE and CSTD should be utilized and strict guidelines for preparation, administration, and disposal must be in place to minimize the potential for spreading of surface contamination throughout the veterinary hospital and limiting exposure to cytotoxic agents by veterinary personnel. One can also not disregard the risk of exposure with contact of contaminated excrement, including urine and feces, in veterinary patients who have received cytotoxic agents. While the amount of exposure necessary to cause adverse effects is unknown, due to the known genotoxic nature of these medications, no amount of exposure should be considered safe, particularly with the risk of repeated, long-term exposure by veterinary healthcare personnel. 

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FOOTNOTES

a Exposure Control B.V.; Wageningen, The Netherlands
b OnGuard Closed Medication System with Tevadaptor Components; B. Braun, Bethlehem, Pennsylvania
c PhaSeal; Becton, Dickinson and Company, Franklin Lakes, New Jersey
d EquaShield; EquaShield, LLC, Port Washington, New York

REFERENCES


