Multicenter study of environmental contamination with ten antineoplastic drugs in 79 Canadian centers: a 2018 follow-up study

Hilliquin D[1], Tanguay C[1], Gagné S[2], Caron N[2], Bussières JF[1,3]

[1] Unité de Recherche en Pratique Pharmaceutique, Département de pharmacie, CHU Sainte-Justine, Montréal, Québec, Canada [2] Centre de Toxicologie du Québec, Institut national de santé publique du Québec, Québec, Québec, Canada, [3] Faculté de pharmacie, Université de Montréal, Montréal, Québec, Canada

Background

- Exposure to antineoplastic drugs put healthcare workers at risks of adverse health effects (mutagenic, teratogenic, etc).
- Environmental surveillance is recommended at least once a year.
- Our research group has been conducting an annual monitoring of surface contamination in Canadian healthcare centers since 2008.

Objectives

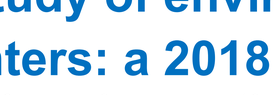
- To monitor environmental contamination with nine antineoplastic drugs in Canadian oncology pharmacy and patient care areas.
- To explore the impact of factors that may explain contamination.

Methods

12 standardized sites (600 cm^2) sampled per center in Jan-Apr 2018:

6 in the pharmacy

6 in patient care areas



Two sampling sites examples are shown (front grille of the hood and arm rest)

Analysis conducted by the Institut National de Santé Publique du Québec by ultra-performance liquid chromatography-tandem mass spectrometry technology

Sampling tubes are shown

6 drugs were quantified: cyclophosphamide, 5-fluorouracile, gemcitabine, ifosfamide, irinotecan, methotrexate

3 drugs were detected, but not quantified (present or absent): docetaxel, paclitaxel, vinorelbine

Descriptive analyses were done

Sub analyses were performed according to working practices and cyclophosphamide contamination (Kolmogorov-Smirnov test for independent samples).

Limits of detection (LOD) were, in ng/cm^2:

cyclophosphamide (0.001); cytarabine (0.040); 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).

Contact : jf.bussieres@ssss.gouv.qc.ca

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Results

79 Centers in 4 provinces (Quebec, Ontario, New Brunswick, Manitoba) participated

45% (397/887) sites positive to at least one antineoplastic drug (Tab I)

The three most contaminated sites were: front grille inside the hood, the floor in front of the hood and the arm rest (Tab I)

The majority of centers used sodium hypoclhorite once a month for cleaning the front grille inside the hood, but other cleaning practices were highly variable

The three most frequent drugs measured were the most used: cyclophosphamide (mean 251 g used/year), gemcitabine (302 g and 5-fluororouracile (1,756 g).

Tab I Contamination per sampling site

Sample sites (n samples)	Positive samples n (%)	Concentration (ng/cm²) 75th perc.	90th perc.
Pharmacy areas			
Front grid inside the hood (78)	63 (80.8%)	0.022	0.19
Floor in front of the hood (78)	47 (60.3%)	0.015	0.11
Storage shelf (78)	48 (61.5%)	0.0042	0.015
Trays used for drug delivery (78)	24 (30.8%)	<LOD	0.0017
Service hatch or preparation validation counter (78)	22 (28.2%)	<LOD	0.019
Shipment reception counter (77)	15 (19.5%)	<LOD	<LOD
Total - pharmacy areas (467)	**219 (46.9%)**	**0.0034**	**0.020**
Patient care areas			
Arm rest (76)	60 (78.9%)	0.030	0.098
Counter used for priming or validation (68)	29 (42.6%)	0.0014	0.032
Exterior surface of container (e.g. bag/syringe) (75)	24 (32.0%)	<LOD	0.0017
Patient room counter (58)	25 (43.1%)	0.0017	0.018
Outpatient clinic counter (71)	20 (28.2%)	<LOD	0.0017
Storage shelf (72)	20 (27.8%)	<LOD	0.0017
Total - patient care areas (420)	**178 (42.4%)**	**0.0017**	**0.022**
Total - pharmacy & patient care areas (887)	**397 (44.8%)**	**0.0017**	**0.021**

LOD: limit of detection, perc.: percentile

. 15 centres participed in all the environmental monitoring studies since 2008-2010

. For these centers, the 75th percentile of cyclophosphamide concentration measured on surfaces is decreasing (Fig 1)

. A similar trend is observed with the data from all participating centers (data not shown)

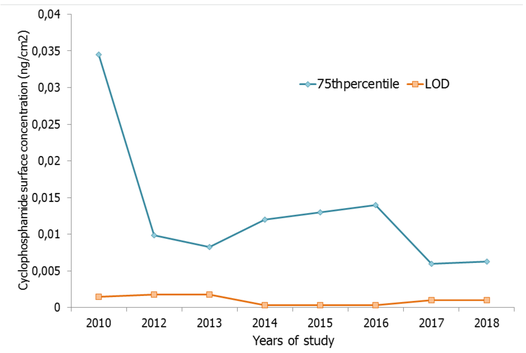

Fig 1 Cyclophosphamide surface contamination over the years for 15 centres that participated in all monitoring studies

Six variables were associated with higher cyclophosphamide contamination (Tab II). They were mostly related to the size of the center and the quantity of drugs used.

Tab II Impact of factors that may explain cyclophosphamide contamination

Comparisons (n samples)	Distribution of cyclophosphamide concentration (ng/cm²) 75th perc.	90th perc.	Difference between groups P value
Participation in multicenter studies			0.010
Participation in 8 studies (n=176)	0.0063	0.028	
Participation in 1-7 studies (n=711)	0.0017	0.020	
Size of oncology clinics - inpatient beds			<0.0001
<15 (n=633)	0.0017	0.016	
≥15 (n=243)	0.0085	0.039	
Size of oncology clinics - outpatient stretchers/chairs/beds			<0.0001
<15 (n=528)	0.0017	0.013	
≥15 (n=348)	0.0068	0.034	
Antineoplastic drugs preparations/year			<0.0001
<4000 (n=345)	<LOD	0.0058	
≥4000 (n=460)	0.0046	0.028	
Cyclophosphamide usage/year (g)			<0.0001
<250 (n=417)	<LOD	0.0099	
≥250 (n=460)	0.0060	0.031	
Removal of outer packaging after receipt			0.314
Removal (n=770)	0.0017	0.020	
No removal (n=117)	0.0078	0.031	
Cleaning of vials after receipt			0.025
Cleaning (n=723)	0.0017	0.016	
No cleaning (n=164)	0.0084	0.044	
Use of closed-system drug transfer devices			0.025
For ≥ 90% of preparations (n=191)	0.0017	0.015	
For 0-90% of preparations (including no use) (n=684)	0.0029	0.023	
Priming of antineoplastic IV tubing			0.998
In healthcare unit (for ≥90% of preparations) (n=198)	0.0037	0.019	
In pharmacy (for ≥90% of preparations) (n=666)	0.0017	0.021	

Discussion / Conclusion

- The same three sites are systematically the most contaminated year after year; they are sites that are frequently exposed to the drugs and they might be harder to clean
  - To note, sampling was performed before any surface was cleaned, so a certain amount of traces is expected
- Even if the proportion of surfaces contaminated by antineoplastic drugs have decreased over the years, the remaining traces are hard to eradicate
- Large centers had higher concentrations of cyclophosphamide on their surfaces
- The use of personnal protective equipment remains indisputable
- Performing an annual monitoring is a good indicator to monitor trends over time and to benchmark a center in relation with other Canadian centers