Rapport de veille n° 62

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

1er juillet 2023 – 31 août 2023

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)***

Rodier S., Saint-Lorant G., Since M., Lagadu S., Benoist H., Palix A., Guilloit J.M., Faveyrial A., Divanon F., Delepee, R.
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, juin 2023

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

Speranza E. D., Jeronimo M., Colombo M.
Initial assessment of multi-compound antineoplastic drug surface contamination in Argentinean healthcare centers: Insights into occupational exposures in South America.
Journal of Oncology Pharmacy Practice, 20 juillet 2023

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/10.1177/10781552231188320

Campos D., Silva I., Rego M., Correia P., Moreira F.
Characterization of education, technical practices and attitudes of Portuguese pharmacy technicians towards manipulation of cytotoxic drugs.
Journal of Oncology Pharmacy Practice, 25 juillet 2023

Résumé : *Pharmacy professionals that manipulate cytotoxic drugs need to undergo educational programs, adopt the most convenient practices, and use appropriate equipment to avoid, as far as possible, occupational exposure to cytotoxic drugs. The main goal of this work is to characterize the education, technical practices, and attitudes towards cytotoxic drugs, of Portuguese pharmacy technicians. A questionnaire comprising eleven questions deemed pertinent was elaborated and subsequently validated by a pilot test. The anonymous, web-based survey was conducted between December 2022 and January 2023, by graduated pharmacy technicians that had manipulated cytotoxic drugs between 2017 and 2022. A total of 77 pharmacy technicians responded to the survey. Although sixty-six pharmacy technicians (86%) had been trained before beginning to manipulate cytotoxic drugs, the promotion of regular post-admission training by the institutions is sparse - only assumed by 53% of the pharmacy technicians (n = 41). All participants reported using gloves and gown during manipulation and the use of double gloves was common (99%; n = 76). Compliances with the recommended limit time for uninterrupted manipulation activity (82%; n = 63) and systematic double-checking (86%; n = 66) were high, but the regular use of sterile gauze around syringe connection sites 58% (n = 45), was less frequent. None of the surveyed pharmacy technicians used closed-system transfer devices (CSTD) and 41 (53%) of those who used spikes did not thoughtfully use these devices. The implementation of regular training programs in manipulating cytotoxic drugs should be fostered, to promote the more judicious use of engineering controls and transversal adoption of the safest technical practices.*

https://doi.org/10.1177/10781552231190025

- ***Articles de périodique***

Quartucci C., Rooney J.P.K., Nowak D., Rakete S. (Préprint dans Bulletin n° 60)
Evaluation of long-term data on surface contamination by antineoplastic drugs in pharmacies.
International archives of occupational and environmental health, Volume 96, Numéro 6, août 2023, Page 785-796

Résumé : *PURPOSE: The handling of antineoplastic drugs represents an occupational health risk for employees in pharmacies. To minimize exposure and to evaluate cleaning efficacy, wipe sampling was used to analyze antineoplastic drugs on surfaces. In 2009, guidance values were suggested to facilitate the interpretation of results, leading to a decrease in surface contamination. The goal of this follow-up was to evaluate the time trend of surface contamination, to identify critical antineoplastic drugs and sampling locations and to reassess guidance values. METHODS: Platinum, 5-fluorouracil, cyclophosphamide, ifosfamide, gemcitabine, methotrexate, docetaxel and paclitaxel were analyzed in more than 17,000 wipe samples from 2000 to 2021. Statistical analysis was performed to describe and interpret the data. RESULTS: Surface contaminations were generally relatively low. The median concentration for most antineoplastic drugs was below the limit of detection except for platinum (0.3 pg/cm(2)). Only platinum and 5-fluorouracil showed decreasing levels over time. Most exceedances of guidance values were observed for platinum (26.9%), cyclophosphamide (18.5%) and gemcitabine*

