Rapport de veille n° 46

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

1er novembre 2020 – 31 décembre 2020

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)***

Palamini M., Floutier M., Gagné S., Caron N., Bussières J.F.
Evaluation of decontamination efficacy of four antineoplastics (ifosfamide, 5-fluorouracil, irinotecan, and methotrexate) after deliberate contamination.
Journal of Occupational and Environmental Hygiene, 26 décembre 2020

Résumé : *The main objective was to determine the decontamination efficacy of quaternary ammonium, 0.1% sodium hypochlorite, and water after deliberate contamination with four antineoplastics (ifosfamide, 5-fluorouracil, irinotecan, methotrexate). A stainless-steel surface was deliberately contaminated with ifosfamide (15 µg), 5-fluorouracil (10 µg), irinotecan (1 µg), and methotrexate (1 µg). First, a single decontamination step with either water, quaternary ammonium, or 0.1% sodium hypochlorite was tested. Then, the effect of up to four successive decontamination steps with either quaternary ammonium or 0.1% sodium hypochlorite was tested. Commercial wipes consisting of two layers of non-woven microfibers with an inner layer of highly absorbent viscose fibers were used. Triplicate surface samples were obtained and tested by ultra-performance liquid chromatography tandem mass spectrometry. The limits of detection were 0.004 ng/cm^2 for ifosfamide, 0.040 ng/cm^2 for 5-fluorouracil, 0.003 ng/cm^2 for irinotecan, and 0.002 ng/cm^2 for methotrexate. After a single decontamination step, the 0.1% sodium hypochlorite eliminated 100% of contamination with 5-fluorouracil, irinotecan, and methotrexate and 99.6 ± 0.5% of ifosfamide contamination. Quaternary ammonium and water also removed 100% of the 5-fluorouracil, and 99.5% to 99.9% of the other three antineoplastics. For ifosfamide, irinotecan, and methotrexate, the decontamination efficacy increased with successive decontamination steps with quaternary ammonium. 5-fluorouracil was undetectable after a single decontamination step. Methotrexate was the only drug for which decontamination efficacy was less than 100% after four decontamination steps. 100% decontamination efficacy was achieved from the decontamination step with 0.1% sodium hypochlorite for 5-fluorouracil, irinotecan, and methotrexate. For ifosfamide, 100% efficacy was achieved only after the third decontamination step. It was possible to make all traces of antineoplastic undetectable after deliberate contamination with 5-fluorouracil, irinotecan, and methotrexate with a 0.1% chlorine solution; up to three decontamination steps were needed to make ifosfamide undetectable. Water or quaternary ammonium removed more than 99.5% of deliberate contamination. In several scenarios, it was necessary to repeat the decontamination to eliminate residual traces. More work is needed to identify the optimal decontamination approach for all of the antineoplastic drugs used.*

https://doi.org/10.1080/15459624.2020.1854458

- ***Articles de périodique***

Claraz P., Riff I., Vert C., Wolff E., Perriat S., Grand A., Cretu Y., Hennebelle I., Canonge J.M., Puisset F.
Assessment of efficacy of postinfusion tubing flushing in reducing risk of cytotoxic contamination.
American Journal of Health-System Pharmacy, Volume 77, Numéro 22, 15 novembe 2020, Pages 1866-1873

Résumé : *Infusion of cytotoxic drugs carries the risk of occupational exposure of healthcare workers. Since disconnecting an infusion line is a source of contamination, flushing of tubing after infusion of cytotoxic agents is recommended, but the optimal volume of rinsing solution is unknown. The objective of this study*

