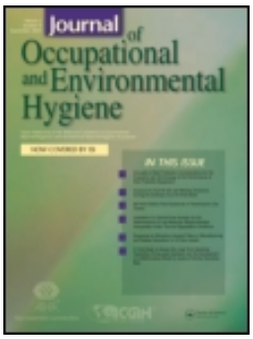

Journal of Occupational and Environmental Hygiene

ISSN: 1545-9624 (Print) 1545-9632 (Online) Journal homepage: www.tandfonline.com/journals/uoeh20

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To cite this article: Derry Stover & Chandran Achutan (2011) Case Study, Journal of Occupational and Environmental Hygiene, 8:1, D1-D6, DOI: 10.1080/15459624.2011.537510

To link to this article: https://doi.org/10.1080/15459624.2011.537510

Published online: 05 Feb 2011.

Journal of Occupational and Environmental Hygiene, 8: D1–D6
ISSN: 1545-9624 print / 1545-9632 online

DOI: 10.1080/15459624.2011.537510

Case Study
Occupational Exposures to Antineoplastic Drugs in an Oncology-Hematology Department

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INTRODUCTION

Approximately 100 antineoplastic drugs are used for the treatment of cancer and other diseases. Commonly referred to as chemotherapy drugs, antineoplastics act by preventing or inhibiting the growth of neoplasms. However, due to the nonselective nature of these agents, noncancerous cells can also be affected. In vitro and in vivo studies demonstrate that antineoplastic drugs possess mutagenic, teratogenic, and carcinogenic properties.[1,2]

Because cytotoxic and genotoxic effects are associated with these drugs, significant risks exist for health care workers who handle antineoplastics. Occupational risks associated with antineoplastic drug exposures were identified in the 1970s by the observation of an increase in sister chromatic exchanges in nurses who handle antineoplastic drugs.[3] Since then, several studies using environmental sampling and biomonitoring suggest health care workers are occupationally exposed to antineoplastic agents.[4–7]

The National Institute of Occupational Safety and Health (NIOSH) has compiled several case studies that suggest both acute and long-term health effects due to antineoplastic drug exposures.[8] Pharmacy staff who prepare antineoplastics and nursing staff who handle or administer these drugs to patients have reported acute effects, such as hair loss, irritation, hypersensitivity, and headaches after reported skin contact.[9] Negative reproductive health outcomes are also associated with antineoplastic exposure.[10–12]

NIOSH and the Occupational Safety and Health Administration (OSHA) have developed guidelines to protect nursing staff against antineoplastic drug exposure. These include (1) the use of two protective gloves and gowns when preparing, administering, or handling waste or excreta containing antineoplastic agents, (2) training for all employees who are involved in their use upon start of employment, and (3) continuing education on how to handle hazardous drugs.[8,13]

Adhering to OSHA and NIOSH guidelines and wearing appropriate personal protective equipment (PPE) can reduce exposures to antineoplastic drugs.[14,15] Physical, psychological, and workplace-related barriers can all affect health care workers' compliance with these recommendations; therefore, evaluating health care workers' use of these measures is an important research objective.[16] Despite its significance, only a limited number of studies have addressed this subject.

The purpose of this study was to evaluate the occupational risks of antineoplastic drug exposure in a hospital oncology-hematology department and to document compliance with the NIOSH guidelines. Study results can provide a means of education to help change employees' attitudes and modify unsafe behaviors. Recommendations are made to help reduce the risk of exposure.

METHODS

Nursing Staff Survey

A questionnaire was administered to nurses, nursing aides, and nursing technicians working in a hospital oncology and hematology department. The questionnaire was administered on 4 days at the beginning of the morning and night shifts. Fifty employees participated. The questionnaire, which was previously reviewed by a hospital research coordinator for content, measured self-reported demographic information, perceptions of chemotherapy exposures, level of training, and personal protective equipment (PPE) use.

Demographic variables included in the survey were age, gender, education, job type, hours working per week, and start date of employment. The frequency of handling 21 antineoplastic drugs was measured by asking nursing staff if they handled or administered the drug at least once a day, at least once a week, at least once a month, sporadically, or never. Nursing staff also rated their individual concerns and their perceived concerns of supervisors and co-workers regarding exposures to antineoplastic drugs. Nursing personnel were also asked if they were certified to administer chemotherapy and what type, if any, training they have received on how to handle chemotherapy drugs.

