Rapport de veille n° 55

Surveillance biologique de l'exposition professionnelle aux médicaments cytotoxiques. Etude de terrain.

1er mai 2022 – 30 juin 2022

Objectifs : Disposer d'une connaissance actualisée du sujet en accompagnement des demandes d'assistance qui découlent de la valorisation de l'étude sur la surveillance biologique de l'exposition aux médicaments cytotoxiques en milieu hospitalier.

La validation des informations fournies (exactitude, fiabilité, pertinence par rapport aux principes de prévention, etc.) est du ressort des auteurs des articles signalés dans la veille. Les informations ne sont pas le reflet de la position de l'INRS.

Les liens mentionnés dans le bulletin donnent accès aux documents sous réserve d'un abonnement à la ressource.

- ***Articles de périodique (PREPRINT)***

Benoist H., Busson A., Faveyrial A., Bouhier-Leporrier K., Divanon F., Breuil C., Roger-Leenaert S., Palix A., Odou P., Simon N., Saint-Lorant G.
Perception, knowledge, and handling practice regarding the risk of exposure to antineoplastic drugs in oncology day hospitalization units and compounding unit staff.
Journal of Oncology Pharmacy Practice, 29 mai 2022

Résumé : *BACKGROUND: Antineoplastic drug exposure is a major problem in regard to caregivers' health. The aim of the present study was to assess the perception, knowledge, and handling practices of all occupation level categories of two oncology day hospitalization units and two compounding units regarding the risk of exposure to antineoplastic drugs. METHODS: This descriptive study, performed through face-to-face interviews, concurrently assessed the perception, knowledge, and handling practices of antineoplastic drugs in five different job categories in four different settings. This work was part of a larger comprehensive project examining surface and blood contamination. Different scores were assigned to evaluate responses to a questionnaire about the perception, knowledge, and handling practices of healthcare workers, a risk global score including a risk perception score, and education/knowledge and handling practices scores. RESULTS: In the survey, continuous training was associated with the global risk score ($p = 0.03$), particularly with the handling practices risk score ($p = 0.01$). Job category was also significantly associated with the global risk score ($p < 0.001$), particularly with the handling practices risk score ($p < 0.001$) and the education/knowledge score ($p < 0.001$). Pharmacy technicians had the highest score regarding risk perception (71.4%), indicating a higher perception of risk, and had a lower score regarding handling practices (25.0%) as well as a lower score (15.7%) regarding risk knowledge. Nurses and physicians had a high score (50%) regarding the risk of handling practices and a score of 57.1% regarding risk perception, indicating an increased perception of safety. Auxiliary caregivers had the highest global score (43.5%) and a score of 30.0% regarding handling practices. CONCLUSIONS: This study identified significant differences among healthcare workers depending on job categories in the antineoplastic drug handling practices and in the knowledge of the risks associated with occupational exposure to antineoplastic drugs. These differences were particularly important between trained and untrained participants, revealing the importance of implementing a continuous training program.*

https://doi.org/10.1177/10781552221103803

Gonzalo N., Rey M., Fontanals S., Quer N., Clopes A., Munoz C.
Simultaneous determination of five cytotoxic drugs in surface wiped samples using liquid chromatography and tandem mass spectrometry for the control of environmental contamination in a comprehensive cancer centre.
International Journal of Environmental Analytical Chemistry, 22 mai 2022

Résumé : *The most common strategy to assess the occupational exposure risk to hazardous drugs in cancer healthcare settings is by monitoring environmental contamination of work surfaces with cytotoxic drugs. Healthcare workers, especially pharmacy technicians and nursing, handle multiple hazardous drugs, so they really may be exposed to different cytotoxic drugs simultaneously. Therefore, simultaneous determination of several cytotoxic drugs provides a more accurate assessment of the real occupational exposure risk in healthcare settings. Our objective was to develop a method for surface wipe sampling and a quantification method for five cytotoxic drugs commonly used in chemotherapy treatments preparation: cyclophosphamide, 5-fluorouracil, epirubicin, gemcitabine and paclitaxel. Wiping*