(16.6%). The most affected wipe sampling locations were isolators (24.4%), storage areas (17.6%) and laminar flow hoods (16.6%). However, areas with no direct contact to antineoplastic drugs were also frequently contaminated (8.9%). CONCLUSION: Overall, the surface contaminations with antineoplastic drugs continue to decrease or were generally at a low level. Therefore, we adjusted guidance values according to the available data. The identification of critical sampling locations may help pharmacies to further improve cleaning procedure and reduce the risk of occupational exposure to antineoplastic drugs.

https://doi.org/10.1007/s00420-023-01963-y

Huang H., Gu Y., Liu S., Hu S., Zhong X., Huang Y., Peng J., Huang X. (Préprint dans Bulletin n° 60)
The meta-analysis of cytogenetic biomarkers as an assessment of occupational risk for healthcare workers exposed to antineoplastic drugs.
International archives of occupational and environmental health, Volume 96, Numéro 5, juillet 2023, Page 675-683

Résumé : *OBJECTIVE: Antineoplastic drugs (ADs) are widely used in clinical practice and have been demonstrated to be effective in treating malignant tumors. However, they carry a risk of cytogenotoxicity for healthcare workers. Studies have reported that genotoxic biomarkers can be applied to assess the occupational health status of healthcare workers at an early stage, but results of different studies are variable. The objectives of the review were examine the association between long-term exposure to ADs and cytogenetic damage to healthcare workers. METHODS: We systematically reviewed studies between 2005 and 2021 using PubMed, Embase and Web of Science databases that used cytogenetic biomarkers to assess occupational exposure to ADs in healthcare workers. We used RevMan5.4 to analyze the tail length parameters of the DNA, frequency of the chromosomal aberrations, sister chromatid exchanges and micronuclei. A total of 16 studies were included in our study. The studies evaluate the quality of the literature through the Agency for Healthcare Research and Quality. RESULTS: The results revealed that under the random-effects model, the estimated standard deviation was 2.37 (95% confidence interval [CI] 0.92-3.81, P = 0.001) for the tail length parameters of the DNA, 1.48 (95% CI 0.71-2.25, P = 0.0002) for the frequency of chromosomal aberrations, 1.74 (95% CI 0.49-2.99, P = 0.006) for the frequency of sister chromatid exchanges and 1.64 (95% CI 0.83-2.45, P < 0.0001) for the frequency of micronuclei. CONCLUSIONS: The results indicate that there is a significant association between occupational exposure to ADs and cytogenetic damage, to which healthcare workers should be alerted.*

https://doi.org/10.1007/s00420-023-01969-6

Hu J., Zhao F., Liu L., Huang H., Huang X.
The meta-analysis of sister chromatid exchange as a biomarker in healthcare workers with occupational exposure to antineoplastic drugs.
Medicine, Volume 102, Numéro 34, 25 août 2023, Page e34781

Résumé : *BACKGROUND: Sister chromatid exchange (SCE) can be used to identify early occupational health status in health care workers. Our aim is to comprehensively assess the relationship between long-term exposure to antineoplastic drugs (ADs) and SCE in health care workers via meta-analysis. METHODS: Five databases were systematically searched for relevant articles published from inception to November 30, 2022. Literature data are expressed as mean difference and 95% confidence intervals (CI) or relative risk and 95% CI. For I2 > 50% trials, random effect model is used for statistical analysis, otherwise fixed effect model is used. This review was registered in the International Prospective Register of Systematic Reviews (identifier CRD42023399914). RESULTS: Fourteen studies were included in this study. Results showed the level of SCE in healthcare workers exposed to ADs was significantly higher*

than in controls. The mean difference of the SCE trial was 0.53 (95% CI: 0.10-0.95, P = .01) under a random-effects model. CONCLUSIONS: The findings suggested a significant correlation between occupational exposure to ADs in health care workers and SCE, requiring the attention of health care workers in general.

https://doi.org/10.1097/MD.0000000000034781