Assessment of the Occupational Dermal Exposure Potential of British Columbian Healthcare Workers to Antineoplastic Drugs

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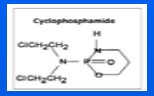
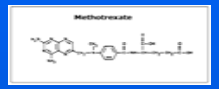
Background

Antineoplastic drugs are routinely used for the treatment of cancer. However, despite the use of control measures, numerous studies have found antineoplastic drug contamination of work areas in healthcare facilities. Such widespread surface contamination makes the potential for skin contact highly probable, which is significant since dermal absorption has been deemed the main route of exposure. Occupational exposure to these drug products has been reported to cause a variety of health effects including liver toxicity, adverse reproductive outcomes as well as cancer.

This pilot study aimed to assess the potential dermal exposure risk in six hospitals with pharmacies throughout the Metro Vancouver region that regularly handle and prepare antineoplastic drugs. To our knowledge, this is the first evaluation of antineoplastic surface and dermal contamination to be conducted in British Columbian hospitals. This study focused on methotrexate (MTX) and cyclophosphamide (CP) – two of the most commonly used antineoplastic drugs. These two agents served as markers of drug contamination.





Objectives

The main objectives of this study were:

1) To identify surfaces/objects that pharmacy workers contact and the frequency of such contact, and
2) Evaluate the occupational dermal exposure risk to antineoplastic agents due to contact with potentially drug-contaminated surfaces/objects.

Methods

Observational review

A member of the research team observed three pharmacy workers per facility, each for at least 90 minutes, to ascertain the specific location of the touched surfaces and the associated frequency of contact. An observational checklist was used to document findings.

Hand wipe samples

Ethics approval was obtained prior to collection of any personal samples. Four pharmacy workers from each of the six facilities were asked to participate in the study – one of whom was responsible for preparing the antineoplastic drugs and three who were not involved in preparation but worked in the pharmacy department. This resulted in a total of 24 hand wipe samples. Each worker that was approached was provided with an overview of the study and then asked to sign a consent form before sample collection. Potential subjects were selected by random convenience sampling. Subjects wearing gloves were asked to remove the barriers prior to collecting the hand wipe.

The sample collection method was a modified version of the protocol developed by Sabatini et al [2005][1]. Briefly, this involves wiping the top and bottom of both of the worker's hands with a Kimwipe™ that was pre-moistened with 0.75 mL of 0.1M ammonium acetate solution. The Kimwipe™ was then placed in a 20 mL vial which was subsequently labeled and kept cold.

Sample analyses

All collected samples were transported to the Laboratory Division of The School of Environmental Health at The University of British Columbia on the day of sampling. The samples were then transferred from the portable cooler and stored in a –20°C freezer until analysis. Samples were analyzed by high-performance liquid chromatography (HPLC) tandem mass spectrometry (MS/MS) and was based on an analytical method developed by Sabatini et al [2005]. Our limit of detection for MTX and CP was 0.90 ng and 1.43 ng, respectively.

[1] Sabatini L, Barbieri A, Tosi M, Violante FS (2005). A new high-performance liquid chromatographic/electrospray ionization tandem mass spectrometric method for the simultaneous determination of cyclophosphamide, methotrexate and 5-fluorouracil as makers of surface contamination for occupational exposure monitoring. *J. Mass Spectrom.* 40: 669-674.

Results & Discussion

Table I : The most frequently contacted surfaces/objects at each site

Surfaces/Objects Contacted	Site A	Site B	Site C	Site D	Site E	Site F
Cytotoxic waste lid	N/A	N/A	N/A	N/A	5	2
Pen inside biological safety cabinet	5	6	1	12	15	14
Hooks inside biological safety cabinet	N/A	N/A	N/A	1	N/A	5
Handle (door or cabinet)	3	N/A	4	1	7	10
Tray	4	2	4	4	N/A	3
Biological safety cabinet counter	7	3	6	N/A	8	2
Scissors	N/A	3	N/A	N/A	3	N/A

N/A = Not Applicable

Table II: Methotrexate (MTX) and Cyclophosphamide (CP) contamination levels detected on the hands of pharmacy workers

Site	Worker #1*		Worker #2		Worker #3		Worker #4	
	MTX (ng)	CP (ng)	MTX (ng)	CP (ng)	MTX (ng)	CP (ng)	MTX (ng)	CP (ng)
A	-	-	-	-	-	-	-	-
B	0.247	-	0.124	-	-	-	0.082	-
C	-	-	-	-	-	-	-	-
D	-	3.96	-	-	-	3.54	-	-
E	-	2.02	-	-	-	-	-	1.57
F	-	2.39	-	-	-	1.98	-	2.72

- = could note be detected with confidence

** Where 1 = Pharmacy technician preparing the drugs (direct exposure)*
2 = Pharmacist who checks the prepared drugs (indirect exposure)
3 = Technician#1 who did not handle drugs (indirect exposure)
4 = Technician #2 who did not handle drugs (indirect exposure)

Our study suggests that the objects/surfaces contacted in the pharmacy department vary from site to site. The most common were the pen, handles and the biological safety cabinet counter. Drug contamination of the hands of pharmacy workers was detected - even if the staff member was not responsible for preparing the drug products. Overall, this indicates that antineoplastic drug contamination of the pharmacy department is likely in British Columbian hospitals. As such, there is a need to explore the degree and spread of drug contamination within a hospital further as well as to evaluate any possible drug uptake (body burden) amongst exposed workers.

Questions for Future Studies

- What other areas of the hospital are contaminated with antineoplastic drugs?
- What is the amount of antineoplastic drug contamination within a hospital?
- Which other healthcare occupations are at risk of dermal exposure to antineoplastic drugs?
- What factors or determinants lead to an increased or decreased risk of exposure? e.g. individual, environmental and organizational factors
- Does a relationship exist between dermal contamination levels and body burden levels?

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