The use of PPE and other exposure reduction measures such as gloves, gowns, and hand washing was determined by asking nursing staff if they always, usually, seldom, or never engaged in the activity when working with chemotherapy drugs or handling waste containing chemotherapy agents.

Wipe Sampling

Wipe sampling was conducted to measure levels of cyclophosphamide, methotrexate, and cytarabine on contaminated surfaces with human activity. Surfaces were wiped using previously described methods.[17,18] Sampling was performed on 1 day, and a total of 13 samples were collected on flat and irregular-shaped surfaces. Two patient rooms were selected for sampling and were reserved for testing after the patients receiving chemotherapy were discharged. Several surfaces in these two rooms, Room A and Room B, were wiped, and these surfaces are shown in Figure 1.

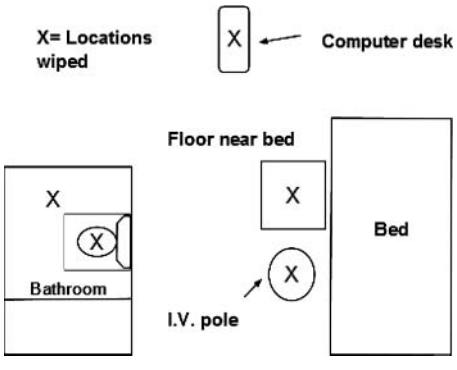

FIGURE 1. Wipe sample locations in patient rooms

In patient rooms, samples were collected on the floor next to the patient bed, intravenous (I.V.) pole apparatus, computer station, chemotherapy waste bin, bathroom floor, and toilet. We also collected samples at two nursing workstations and on the outer plastic bag used for delivery of a cytarabine infusion.

Wipe samples were collected using 3 × 3-inch sterile gauze pads (Type VII, Medline Industries Inc., Mundelein, Ill.) wetted with sodium hydroxide (0.03 M). For flat surfaces such as floors, 20 mL was deposited on a 70 × 70-cm area, and the section was wiped in a raster pattern using two gauze pads. Both pads were sealed in a plastic conical tube. For irregular surfaces, such as the I.V. pole and computer stations, the process was split into two 10-mL samples, both of which were combined in the same container. A blank sample was prepared by depositing 20 mL on gauze and sealing it in a plastic conical tube. All 13 samples and the field blank were stored at –20°C and shipped on ice to a laboratory for quantification of cyclophosphamide, methotrexate, and cytarabine.

Statistical Analysis

Statistical analysis was performed using SPSS (version 16.0, SPSS Inc., Chicago, Ill.). Due to small sample size, frequencies of handling specific antineoplastic drugs were collapsed into two groups that were handling at least monthly and more frequently than monthly. Pearson's chi-squared tests were conducted to determine associations between variables, such as length of employment, amount of training, and use of PPE.

RESULTS

Nursing Staff Survey

We obtained a response rate of 70.4% (N = 50) of nursing staff who completed the questionnaire. Table I summarizes the respondents' use of PPE and other protective measures. The majority of the nursing staff were female (n = 45), 21 to 30 years old (n = 29), and who had a 4-year college degree (n = 36). Forty of the respondents were nurses, while 10 reported working as nurses' aide or nursing technician. The mean length of employment in the department was 3.66 years.

Only antineoplastic drug administration was performed by nursing staff, and no antineoplastics were prepared in the department. Among nursing staff who handled antineoplastic agents, the most commonly handled drugs, in order, were cytarabine, cyclophosphamide, etoposide, methotrexate, and ifosfamide. More than 65% of the nursing staff reported handling these drugs at least once a month.

Out of the 50 respondents, 46% of the nursing staff reported being certified through the hospital to administer chemotherapy, while 82% reported receiving training on how to handle chemotherapy drugs safely. Nursing staff answered questions relating to concerns of occupational antineoplastic exposures

TABLE I. Employees' Use of PPE and Other Protective Measures

When handling chemotherapy or waste containing chemotherapy, how often do you?	Percentage of Responses	
	Seldom or Never	Usually or Always
Wear at least one type of glove	4	96
Wash hands after handling chemotherapy or waste containing chemotherapy	13	87
Wear chemotherapy-resistant gown	14	86
Wear gloves when removing drugs from bag	31	69
Wear two pairs of chemotherapy-resistant gloves	51	49
Reuse chemotherapy-resistant gown	81	19
Wear any type of mask	97	3
Wear safety glasses	97	3

using a scale of 1 to 5, with 1 being "not at all" and 5 being "very." When asked about their individual concerns of exposure, the median answer was 3. The median rating when nursing staff rated their supervisor's concern was 4, while the median of perceived co-workers' concerns was 3.

