Bulletin de veille n° 65

1ee janvier 2024 – 29 février 2024

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

Objectif : *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 éléments issus de cette veille sont founis sans garantie d'exhaustivité.

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

Sessink P.J., Tans B., Spriet I., Devolder D.
Longitudinal evaluation of environmental contamination with hazardous drugs by surface wipe sampling.
Journal of Oncology Pharmacy Practice, décembre 2023

Résumé : *Introduction: Exposure of healthcare workers to hazardous drugs can lead to adverse health effects supporting the importance of a continuous monitoring program, for example, by taking surface wipe samples. The objective was to describe the results of repeated monitoring of contamination with hazardous drugs on multiple surfaces in a hospital pharmacy and at two wards using standardized preparation techniques and cleaning procedures. Methods: Twelve surfaces in the hospital pharmacy and at two wards were sampled and analyzed for contamination with the hazardous drugs cyclophosphamide, doxorubicin, 5-fluorouracil, gemcitabine, methotrexate, and paclitaxel. The drugs were prepared with a closed-system drug transfer device (CSTD). Sampling of the drugs was performed in four trials during eight months. Liquid chromatography tandem mass spectrometry was used for the analysis of the drugs. Results: During the four trials, contamination with five of the six hazardous drugs was found on half of the surfaces in the pharmacy and in a ward. Seventeen out of 288 possible outcomes were positive (6%), with the biological safety cabinet grate (n= 6) and scanner (n= 5) most frequently contaminated. The highest level of contamination was observed on the pass-thru window (cyclophosphamide: 2.90 ng/cm(2)) and the touch screen of the Diana device (5-fluorouracil: 2.38 ng/cm(2)). Both levels were below the action level of 10 ng/cm(2). Conclusions: The long-term use of a CSTD in combination with appropriate cleaning has proven effective in achieving low levels of surface contamination with hazardous drugs.*

https://doi.org/10.1177/10781552231205481

- ***Articles de périodique***

Abu-Alhaija D., Miller E., Shaughnessy E., Bakas T.
Psychometric Testing of the Oncology Nurses Health Behaviors Determinants Scale: A Cross-Sectional Study.
Seminars in Oncology Nursing, Volume 9, Numéro 6, décembre 2023, Article 151515

Résumé : *Objectives: Adherence by oncology nurses to chemotherapy safe handling guidelines is essential to prevent hazards of chemotherapy exposure. A review of the literature revealed the need for an instrument with evi-dence of reliability and validity to measure factors influencing adherence to safe chemotherapy-handling guidelines among oncology nurses. The purpose of this study was to psychometrically test the Oncology Nurses' Health Behaviors Determinants Scale (HBDS-ON) that measures the mentioned factors. Data Sources: Methodological research of a quantitative cross-sectional survey design was used. The study surveys were administered by email to a sample of 108 oncology nurses. Cronbach alpha, item analysis, exploratory factor analysis using principal axis factoring, and convergence validity testing were used to test reliability and validity.Conclusion: Factor analysis yielded six subscales, each having acceptable internal consistency reliability (Cronbach alpha between 0.70 and 0.88). The subscales included four oncology nurse health beliefs (per-ceived threat, benefits, barriers, and self-efficacy), cues to action, and personal protective equipment avail-ability and accessibility.*

Convergence validity testing results support the Oncology Nurses Health Behaviors Determinant Scale (HBDS-ON) construct validity. Oncology nurses' self-efficacy to adherence to chemother-apy-handling guidelines, the perceived barriers to adhere to chemotherapy-handling guidelines, and cues to action are associated with adherence to chemotherapy-handling guidelines. Implications for Nursing Practice: Oncology nurses' health beliefs, the cues to action, and personal protection equipment availability and accessibility are important determinants of nurses' adherence to chemotherapy -handling guidelines. The HBDS-ON is an instrument that has evidence of reliability and validity and could be used in practice to measure these determinants.

http://dx.doi.org/10.1016/j.soncn.2023.151515

Pinet E., Cirtiu C.M., Caron N., Bussières J.F., Tanguay C. (Préprint dans Bulletin n° 60)
Canadian monitoring program of the surface contamination with 11 antineoplastic drugs in 124 centers.
Journal of Oncology Pharmacy Practice, Volume 30, Numéro 1, janvier 2024, Page 19-29