procedure was performed using cellulose swabs moistened in a mixture solution containing acetonitrile, water, 2-propanol and methanol with 0.1% formic acid. The obtained extracts were simultaneously quantified by an LC-MS/MS method. Chromatographic separation was achieved using an Acquity UPLC (R) BEH C18 column by a gradient elution, and detection was carried out in multiple reaction monitoring mode with electrospray source operating in positive and negative ion mode. Wipe and extraction procedures developed were simple and easy to implement, being able to recover the cytotoxic target drugs from two type surfaces sampling, stainless steel surfaces and polyethylene bags surfaces. The analytical method was linear over the calibration range and the limits of quantification were 1 ng/mL for cyclophosphamide, gemcitabine and paclitaxel, 1.5 ng/mL for epirubicin and 5 ng/mL for 5-fluorouracil. Intra- and inter-day precision and accuracy for all drugs were always inferior to 15%. This work provides a suitable procedure to identify cytotoxic contamination on work surfaces, being a useful tool to monitor occupational exposure risk to hazardous drugs, as well as to evaluate the effectiveness of decontamination protocols applied and hazardous drug handling protocols in cancer healthcare settings.

https://doi.org/10.1080/03067319.2022.2070013

Acramel A., Fouque J., Blondeel-Gomes S., Huguet S., Rezai K., Madar O., Escalup L.
Application of an Environmental Monitoring to Assess the Practices and Control the Risk of Occupational Exposure to Cyclophosphamide in Two Sites of a French Comprehensive Cancer Center.
Annals of work exposures and health, 21 mai 2022

Résumé : *OBJECTIVES: The risk of chronic exposure to antineoplastic agents in hospitals, mainly by skin contact with contaminated surfaces, is well established. The aim of this study was to assess indirectly the risk of occupational exposure to antineoplastics drugs at two hospitals by using an environmental monitoring, and to suggest ways of improving the exposure to healthcare workers. METHODS: An observational study of care practices on both sites was carried out. A wipe sampling campaign was then designed to study environmental contamination throughout the chemotherapy process: receipt, storage, compounding, transport, administration, and elimination areas. Samples were analyzed by a validated LC-MS/MS method allowing trace quantification of cyclophosphamide. A guidance 'safe value' of 0.10 ng/cm2 was considered. RESULTS: A total of 293 samples were analyzed, of which 58% were found to be positive. In the compounding units, the drug vials were contaminated before [range = (non-quantifiable [NQ]-0.71) ng/cm2] and after cleaning procedure [(NQ-0.62) ng/cm2], particularly when the flip-off lid was removed during cleaning. The contamination found on manual preparations was operator-dependent: [non-detectable (ND)-3.51] ng/cm2 on infusion bag surfaces; (780.61-24 698.98) ng/cm2 on medication ports. In the case of automated preparations, the average contamination was higher on infusion bag surfaces [(2.43-36.86) ng/cm2] and lower on medication ports [(0.43-7.65) ng/cm2] than manual preparations. Contamination of the analytical control area was also highlighted. In the daily care unit, the contamination was located near the infusion area (armchairs, infusion stands, floor, and patient toilets), and varied somewhat between the two sites, especially on the floor with (0.46-27.32) compared to (ND-0.18) ng/cm2. We did not detect contamination on the transport boxes, on the door handles or in the disposal areas. CONCLUSIONS: The variability of contamination observed between the two sites can be explained in part by the difference in routine practices, especially training of the staff, and cleaning procedures. Findings were communicated to healthcare workers, and news interventions were implemented based on wipe sampling results. This study demonstrated a method for routine environmental monitoring and worker education as a strategy to reduce occupational exposure.*

https://doi.org/10.1093/annweh/wxac035

- ***Articles de périodique***

Tang Y., Che X., Wang Y.L., Ye X., Cao W.L., Wang Y.
Evaluation of Closed System Transfer Devices in Preventing Chemotherapy Agents Contamination During Compounding Process-A Single and Comparative Study in China.
Frontiers in Public Health, Volume 10, 18 avril 2022, Page 827835

Résumé: *AIM: We performed a comparative study to investigate the efficacy of closed system transfer devices (CSTDs) on the safe handling of injectable hazardous drugs (HDs). METHODS: The exposure assessments of cyclophosphamide and cytarabine were performed under traditional or CSTDs. For preparation activity, chemotherapy contamination samples on protective equipment (such as gloves and masks) were collected. The contamination analysis was performed by liquid chromatography with tandem mass spectrometry (LC-MS/MS). A 6-item form was distributed monthly (form M1-M6, total 6 months) to assess the pharmacists' experience on ergonomics, encumbrance, and safety impression. RESULTS: Totally, 96 wiping samples were collected throughout the study. The numbers of contaminated cyclophosphamide samples reduced under CSTD were -37.8, -41.6, -67.7, -47.3, and -22.9% and cytarabine were -12.3, -12.1, -20.6, -69.6, and -56.7% for left countertop, right countertop, medial glass, air-intake vent and door handle, as compared to traditional devices. The reduction was similar to pharmacist devices, i.e., -48.2 and -50.0% for masks and gloves cyclophosphamide contamination, -18.0 and -42.4% for cytarabine. This novel system could improve contamination on dispensing table, transfer container, and dispensing basket by -16.6, -6.0, and -22.3% for cyclophosphamide and -28.5, -22.5, and -46.2% for cytarabine. A high level of satisfaction was consistently associated with ergonomics for CSTD during the compounding process. Meanwhile, a slightly decreased satisfaction on ergonomics, encumbrance, and safety impression was observed for the traditional system between M2 and M3. CONCLUSION: Closed system transfer devices are offering progressively more effective alternatives to traditional ones and consequently decrease chemotherapy exposure risk on isolator surfaces.*