Several questions pertained to the use of PPE and other exposure reduction measures when handling antineoplastic drugs or waste containing these agents. Questionnaire results are summarized in Table I. Some respondents did not answer these questions. Overall, approximately 96% of nurses wear at least one type of chemotherapy-resistant glove when handling antineoplastic drugs. Forty-nine percent of nursing staff reported wearing double chemotherapy-resistant gloves usually or always, while 51% responded seldom or never.

When removing antineoplastic drugs from the outer plastic delivery bag, 69% of nursing staff reported wearing gloves either usually or always. Chemotherapy-resistant gowns are worn usually or always in 86% of respondents, and 18.9% of nursing staff reported reusing their gowns. Less than 3% of nursing staff reported usually or always wearing surgical masks, N95 respirators, or safety glasses. Hand washing after handling antineoplastic drugs or waste containing these agents was reported in 87% of nursing personnel. We did not find a significant association between amount of training and the use of PPE. There was also no significant association between individual concerns of exposure and use of PPE.

Wipe Sampling

Results of the wipe samples are summarized in Table II. Detectable amounts of antineoplastic drugs were found on 7 of the 13 samples. In positive samples, only one antineoplastic agent was detected. Cytarabine was not detected in any sample.

Only methotrexate was detected on surfaces in Room A, which included the bedside floor, I.V. pole apparatus, bathroom floor, and toilet. In Room B, only cyclophosphamide was detected in wipe samples of the bedside floor, I.V. pole apparatus, and toilet. Antineoplastic drugs were not detected on surfaces of computer stations inside the patient rooms and a chemotherapy waste bin. Cytarabine, cyclophosphamide, and methotrexate were not detected on surfaces outside the patient rooms.

DISCUSSION

Nearly all nursing staff handles antineoplastic drugs or waste containing these drugs on a daily or weekly basis, and thus, the potential for exposure is high. The cytotoxic and genotoxic drugs cytarabine, cyclophosphamide, etoposide, and methotrexate were handled most frequently. Although overall cumulative exposures are likely to be low because most nurses are young and had worked in the department for only a few years, every effort should be taken to prevent unnecessary exposures to these carcinogenic agents.

Work practices such as PPE use and hand washing can reduce antineoplastic exposures, and guidelines for best practice are recommended by organizations including OSHA, NIOSH, the American Society of Health-System Pharmacists, and the Oncology Nursing Society.[8,13,19,20] Our results reveal that most nursing staff take many precautions during antineoplastic drug administration, as evidenced by the high percentage of staff (96%) who wear at least one type of chemotherapy-resistant glove when handling these drugs. This finding is similar to previous studies indicating glove use to be between 82–94%.[9,21–23]

Although double gloving and chemotherapy -resistant glove use is recommended by OSHA and NIOSH, few studies have measured the rates of double gloving and chemotherapy-resistant glove use. Eisenberg[16] reports that a survey of 678 oncology nurses found less than 15% of the nurses usually wore two pairs of gloves.[16] Although the percentage of respondents who said they wear two pairs of gloves was higher in our study, nearly half are not in compliance with recommended guidelines.

Past studies have found gown use to be between 21% and 31%.[21–23] The use of chemotherapy-resistant gowns by the nursing staff was higher than previous studies, as 86% reported using chemotherapy-resistant gowns usually or always. Our results indicate more than 10% of nursing staff do not usually or always wash their hands after handling these drugs. Since wipe sampling conducted in this study inside patient rooms indicated surfaces are contaminated with antineoplastic drugs, the risk for dermal exposures for these employees is high.

TABLE II. Contamination of Antineoplastic Drugs on Various Surfaces

		Level of Contamination[A]			
		Cyclophosphamide		Methotrexate	
Workplace	Location of Sampled Surface	ng/cm^2	ng/sample	ng/cm^2	ng/sample
Room A	Bedside floor	ND		6.12	
	I.V. pump apparatus		ND		92000
	Computer station		ND		ND
	Chemotherapy waste bin		ND		ND
	Bathroom floor	ND		1.33	
	Toilet		ND		800
Room B	Bedside floor	0.07		ND	
	I.V. pump apparatus		200		ND
	Computer station		ND		ND
	Toilet		740		ND
Nurse's station	Computer station North		ND		ND
	Computer station South		ND		ND
	Outer plastic transport bag		ND		ND

Note: Reporting limits: cyclophosphamide = 100 ng/sample; methotrexate = 20 ng/sample.
[A]Cytarabine not detected in any sample.

