

Surfaces contamination with 5-Fluorouracil in two Portuguese Hospitals

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ABSTRACT

During the last years there has been an increasing concern about occupational exposure to cytostatic drugs in Hospitals. The first findings on occupational exposures among hospital personnel administering chemotherapy were reported only in 1979. Since then a great number of studies have been published describing possible exposure-related health effects. Consequently, rigorous guidelines for the safe handling of cancer chemotherapeutic agents were devised and the handling facilities in hospitals were extensively improved. However, recent studies developed in European countries revealed detectable amounts of several drugs in surface wipe samples. Dermal absorption after contact with contaminated surfaces can play an important role in exposure to antineoplastic drugs. Therefore, the existence of contamination in workplace surfaces implies an increased risk of exposure for health care workers. Since there is no recent report in Portugal, regarding the occupational exposure to antineoplastic drugs, a study was developed aiming to determine the 5-fluorouracil (5-FU) contamination on work surfaces of two Portuguese hospitals. In order to assess surfaces contamination by 5-FU, two different areas were wipe sampled: preparation and administration of antineoplastic drugs. The analysis of the extracted wipe samples was blinded and performed using a HPLC-DAD procedure (LOQ = 10 ng/cm²). In a total of 348 samples, 39 (11.2%) showed measurable levels of 5-FU (Hospital A: 17 (24%); Hospital B: 22 (8%)) with the administration areas presenting a higher number of contaminated samples in both hospitals (Hospital A: 43% vs 12%; Hospital B: 13% vs 5%). However, and in agreement with previous studies, the highest level of contamination was obtained in preparation area (storage cabinet of Hospital A - 78.8 ng/cm²). In conclusion, both hospitals showed surfaces contaminated with 5-FU, suggesting possible exposure to cytostatic drugs by dermal absorption. These results stress the need of constantly promote good practices and safety procedures among professionals and the need to perform routine monitoring of surfaces contamination in this occupational setting.

Keywords: cytostatic drugs; occupational exposure; dermal absorption; wipe sampling

1. INTRODUCTION

The use of antineoplastic drugs in cancer therapy is increasing due to their cytotoxic activity. However, they can also affect the growth and reproduction of healthy cells and can have carcinogenic, mutagenic or teratogenic properties (IARC, 1987, 1997; Schierl et al., 2009). In 1979, Falck et al. recognized the potential health hazard in occupational exposure describing mutagenic activity detected in the urine of nurses handling cytostatic drugs without protective measures. Additionally, toxic effects on reproductive health of female nurses have been reported (Stuecker et al., 1990; Valanis et al., 1997; Dranitsaris et al., 2005). Several biomonitoring studies demonstrated that nurses and pharmacy personnel involved in preparation or administration are exposed to antineoplastic drugs, by detecting cytotoxic agents or their metabolites in urine and blood (Pethran et al., 2003; Turci et al., 2003; Fransman et al., 2007).

Contact with contaminated surfaces can play an important role in exposure to antineoplastic drugs due to dermal absorption, therefore, the contamination levels of antineoplastic drugs in the workplace surfaces should be as low as possible, since this also indicates that dermal exposure is low. Considering this, the monitoring of surfaces contamination is a common way to assess occupational exposure and the most common method used is wipe sampling (Hedmer et al., 2004, 2008).

5-Fluorouracil (5-FU) is one of the most frequently antineoplastic agents used in Portuguese Hospitals and can be easily absorbed through the skin. Considering these two factors, this drug can be used as an indicator of surfaces contamination and exposure and have been extensively discussed in other studies (Larson et al., 2003; Castiglia et al., 2008; Schierl et al., 2009; Hedmer and Wohlfart, 2012; Kopp et al., 2013).

Since there is no recent report in Portugal related with occupational exposure to antineoplastic drugs, a study was developed aiming to determine 5-FU contamination on work surfaces of two Portuguese hospitals.