Résumé *: INTRODUCTION: Occupational exposure to antineoplastic drugs can lead to long-term adverse effects on workers' health. A reproducible Canadian surface monitoring program was established in 2010. The objective was to describe contamination with 11 antineoplastic drugs measured on 12 surfaces among hospitals participating in this annual monitoring program. METHODS: Each hospital sampled six standardized sites in oncology pharmacies and six in outpatient clinics. Ultra-performance liquid chromatography coupled with tandem mass spectrometry was used for cyclophosphamide, docetaxel, doxorubicin, etoposide, 5-fluorouracil, gemcitabine, irinotecan, methotrexate, paclitaxel, and vinorelbine. Platinum-based drugs were analyzed by inductively coupled plasma mass spectrometry; this excludes inorganic platinum from the environment. Hospitals filled out an online questionnaire about their practices; a Kolmogorov-Smirnov test was used for some practices. RESULTS: One hundred and twenty-four Canadian hospitals participated. Cyclophosphamide (405/1445, 28%), gemcitabine (347/1445, 24%), and platinum (71/756, 9%) were the most frequent. The 90th percentile of surface concentration was 0.01 ng/cm² for cyclophosphamide and 0.003 ng/cm² for gemcitabine. Centers that prepared 5000 or more antineoplastic per year had higher concentrations of cyclophosphamide and gemcitabine on their surfaces ($p = 0.0001$). Almost half maintained a hazardous drugs committee (46/119, 39%), but this did not influence the cyclophosphamide contamination ($p = 0.051$). Hazardous drugs training was more frequent for oncology pharmacy and nursing staff than for hygiene and sanitation staff. CONCLUSIONS: This monitoring program allowed centers to benchmark their contamination with pragmatic contamination thresholds derived from the Canadian 90th percentiles. Regular participation and local hazardous drug committee involvement provide an opportunity to review practices, identify risk areas, and refresh training.*

https://doi.org/10.1177/10781552231167329

Karedal M., Ozdemir J., Tinnert A., Wetterling M., Hedmer M. (Préprint dans Bulletin n° 60)
Pilot study: External surface contamination of gemcitabine and 5-fluorouracil on drug packaging.
Journal of Oncology Pharmacy Practice, Volume 30, Numéro 1, janvier 2024, Page 9-14

Résumé *: INTRODUCTION: Antineoplastic drugs (ADs) are commonly used pharmaceuticals for anticancer treatments. It has previously been shown that the external surface of drug vials frequently is contaminated with ADs. More than a decade ago methods to prevent occupational exposure were*

introduced by using plastic coverage of the glass vials or packing vials in a secondary plastic container. The aim of the pilot study was to determine contamination levels of ADs on different parts of AD packaging of two different commercially available drug vials on the Swedish market and to investigate the occurrence of cross contamination of ADs. METHODS: Packagings of gemcitabine (GEM) and 5-fluorouracil (5-FU) were tested by wipe sampling. Five ADs; GEM, 5-FU, cyclophosphamide (CP), ifosfamide and etoposide were quantified using liquid chromatography mass spectrometry. RESULTS: AD contaminations were detected in 69% and 60% of the GEM and 5-FU packaging samples. Highest levels, up to approximately 5 µg/sample, were observed on the glass vials. The protective shrink-wrap of 5-FU vials and the plastic container of GEM were contaminated with low levels of 5-FU and GEM, respectively, and furthermore the 5-FU vials with shrink-wrap were cross-contaminated with GEM. Cross-contamination of CP and GEM was detected on 5-FU vials with plastic shrink-wrap removed. CONCLUSIONS: External contamination of ADs are still present at primary drug packagings on the Swedish market. Protection of AD vials by plastic shrink-wrap or a secondary plastic container does not remove the external contamination levels completely. The presence of cross contamination of ADs on drug packagings was also observed.

https://doi.org/10.1177/10781552231163544

Rodier S., Saint-Lorant G., Since M., Lagadu S., Benoist H., Palix A., Guilloit J.M., Faveyrial A., Divanon F., Delepee, R. (Préprint dans Bulletin n° 62)
UHPLC-MS/MS method for the quantification of ultra-traces of irinotecan and its metabolites in red blood cells and plasma to detect caregivers' contamination.
Drug testing and analysis, Volume 16, Numéro 2, février 2024, Page 236-246