https://doi.org/10.3389/fpubh.2022.827835

Huang X., Gao C., Cai W., Tao Y., Zhong X., Liu H., Hong X., Ding X., Lu H., Lai W., Yi X. & Gu Y.
(Préprint dans Bulletin n° 52)
Effect of Occupational Exposure to Antineoplastic Drugs on DNA Damage in Nurses: A Cross-Sectional Study.
Occupational and Environmental Medicine, Volume 79, Numéro 4, Avril 2022, Page 253-258

Résumé : *Background : Although the therapeutic effect of antineoplastic drugs is incontestable, these agents can also potentially act as carcinogens, mutagens and/or teratogens in people. The aim of this study was to assess the effect of occupational exposure to antineoplastic drugs on DNA damage, assessed by the comet assay and cytokinesis-block micronucleus (CBMN) assay, in nurses. Methods : The cross-sectional study enrolled 305 nursing staff members from 7 public hospitals in Shenzhen who handled antineoplastic drugs, and 150 healthy nursing staff members who were not exposed to antineoplastic drugs as the control group. DNA damage was assessed by the comet and CBMN assay. Multiple linear regressions and logistic regressions models were used to analyse the effect of occupational exposure to antineoplastic drugs on DNA damage. Results : After adjustment for confounding factors, compared with non-exposure to antineoplastic drugs, exposure to antineoplastic drugs was positively related to tail moment, olive moment, tail length and tail DNA per cent, and adjusted β or OR (95% CI) was 0.17 (0.08 to 0.26), 0.18 (0.10 to 0.27), 1.03 (0.47 to 1.60) and 1.16 (1.04 to 1.29) (all p<0.05). Moreover, similar*

significant relationships were observed for the biomarkers of the CBMN assay. Additionally, other than age, there was no interaction between antineoplastic drug exposure and other variables for the levels of biomarkers of the CBMN assay and the comet assay. Conclusions : The present results showed that exposure to antineoplastic drugs was positively related to the risk of DNA damage in nurses. The results imply that occupational exposure to antineoplastic agents is an important global public health problem that requires urgent attention.

http://dx.doi.org/10.1136/oemed-2021-107913.

Verscheure E., Creta M., Vanneste D., Vanoirbeek J., Zakia M., Abdesselam T., Lebegge R., Poels K., Ghosh M., Duca R. C., Godderis, L.
Quantification of three antineoplastic agents in urine using the UniSpray ionisation source.
Journal of Chromatography B, Volume 1205, 1er août 2022, Article 123331

Résumé : *BACKGROUND: Many guidelines and safety measures led to a decrease in exposure to antineoplastic agents. Since healthcare workers are often exposed to lower concentrations than patients, a sensitive method is needed to quantify occupational exposure. OBJECTIVE: The aim of this study was to develop and validate a sensitive method for simultaneous detection and quantification of cyclophosphamide, ifosfamide and paclitaxel in urine by use of UPLC-MS/MS with a UniSpray ionisation source. METHODS: Compounds were extracted from urine using Novum simplified liquid extraction cartridges, separated on a C18 column, ionised by a UniSpray ionisation source and detected with MS/MS. In the second part of the study, a field study was performed to assess occupational exposure to antineoplastic agents. RESULTS: Eighty-three samples from healthcare workers were analysed and resulted in seventeen samples containing quantifiable concentrations of at least one compound. In conclusion, a sensitive method for simultaneous detection and quantification of cyclophosphamide (LLOQ 0.05 ng/mL), ifosfamide (LLOQ 0.3 ng/mL) and paclitaxel (LLOQ 0.7 ng/mL) was developed and validated.*

https://doi.org/10.1016/j.jchromb.2022.123331