Multicenter Study of Environmental Contamination With Antineoplastic Drugs in 51 Canadian Hospitals

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Introduction

- Healthcare workers are exposed to hazardous drugs.

  → This occupational exposure can lead to adverse health effects. No health-based exposure limit is known.

- According to the 2014 NIOSH list, there are 184 hazardous drugs (97/184 are antineoplastic drugs).
- 2014: A new guideline from the Ordre des Pharmaciens du Québec recommends environmental monitoring twice per year, for sterile compounding.
- Since 2008: our group has performed 3 multicenter studies of environmental contamination with antineoplastics in Quebec hospitals.

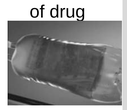
Objectives

- To describe environmental contamination of cyclophosphamide (CP), ifosfamide (IF) and methotrexate (MTX) in Canadian hospitals.
- To describe trends over the years since 2008.

Methods

- Descriptive, comparative study.
- Head of pharmacy departments from hospitals with >50 acute care beds contacted:
  - on December 20th, 2013 for Quebec hospitals (n=58);
  - on January 10th, 2014 for other Canadian provinces (n=137).
- 12 standardized sampling sites (surface of 600 cm²) were collected in Feb-Sep 2014 (at the end of the day, before cleaning).

Tab I Sampling sites

Pharmacy areas					
Reception counter	Storage shelf	Front grille inside the hood	Floor in front of the hood	Service hatch	Tray for drug delivery
					
Patient care areas					
Storage shelf	Counter for priming	Arm rest	Patient room counter	Outpatient clinic counter	Outer surface of drug
					

Working pratices

- Centers were asked if:
  - They removed the outer packaging of drugs after receipt;
  - They cleaned the vials after receipt;
  - They used a closed-system transfer device (CSTD).

Analytical procedure

- Samples were analyzed for the presence of the antineoplastics by UPLC-MS-MS.

Table II. Limits of detection (LOD) and limits of quantification (LOQ)

	LOD (pg/cm²)	LOQ (pg/cm²)
Cyclophosphamide (CP)	0.36	1.2
Ifosfamide (IF)	0.95	3.2
Methotrexate (MTX)	0.97	3.3

Comparison

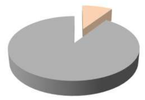
- A comparison of surface contamination between centers that participated in the 4 studies (2008-2010, 2012, 2013 and 2014) was made.
- Kolmogorov-Smirnov test for two unpaired samples was used for working practices.

Results

Surface contamination with antineoplastics

- 34/58 hospitals from Quebec participated (response rate 59%).
- 17/137 centers from 5 other Canadian provinces participated (response rate 12%).

Tab.III Global 2014 results

Cyclophosphamide	Ifosfamide	Methotrexate
Proportion of positive samples		
50% (294/584)	21% (125/584)	9% (54/584)
		
75th percentile of drug concentration		
10.8 pg/cm²	1.59 pg/cm²	Lower than the LOD

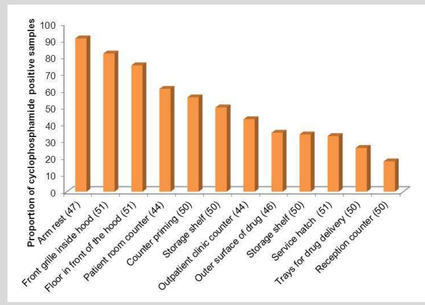


Fig.1 Proportion of positive sampling sites for cyclophosphamide

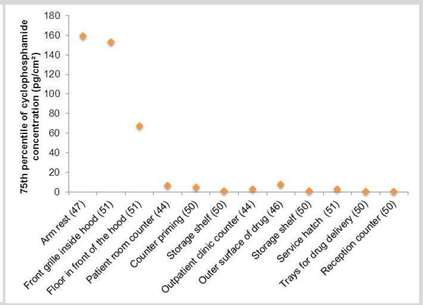
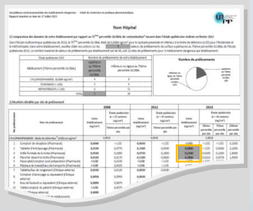


Fig.2 75th percentile of cyclophosphamide concentration

Personnalized report

- Each center received a personnalized report which included their hospital's results, and a comparison with global results.
  - The **75th percentile** was set as a **target**, and each sampling site with a higher concentration was highlited, and should be targeted for corrective measures.



Impact of working practices

- Centers who used CSTDs, removed the outer packaging of vials or cleaned vials after receipt had a lower 75th percentile of CP concentration (not significant).

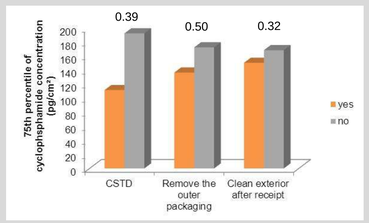


Fig.3 75th percentile of cyclophosphamide concentration on the front grille of the hood

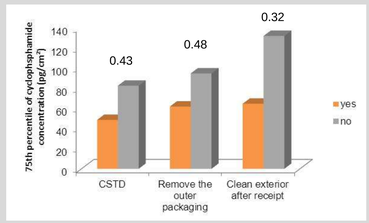
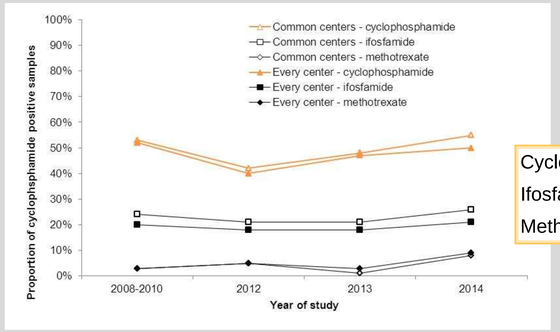


Fig.4 75th percentile of cyclophosphamide concentration on the floor in front of the hood

Trend 2008-2014

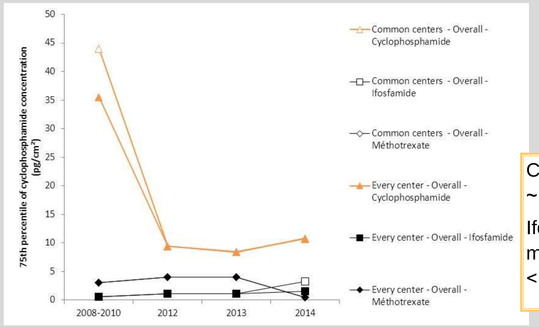
- 19 centers participated in the 4 studies (common centers).
  - Similar results were obtained with common centers and all centers.
- The proportion of antineoplastic positive sites remained constant over the years.



Cyclophosphamide: ~50%
Ifosfamide : ~20%
Methotrexate: ~5%

Fig.5 Proportion of positive samples over the years

- The concentration of cyclophosphamide have been reducing over the years
  - Reached a plateau in 2012
- Concentration of ifosfamide and methotrexate on surfaces remained low



Cyclophosphamide: ~10pg/cm²
Ifosfamide and methotrexate: < 1pg/cm²

Fig.6 75th percentile of cyclophosphamide concentration over the years

Discussion / Conclusions

- The most contaminated sites were: front grille of the hood, armrest, floor in front of the hood.
- The 75th percentile CP concentrations decreased over the years: a plateau was observed since 2012.
- CP is a good marker to evaluate surface contamination with antineoplastic.
- **Local and attainable goals** for surface contamination with hazardous drugs should be set **annually**, as long as no health-based limit is known.
- For Canadian hospitals, we set the value of the annual **global 75th percentile** as a **manageable target**.

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