Résumé : *The occupational exposure of caregivers to antineoplastic agents has been demonstrated since 1979. Since the early 1990s, numerous studies from several countries have demonstrated the contamination of care facilities by antineoplastic drugs. As it is easier to sample, most contamination measurements in workers are carried out in urine sample. The distribution and elimination half-lives of irinotecan suggest that blood can be considered as better than urine for the biomonitoring of a potential contamination of healthcare workers. We describe here the development and the validation of a UHPLC-MS/MS method to simultaneously quantify irinotecan, and two of its main metabolites, APC and SN-38, at ultra-trace levels in plasma and red blood cells (RBC). This method has been applied to blood samples collected from several healthcare services in a French comprehensive cancer center. The results demonstrate that the method is sensitive enough to identify a contamination of healthcare workers by irinotecan and SN-38 at very low concentrations. Moreover, the results show that analysis of RBC is of great interest and complementary to that of serum.*

https://doi.org/10.1002/dta.3539

Dugheri S., Squillaci D., Saccomando V., Marrubini G., Bucaletti E., Rapi I., Fanfani N., Cappelli G., Mucci N.
An Automated Micro Solid-Phase Extraction (µSPE) Liquid Chromatography-Mass Spectrometry Method for Cyclophosphamide and Iphosphamide: Biological Monitoring in Antineoplastic Drug (AD) Occupational Exposure.
Molécules, Volume 29, Numéro 3, février 2024, Article 638

Résumé : *Despite the considerable steps taken in the last decade in the context of antineoplastic drug (AD) handling procedures, their mutagenic effect still poses a threat to healthcare personnel actively involved in compounding and administration units. Biological monitoring procedures usually require large volumes of sample and extraction solvents, or do not provide adequate sensitivity. It is here proposed a fast and automated method to evaluate the urinary levels of cyclophosphamide and iphosphamide, composed of a miniaturized solid phase extraction (mu SPE) followed by ultrahigh-performance liquid chromatography-tandem mass spectrometry (UHPLC-MS/MS) analysis. The extraction procedure, developed through design of experiments (DoE) on the ePrep One Workstation, required a total time of 9.5 min per sample, with recoveries of 77-79% and a solvent consumption lower than 1.5 mL per 1 mL of urine sample. Thanks to the UHPLC-MS/MS method, the limits of quantification (LOQ) obtained were lower than 10 pg/mL. The analytical procedure was successfully applied to 23 urine samples from compounding wards of four Italian hospitals, which resulted in contaminations between 27 and 182 pg/mL.*

https://doi.org/10.3390/molecules29030638

Yamamoto S., Sanefuji M., Suzuki M., Sonoda Y., Hamada N., Kato W., Ono H., Oba U., Nakashima K., Ochiai M., Kusuhara K., Koga Y., Ohga S.
Pediatric leukemia and maternal occupational exposure to anticancer drugs: the Japan Environment and Children's Study.
Blood, Volume 143, Numéro 4, 25 janvier 2024, Page 311-319

Résumé : *Occupational exposure to medical agents and ionizing radiation has been suggested as a possible risk factor for childhood cancer. However, the relationship between such exposure and pediatric malignant neoplasms has not yet been comprehensively studied. This cohort study aimed to investigate the association between parental occupational exposure to hazardous medical agents or ionizing radiation and the risk of childhood cancer in offspring. Data from a large birth cohort in Japan, which included 104 062 fetuses, were analyzed. The primary outcome was the development of leukemia or brain tumors diagnosed by community physicians during the first 3 years after birth. Exposure factors were medical agents, including anticancer agents, ionizing radiation, and anesthetics, handled by mothers during pregnancy or by fathers for 3 months before conception. The incidence of leukemia, but not of brain tumors, was higher in mothers exposed to anticancer drugs. Multivariable regression analysis showed that maternal exposure to anticancer drugs was associated with an increased risk of leukemia in offspring older than 1 year (adjusted relative risk, 7.99 [95% confidence interval, 1.98-32.3]). Detailed information obtained from medical certificates of patients with identified leukemia revealed no infant leukemia but acute lymphoblastic leukemias in the exposed group. Our findings suggest that maternal occupational exposure to anticancer drugs may be a potential risk factor for acute lymphoblastic leukemia in offspring older than 1 year. Effective prevention methods may be necessary to prevent maternal exposure to anticancer drugs and to reduce the risk of childhood malignant neoplasms.*

https://doi.org/10.1182/blood.2023021008