Biological monitoring of four antineoplasic drugs among Canadian healthcare workers in two hospitals

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BACKGROUND

- There is a growing number of hazardous drugs used in healthcare settings. Antineoplastic drugs are part of the group 1 of the hazardous drugs, as classified by the National Institute for Occupational Safety and Health. Adverse effects of these drugs have been documented in exposed healthcare workers.
- Studies have been conducted to measure urinary excretion of antineoplastic agents and their metabolites.

OBJECTIVES

The aim of this study was to assess the feasibility of the biological monitoring of four antineoplastic drugs in two adult oncology centers: cyclophosphamide, ifosfamide, methotrexate and 5-fluorouracile.

MATERIAL AND METHODS

- Exposed workers were recruited from two Canadian teaching hospitals oncology departments: center A (450 beds, 30 oncology stretchers, 30 inpatient beds) and center B (530 beds, 30 oncology stretchers, 25 inpatient beds).
- Both oncology clinics had dedicated satellite pharmacy equipped with three IIB2 hoods for hazardous drugs preparations.
- No closed-system drug transfer devices were used.
- Before the study, an information period was offered during which we aimed at enhancing the workers' awareness and knowledge of the risk of occupational exposure. Two presentations were offered: one for the pharmacy staff and one for the nurses.

POPULATION
- **3 occupational categories : nurses, pharmacists, pharmacy technicians**
- Voluntary participation and consent required
- Inclusion criteria:
  - Working at least 3 consecutive days or 5 non-consecutive days in a 10-day period
  - Not being in contact with any of the four antineoplastic drugs outside the workplace

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- Each participant filled out a journal about:
  - Demographic informations
  - **Activities** performed during the 5 days prior to sampling
  - **Personal protective equipment** worn during these activities

URINE SAMPLE
- One urine sample per participant provided at the end of the working shift
- Analyzed for the presence of cyclophosphamide (limit of detection 9.0 pg/mL), ifosfamide (9.7), methotrexate (75) and alpha-fluoro-beta-alanine (120) (5-fluorouracile's main urinary metabolite)
- Quantified by positive electrospray MRM by ultra-performance liquid chromatography tandem mass spectrometry technology

RESULTS
- Descriptive statistics were performed
- Anonymized and global results were provided to participants.
- No individual results were provided.

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RESULTS

POPULATION

- Samples were collected between January 17th, 2017 and February 1st, 2017 for center A and between June 5th, 2017 and June 23rd, 2017 for center B.

Table I Demography

Variables		Participants working in center A (n=28)	Participants working in center B (n=28)
Occupational categories	Nurses	13	11
	Pharmacists	9	8
	Pharmacy technicians	6	9
Sex	Women	26	25
	Men	2	3
Age	20-29 years	2	4
	30-39 years	11	10
	40-49 years	10	10
	≥ 50 years	5	4
Experience in oncology In years (average±SD)	Nurses	3.2 ± 2.7	5.1 ±5.9
	Pharmacists	8.6 ± 5.0	9.1 ± 8.5
	Pharmacy technicians	5.4 ± 4.2	9.1 ± 6.2

URINE SAMPLES

- None of the samples analyzed (0/56) had detectable concentrations of any of the four drugs evaluated.

ACTIVITIES

- In the five days before sampling, 51/56 (91.0%) participants performed at least one activity with one of the four antineoplastic drugs.
- No accidental exposure was reported during the study.

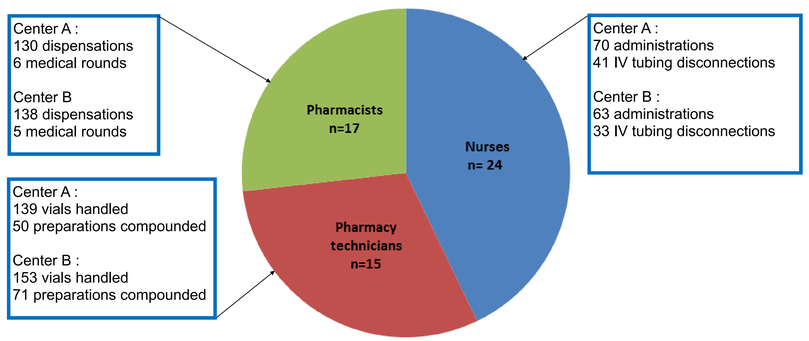

Figure 1 Activities performed during the five days before sampling

PERSONAL PROTECTIVE EQUIPMENTS

- Nurses wore the complete recommended protection for technical activities (Center A = 72.6%, Center B = 54%), but incomplete for non technical activities (Center A et B = 0 %).

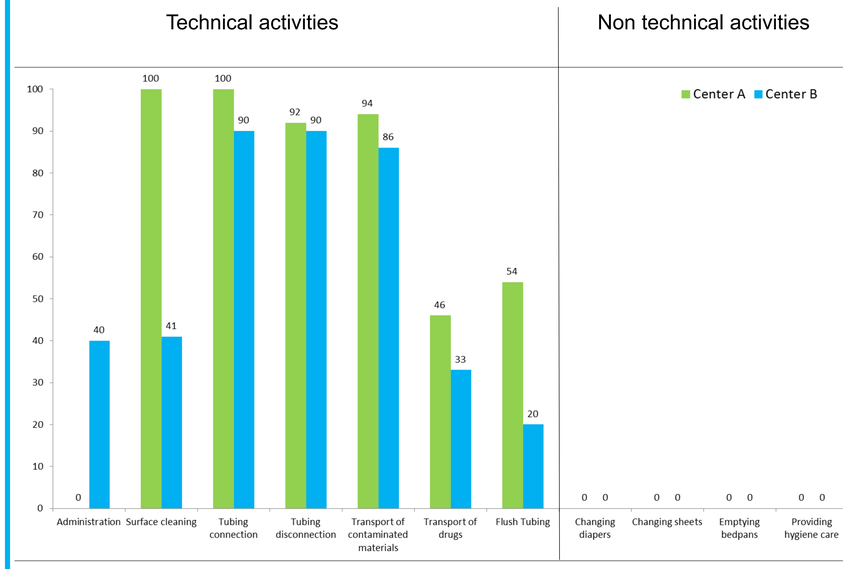

Figure 2 Proportion of nurses wearing complete protective equipment for technical and non technical activities

- All pharmacists and pharmacy technicians wore all of the recommended protection for all activities for the center A.
- Four pharmacists (50%) and two pharmacy technicians (22.2%) wore all of the recommended protection for all activities for the center B.

DISCUSSION/CONCLUSIONS

- We were able to implement a study of biological monitoring in two adults oncology centers.
- No urine sample had detectable concentrations in nurses, pharmacists and pharmacy technicians.
- The absence of positive samples did not allow us to identify activities that were associated with exposure.
- The personal protective equipments were efficient to avoid biological intake of these four drugs. However, it could be enhanced, especially for nurses during drugs administration and during non technical activities.
- Repeated biological monitoring of hazardous drugs in urine may contribue to increase workers' awareness of risk exposure to hazardous drugs. Optimal frequency for such surveillance remains to be determined.