Several surfaces inside patient rooms were contaminated with antineoplastic agents, and these results are similar to previous studies.[18,24–26] Concentration of methotrexate on the I.V. pump in one patient room was significantly higher than the concentration of cyclophosphamide on the I.V. pump in the other room, although the sampling technique was identical on both I.V. pumps. One possible explanation is that the patient may have contaminated the I.V. pump while in the bathroom, or spillage may have occurred during the administration of the I.V. The presence of only methotrexate in Room A and only cyclophosphamide in Room B may indicate that these surfaces were recently contaminated during the patient's treatment. We were informed by the nursing staff that a patient in Room B had recently received cyclophosphamide and cytarabine, but studies show that cyclophosphamide can persist on surfaces even after extended periods of time.[27]

No antineoplastic drugs were detected on surfaces of computers in the patient rooms or at computer stations (computer keyboard, mouse, phone, and countertop) outside the patient room. These negative findings, combined with survey data indicating that glove use, gown use, and hand washing were high, suggest that nursing staff in the department reduce cross-contaminating surfaces that are commonly touched, thereby reducing the potential for dermal exposures. In personal conversations, some nursing staff personnel expressed concern over potential exposures when removing antineoplastic products from their outer bag. While only one bag was wiped and antineoplastic products themselves were not wiped, the lack of measurable amounts on the outer bag may suggest that the outer bag is free from contamination. Nevertheless, several studies have shown contamination on the outside of drug vials and packages received from the pharmacy.[28–30] Storage bins for the I.V. bags should be sampled to determine the extent of outer bag contamination.

Measurable amounts of antineoplastics on bedside floors and I.V. pole apparatus suggest that spillage or leakage may occur when nurses administer these drugs, consistent with previous studies.[18,31] The hospital's hazardous drug policy states that OSHA-recommended drug administration protocols, PPE, and administrative controls are required to reduce exposures during administration. Many of these measures are already being followed by nursing staff; however, our results indicate that surface contamination is still an issue.

The presence of these agents on bathroom surfaces also suggests that patients' excreta are a significant source of surface contamination. While disposing of urine in the toilet, the possibility for splashing, spraying, and droplet aerosolization exists. Previous research suggests that exposures via excreta are larger than previously thought.[31] Exposures can result due to direct dermal contact from splashing, indirect dermal contact from surface cross-contamination, and inhalation of droplets containing antineoplastic agents. Less than 3% of nursing staff reported wearing masks, respirators, or safety glasses; therefore, there is a risk for exposure in bathroom-related or excreta-disposal work activities.

Some nursing aides and nursing technicians did not answer questions related to drug handling or PPE use because they stated they did not directly administer the drug to the patient. This observation suggests that some nursing aides or nursing technicians are unaware of the exposure risks due to

patients' excreta handling. In the survey's comment section, some nurses expressed concern over exposures when dumping excreta but stated there was no way to reduce these exposures, suggesting that either (1) some nurses are unaware of the recommended PPE, (2) they do not have access to these PPE in their work environment, or (3) they do not know where to find these PPE.

This study is only one of few to measure nursing staff compliance with OSHA and NIOSH guidelines during antineoplastic drug handling. Our study is novel for the level of detail in our questionnaire data, especially the use of double gloving and chemotherapy-resistant gloves. In addition, our findings add further evidence to the literature that surfaces in hospital oncology departments are frequently contaminated with antineoplastic drugs and that nursing staff face occupational risks via dermal exposure. Findings from this study were communicated to the nursing staff and their supervisors in a written report as well as an oral presentation as a means to educate them on ways to reduce exposure.

CONCLUSION

Most employees in this study took several protective measures when handling antineoplastic agents, thereby reducing their risk for exposures. The use of any type of glove, double gloves, and gowns were higher than previous studies, suggesting a trend of increasing adherence to guidelines. However, many nurses were not in compliance with all recommended measures, such as donning chemotherapy-resistant gloves and gowns, and hand washing. Therefore, an increased risk for exposures exists in these workers. Several surfaces inside patient rooms were contaminated with antineoplastic drugs, further supporting an increased risk for dermal exposures and further stressing the importance of adhering to antineoplastic handling guidelines issued by OSHA and NIOSH.

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