was to assess whether postinfusion line flushing completely eliminates cytotoxics. METHODS: Infusions were simulated with 3 cytotoxics (gemcitabine, cytarabine, and paclitaxel) diluted in 5% dextrose injection or 0.9% sodium chloride injection in 250-mL infusion bags. Infusion lines were flushed using 5% dextrose injection or 0.9% sodium chloride solution at 2 different flow rates. The remaining concentration of cytotoxics in the infusion line was measured by a validated high-performance liquid chromatography (HPLC) method after passage of every 10 mL of flushing volume until a total of 100 mL had been flushed through. RESULTS: All cytotoxics remained detectable even after line flushing with 80 mL of flushing solution (a volume 3-fold greater than the dead space volume within the infusion set). Gemcitabine and cytarabine were still quantifiable via HPLC even after flushing with 100 mL of solution. Efficacy of flushing was influenced by the lipophilicity of drugs but not by either the flushing solvent used or the flushing flow rate. After 2-fold dead space volume flushing, the estimated amount of drug remaining in the infusion set was within 0.19% to 0.56% of the prescribed dose for all 3 cytotoxics evaluated. CONCLUSION: Complete elimination of cytotoxics from an infusion line is an unrealistic objective. Two-fold dead space volume flushing could be considered optimal in terms of administered dose but not from an environmental contamination point of view. Even when flushed, the infusion set should still be considered a source of cytotoxic contamination.

https://doi.org/10.1093/ajhp/zxaa357

Mucci N., Dugheri S., Farioli A., Garzaro G., Rapisarda V., Campagna M., Bonari A., Arcangeli G.
Occupational exposure to antineoplastic drugs in hospital environments: potential risk associated with contact with cyclophosphamide- and ifosfamide-contaminated surfaces.
Medycyna Pracy, Volume 71, Numéro 5, Août 2019, Pages 519-529

Résumé : *Cyclophosphamide (CP) and ifosfamide (IP) contaminations have been detected in hospital environments. This study was conducted to determine if there was any contamination in the spaces (floors and door handles) between the hospital exit and the antineoplastic drugs (ADs) preparation and administration units. At the same time, the authors proposed a new automation of the analytical procedure to considerably decrease the time needed for sample preparation and analysis. MATERIAL AND METHODS: To evaluate the ADs contamination of surfaces, 829 wipe tests were performed in a campaign involving 3 hospitals located in Italy. Sampling was performed using an innovative kit. The levels of ADs were measured in each wipe sample using liquid chromatography/triple quadrupole. RESULTS: On-line solid-phase extraction guarantees the construction of a robust and reproducible analytical method. The CP and IP recoveries from stainless steel, polycarbonate and polyvinyl chloride ranged >80%, and the wipe holders and the automation tested ensured desorption efficiencies close to 100% for both the ADs. Of the 552 wipes taken on the spaces between the hospital exit and the preparation, administration and pharmacy warehouse units, 22 were greater than or equal to the limit of quantification, all adjacent to the administration units. CONCLUSIONS: This study provides an insight into the exposure situation against ADs residues. In order to improve environmental monitoring programs, the authors propose to evaluate the ADs contamination also outside the preparation, administration and pharmacy warehouse units.*

https://doi.org/10.13075/mp.5893.00931

Hilliquin D., Tanguay C., Bussières J.F.
External contamination of commercial containers by antineoplastic agents: a literature review.
European Journal of Hospital Pharmacy, Volume 27, Numéro 5, septembre 2020, Pages 313-314

Résumé : *The aim of this study was to review the literature regarding the external contamination of commercial vials by antineoplastic drugs. A PubMed and CINAHL searches from 1 January 1990 to 1 May 2018 was performed with the terms: << antineoplastic agents >>, << environmental monitoring >>, << drug packaging >>, << vials >> and << contamination >>. Articles that presented results on the external contamination of commercial vials were included. Twenty-four articles were identified from 11 countries. A total of 4248 vials were sampled from 28 manufacturers. Traces were found on 56% (2379/4248) of vials. A maximum of 150 000 ng was measured on a glass vial of fluorouracil. This literature review showed that the exterior of the majority of commercial antineoplastic vials was contaminated. Manufacturers should limit this contamination. Centres are also encouraged to clean the vials on receipt. Personal protection equipment should be worn at all steps of the drug-use process.*

http://dx.doi.org/10.1136/ejhpharm-2018-001705

Hemingway M.W., Meleis L., Oliver J., Silvestri S.
A Protocol for the Safe Use of Hazardous Drugs in the OR.
AORN Journal**,** Volume 111, Numéro 3, avril 2020, Pages 289-300

