

Monitoring campaign for professional exposure to cytostatics

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Introduction

Used in the treatment of cancer, cytostatic drugs have an intrinsic toxicity which can expose the personnel in charge of these drugs, at a very low level but potentially throughout a professional career.

INRS study (1) :

53% of staff participating in the reconstitution of cytostatic drugs had their urine positive for at least one of the following molecules : cyclophosphamide, ifosfamide, methotrexate and alpha-fluoro-beta-alanine (metabolite of the 5-fluorouracil : 5-FU).

85% of the tested surfaces (external sides of bottles and pockets, workplans, doors handles, telephones, etc.) were positive to cyclophosphamides and 5-FU.

INRS study (2) :

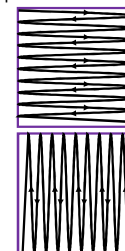
Professional exposure to cytostatic is correlated with the chemotherapy preparation activity.

Materials and methods

The Val d'Ariège Hospital performs 7.000 preparations per year, under isolator. An evaluation of cleaning/decontamination procedures is essential. Thus, it was decided to follow two drugs among the most used which will serve as exposure tracers : 5-FU and platinum-based chemotherapeutic agents (carboplatin, cisplatin and oxaliplatin). Exposure evaluation to these drugs will be assessed by measuring elemental platinum (Pt). 5-FU and platinum-based chemotherapeutic agents are not very volatile and reconstitution process are not very dispersive, searching for these molecules on surface samples is more relevant than on atmospheric samples.

Samples : after two mornings of preparation (25 preparation/d whose 6 5-FU and 4 platinum-based chemotherapeutic agents)

- Kimtech wipes
- Area : 10cm * 10cm (except gloves and handles : completely wiped) – cf. figure opposite)
- Change of the sampler gloves between each sample (no cross contamination)
- Areas selected are the most likely to be contaminated (isolators, exit airlocks, workplans, refrigerators, sheets, transport cases, offices, preparer gloves, doors and door handles)



Assays : analysis were performed by Toxilabo laboratory specialist in chemical risk assessment for companies. For each drug, one wipe is needed. Deadline for reporting results <15d.

Pt : inductively coupled plasma (ICP) and mass spectrometry (MS)
LOQ : 2.5 ng (\leftrightarrow 250 ng/m²).

5-FU : high performance liquid chromatography (HPLC) with ultraviolet detection (UV).
LOQ : 10 ng (formerly 20 ng at the time of the study ; \leftrightarrow 2.0 µg/m²).

Results

55 wipes for 28 areas (no search for Pt on an area).

Area	Pt (ng/m ²)	5-FU (µg/m ²)
49/55 areas	< 250	< 2.0
Workplan isolator*	251	18.3
Exit airlock, left side	288	17.1
Exit airlock, right side	1015	35.9

* Positive control (sampling from the work area before decontamination).

Discussion

Results have shown that the method used (samples and assays) allows to identify the presence of these molecules. Airlock and isolator are positive and the most used, which confirmed that the risk is correlated with the activity. Moreover, these areas are considered to sensitive point of contamination because they correspond to the work area and the exit of the pockets not overwrapped. Other samples are under the LOQ for each molecule, which lead to the conclusion that the decontamination procedures are satisfactory whether at the level of the pharmacy or at the entire circuit (treatment room, patient room, etc.). Otherwise the protective measures seems appropriate, including : the installation of zip pockets for the over-packaging of preparations for dispensing to services; wearing single-use over-gloves changed each time to catch the preparations in the airlock; the frequently cleaning of specific transport cases, raising the awareness of all staff involved (pharmacy, caregivers, nurses, storekeepers, etc.) by the health service and ourselves; they help prevent the spread of potential contamination. The exit airlock cleaning protocol must be changed to improve results at this level.

This monitoring campaign is intended to be repeated each year to verify that the new cleaning procedures are respected and adapted. Samples are also considered in the event of dispersive incident (e.g. break of pocket) to validate that the decontamination allows resumption of work on the exposed areas.

Finally, the benefit of biomonitoring should also be considered, as it is complementary to these surface exposure measurements. Indeed, the assay of these molecules, or of a metabolite in the urine of employees (for which there are biological reference values) would make it possible to conclude individually on the effectiveness of the protective measures.