Multicenter study of environmental contamination with nine antineoplastic drugs in 93 Canadian centers : a 2019 follow-up study

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Background

- Antineoplastic drugs traces are measured on many surfaces in healthcare centers.
- A biannual surveillance of antineoplastic traces is recommended in Canadian guidelines.

Objectives

- To monitor environmental contamination by nine antineoplastic drugs in Canadian oncology pharmacies and outpatient clinics
- To explore the impact of factors that may be associated with surface contamination.

Methods

- 12 standardized sites (600 cm²) sampled per center
  - 6 in oncology pharmacy
  - 6 in outpatient clinic
- Sampling performed after a working day before any cleaning
- Analysis conducted by the Institut National de Santé Publique du Québec (INSPQ) by ultra-performance liquid chromatography-tandem mass spectrometry technology (UPLC-MS/MS)
  - 6 drugs quantified: cyclophosphamide, ifosfamide, methotrexate, gemcitabine, 5-fluorouracil, irinotecan
  - 3 drugs detected, but not quantified : docetaxel, paclitaxel, vinorelbine
- Limits of detection (LOD) were, in ng/cm²: cyclophosphamide (0.001); docetaxel (0.090); 5-fluorouracile (0.040); gemcitabine (0.004); ifosfamide (0.006); irinotecan (0.003); methotrexate (0.002); paclitaxel (0.040) and vinorelbine (0.004)
- Descriptive analyses were conducted
- The impact of some factors was evaluated with a Kolmogorov-Smirnov test for independent samples

Results

- 93 centers in 5 provinces (Quebec, Ontario, New Brunswick, Manitoba, Nova Scotia) participated
- 44.4% (464/1045) sites positive to at least one antineoplastic drug (Table I)
- The 3 most contaminated sites were: front grid inside the hood, the floor in front of the hood and the arm rest (Table I)
- The 3 most frequent drugs measured were the most used: cyclophosphamide (mean 281 g used/year), gemcitabine (336 g) and 5-fluororouracile (1 885 g).

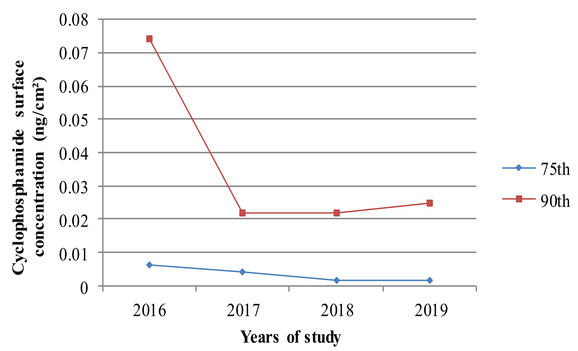
Table I Contamination per sampling site

Sample site (n sample)	Positives to at least one antineoplastic drug n (%)	Cyclophosphamide concentration (ng/cm²)	
		75th perc.	90th perc.
Pharmacy areas			
Front grid inside the hood (n=92)	75 (81.5%)	0.0308	0.2530
Floor in front of the hood (n=92)	60 (65.2%)	0.0110	0.0890
Storage shelf (n=92)	51 (55.4%)	0.0017	0.0062
Trays used for drug delivery (n=92)	31 (33.7%)	<0.0010	0.0046
Service hatch or counter for post-preparation validation (n=92)	27 (29.3%)	<0.0010	0.0111
Shipment reception counter (n=91)	18 (19.8%)	<0.0010	0.0014
Sub-total (Pharmacy areas) (n=551)	**262 (47.5%)**	**0.0017**	**0.0216**
Patient care areas			
Patient treatment chair arm rest (n=91)	69 (75.8%)	0.0280	0.0852
Exterior surface of antineoplastic drug container (n=82)	29 (35.4%)	<0.0010	0.2160
Counter used for priming or validation (n=87)	29 (33.3%)	<0.0010	0.0021
Patient room counter (n=69)	29 (42.0%)	0.0017	0.0092
Outpatient clinic counter (n=79)	23 (29.1%)	<0.0010	0.0017
Storage shelf (n=86)	23 (26.7%)	<0.0010	0.0041
Sub-total (patient care areas) (n=494)	**202 (40.9%)**	**0.0017**	**0.0220**
Total (pharmacy & patient care areas) (n=1045)	**464 (44.4%)**	**0.0017**	**0.0214**

LOD: limit of detection, perc.: percentile

- 53 centers participated in the environmental monitoring studies since 2016
- For these centers, the 90th percentile of cyclophosphamide concentration measured on surfaces has decreased overtime while the 75th remained stable (Figure 1)

Figure 1 Cyclophosphamide surface contamination over the years for 53 centres that participated in the environmental monitoring studies since 2016



- 5 variables were associated with higher cyclophosphamide contamination (Table II). These variables were mainly related to the size of the center and the quantity of drugs used.

Table II Impact of factors that may explain cyclophosphamide contamination

Factors (n samples)	Distribution of cyclophosphamide concentration (ng/cm²)		Difference between groups
	75th perc.	90th perc.	P value
Participation in the last 4 studies (since 2016)			0.644
Yes	0.0017	0.0248	
No	0.0017	0.0195	
Size of oncology outpatient clinics - inpatient beds			<0.0001
<15 (n=751)	0.0017	0.0170	
≥15 (n=277)	0.0073	0.0834	
Size of oncology outpatient clinics - stretchers/chairs/beds			<0.0001
<15 (n=624)	0.0017	0.0170	
≥15 (n=414)	0.0053	0.0405	
Antineoplastic drug preparations/year			<0.0001
<4000 (n=417)	<0.0010	0.0114	
≥4000 (n=490)	0.0044	0.0288	
Cyclophosphamide usage/year (g)			<0.0001
<250 (n=471)	<0.0010	0.0078	
≥250 (n=553)	0.0058	0.0494	
Removal of outer packaging after receipt			1.000
Removal (n=838)	0.0017	0.0200	
No removal (n=207)	0.0017	0.0234	
Cleaning of vials after receipt			0.858
Cleaning (n=826)	0.0017	0.0200	
No cleaning (n=219)	0.0036	0.0310	
Closed-system drug transfer device (CSTD) use for cyclophosphamide			0.136
Use (n=473)	0.0017	0.0126	
No use (n=572)	0.0037	0.0267	
Priming of antineoplastic IV tubing in oncology pharmacy			0.288
In outpatient clinic unit (for ≥90% of preparations) (n=269)	0.0040	0.0640	
In oncology pharmacy (for ≥90% of preparations) (n=752)	0.0017	0.0180	

- While four preventive measures (e.g. removal of outer packaging after receipt, cleaning of vials after receipt, use of CSTDs, priming of IV tubing in oncology pharmacy) are not associated with less contamination of antineoplastic drugs in this study, each hospital should consider each measure for its feasibility, its costs and its potential impacts.
- Cleaning with sodium hypochlorite solution was not associated with less contamination than other products used.

Conclusion

- Some working surfaces were frequently contaminated despite the implementation of safe handling guidelines. The use of personal protective equipment remains essential.
- The same 3 sites are systematically the most contaminated year after year.
- Environmental monitoring can help centers to monitor their practices and identify contaminated areas.

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