Résumé : *Hazardous drug (HD) use in the perioperative environment poses unique challenges and risks for exposure that can have adverse consequences for perioperative personnel. The United States Pharmacopeial Convention has implemented new standards to address the safe handling and administration of HDs by health care workers. To comply with these standards and minimize perioperative personnel's occupational exposure to HDs, a multidisciplinary team at an academic medical center in Boston that was performing an increased number and variety of operative and other invasive procedures using antineoplastic agents updated their protocol for the safe use of HDs in the OR. This article discusses HDs and the risks they pose to health care workers and outlines the new HD safety protocol for the OR that was part of a performance improvement plan to ensure compliance with new standards and staff member safety in the perioperative setting.*

https://doi.org/10.1002/aorn.12960

Scarselli A., Corfiati M., Di Marzio D.; Iavicoli S.
Evaluating Antineoplastic Agents and Occupational Exposures Among Italian Workers Using SIREP Surveillance System.
Journal of Occupational and Environmental Medicine**,** Volume 61, Numéro 8, août 2019, Pages 669-675

Résumé : *The aim of the study is to evaluate exposures to antineoplastic agents at workplaces in healthcare and manufacturing in Italy. METHODS: Data on antineoplastic agents were collected from occupational exposure registries. Statistical analysis was carried out for exposure-related variables. The number of workers potentially exposed was estimated for selected industrial sectors. Concurrent exposures were investigated using cluster analysis. RESULTS: Overall 15,763 exposure situations were analyzed during 1996 to 2016. Most exposures occurred in healthcare (66%). A total of 11,830 workers potentially exposed to antineoplastic agents was estimated. Concurrent exposures were frequently detected in the pharmaceutical industry and among healthcare workers. CONCLUSIONS: Occupational exposure to antineoplastic agents currently represents a matter of concern both in the chemical industry and in the healthcare sector. The growing number of agents in use supports the need to constantly control exposures.*

10.1097/JOM.0000000000001641

- ***Références bibliographiques INRS-Biblio***

Labreche F., Ouellet C., Roberge B., Yennek A., et Coll.
Antinéoplasiques en milieu hospitalier. Etude pilote sur l'exposition potentielle du personnel d'hygiène et de salubrité.
Rapports scientifiques. R-1090, Institut de recherche Robert-Sauvé en santé et en sécurité du travail (IRSST), Montréal (Canada), 2020, 68 p., ill., bibliogr.

Résumé : *L'objectif principal de cette étude était d'évaluer l'exposition potentielle à des antinéoplasiques (ANP) couramment utilisés en mesurant la contamination des surfaces fréquemment touchées lors de tâches d'hygiène et de salubrité en milieu hospitalier. Les objectifs secondaires étaient d'explorer la faisabilité et l'acceptabilité par le personnel d'effectuer des frottis de leurs mains, et de valider l'analyse de sept ANP de plus que les trois pour lesquels une méthode d'analyse était disponible au Centre de toxicologie du Québec (CTQ). Deux centres hospitaliers (CH) de référence en cancérologie ont accepté de participer à l'étude. Le cyclophosphamide et la gemcitabine étaient le plus souvent identifiés, suivis par le 5-fluorouracile et l'irinotécan. Cette étude a estimé pour la première fois au Canada la contamination par les ANP des surfaces de travail manipulées par les travailleurs d'hygiène et de salubrité en milieu hospitalier. Elle met en évidence un potentiel important d'exposition. Bien que ne prouvant pas l'exposition ou l'absorption des ANP par ces travailleurs, les résultats remettent en question les pratiques de gestion de la manipulation des médicaments dangereux et ouvrent un éventail d'actions préventives à développer et de moyens à mettre en place. Il faut notamment mentionner la formation du personnel HS sur la manipulation des médicaments dangereux et une analyse des techniques et équipements de travail d'hygiène et de salubrité visant à optimiser la prévention de la contamination par des médicaments dangereux. Cette étude a permis de valider l'analyse de sept ANP supplémentaires tout en testant l'acceptabilité, pour le personnel, de déceler la contamination cutanée par des frottis des mains. Les résultats obtenus pourront orienter les activités de prévention de l'exposition aux médicaments dangereux dans le secteur de la santé.*