2. MATERIALS AND METHODS

Surfaces contamination by 5-FU was investigated in two Hospitals by wipe sampling in zones where antineoplastic drugs were handled, namely: preparation and administration areas. 5-FU is considered a suitable indicator for occupational exposure to antineoplastic drugs because is frequently used in preparations and in high amounts (Castiglia et al., 2008). Sensitive analytical methods are already established for this drug and there is already some data from other studies developed in other countries that, with some caution, permit to compare results. Sampling campaigns were developed in two different days in both Hospitals. The days were indicated as normal regarding antineoplastic drug preparation and administration. Before wiping, gauzes were moistened with a solvent (ethyl acetate). Sampling was performed by consecutive wiping to cover an area of 10x10 cm. Sampled locations were storage cabinets, preparation and packing benches, hoods, transfers, chairs for drug administration, worktops and others. All wipe samples were

extracted as described elsewhere (Schmaus et al., 2002). The analysis of the samples was blinded and performed by HPLC-DAD (LOQ = 10 ng/cm²), in the same conditions described by Schmaus et al., (2002).

3. RESULTS AND DISCUSSION

A total of 348 samples were taken and 39 (11.2%) showed measurable values of 5-FU. The highest value was obtained in the preparation area (storage cabinet of Hospital A - 78.8 ng.cm⁻²), however, a higher number of contaminated samples were obtained in the administration areas (Table 1).

Table 1 - Results obtained in both Hospitals

	HospitalA (n=70)	HospitalB (n=278)
Contaminated Samples	17 (24%)	22 (8%)
Traces	13 (19%)	81 (29%)
Not detected	40 (57%)	175 (63%)
Preparation samples	n=42	n=173
Contaminated (>LOQ)	5 (12%)	8 (5%)
Mean (ng.cm ⁻²) ± SD	46.2 ± 32.6	16.58 ± 5.1
Administration samples	n=28	n=105
Contaminated (>LOQ)	12 (43%)	14 (13%)
Mean (ng/cm ²) ± SD	16.4 ± 12.32	17.27 ± 6.27

LOD=3 ng/cm² - LOQ=10 ng/cm²

Surface monitoring of antineoplastic drug contamination can be used as a surrogate for dermal exposure, and therefore can be a good indicator of occupational exposure to these drugs. The existence of contamination by antineoplastic drugs on different surfaces in the workplaces implies an increased risk for health care workers to become dermally exposed (Hedmer and Wohlfart, 2012). Our results showed contamination by 5-FU and this indicate possible exposure to this and others antineoplastic drugs.

Moreover, although 5-FU was not handled in the services in all the selected sampling days, contamination was found on the surfaces. Similar observations were also reported by Acampora et al. (2005). This is a very interesting aspect since it is possible to use the most frequent handled antineoplastic drug in the workplace as a marker for antineoplastic drug contamination (Hedmer et al., 2008). It also points out the inefficiency of hygiene procedures as a contributing cause to surfaces contamination (Acampora et al., 2005; Castiglia et al., 2008).

In this work the higher value of contamination was found in a storage cabinet, showing that surfaces unrelated to the direct handling of drugs can also be contaminated. Similar results were found in a study developed in Germany pharmacies by Brouwers and colleagues (2007). This kind of contamination can be related with two phenomena: a wide spread surfaces contamination in these places and/or package contamination as reported by Favier et al. (2005).

Differently from other studies (Fransman et al., 2004; Connor et al., 2010), administration areas presented a higher number of samples contaminated with 5-FU than preparation areas. This fact suggests that in administration areas there is less care in handling the drugs probably due to the lack of implemented good practices and safety procedures.

There are no occupational exposure limits for drugs classified as carcinogen for humans, therefore, it seems appropriate to apply the ALARA principle ("as low as reasonably achievable") in terms of an intension to keep the exposure to carcinogenic substances at the lowest achievable level, usually limited by technological limitations or economic considerations. Considering this, and in theory, all the workplaces should be absent of antineoplastic drugs contamination (Castiglia et al., 2008).

4. CONCLUSIONS

In conclusion, both hospitals presented surfaces contaminated with 5-FU, which also suggests possible contamination by other antineoplastic drugs. Preparation areas presented less contaminated samples than administration areas. These differential results call to attention the need of constantly promote good practices and safety procedures among all the professionals that handled these drugs. The routine monitoring of surfaces contamination is of paramount importance to ensure the appliance of safety procedures.

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