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Antineoplastic drug residues inside homes of chemotherapy patients

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ABSTRACT

Chemotherapy treatment of cancer patients has shifted from inpatient to outpatient administration. Thus, family members are potentially exposed to cytotoxic drug residues from patients' excretions inside their homes. The study's aim was to evaluate the surface contamination and the potential uptake of antineoplastic drug residues by family members at home of chemotherapy patients. Overall, 265 wipe samples from 13 homes were taken at two times after chemotherapy from different surfaces (toilet, bathroom, kitchen). 62 urine samples were collected from patients and family members on three days. Samples were analyzed for cyclophosphamide, 5-fluorouracil (urine: FBAL) and platinum (as marker for cis-, carbo- and oxaliplatin). Substantial contamination was found on every surface type (PT: 0.02–42.5 pg/cm^2, 5-FU: ND-98.3 pg/cm^2, CP: ND-283.3 pg/cm^2) with highest concentrations on toilet and bathroom surfaces. While patients' urinary drug concentrations often were elevated for more than 48 h after administration, no drug residues were detectable in the family members' urine. This study provided an insight in the exposure situation against antineoplastic drug residues at home of chemotherapy patients. As contamination could be found on various surfaces adequate hygienic and protective measures are necessary to minimize the exposure risk for cohabitants.

1. Introduction

In cancer therapy, chemotherapy with antineoplastic drugs (AD) plays a substantial role due to their effective cytotoxic properties. But exactly these properties can also cause harm to persons who are involved in drug preparation, administration and caring of chemotherapy patients, because many ADs are known to express carcinogenic, mutagenic and teratogenic effects (IARC, 2012; Connor et al., 2014). As transdermal absorption after skin contact with contaminated surfaces is suggested to be a major route of accidental incorporation (Sessink et al., 1994; Kromhout et al., 2000; Fransman et al., 2005), dermal contact during all tasks should be avoided and persons with risk of contact should wear protective equipment and adhere to strict hygiene measures. In recent years, a shift has occurred from inpatient chemotherapy treatment in oncology wards to chemotherapy administration in outpatient departments with the patient's short-term presence of only few hours. Thus, patients can spend more time in their familiar surroundings during cancer treatment. However, coming along with this development, the exposure risk for contact to ADs shifts from hospital settings (pharmacies, wards) with strict hygiene and safety regulations (NIOSH, 2004; ISOPP, 2007) to less controlled home environments with uninformed persons (patients, families). Studies on oncology wards and outpatient centres reported frequent and high surface contaminations in areas where chemotherapy infusions and body fluids of patients were handled such as infusion stand and floor beneath, floor under bed, toilet surfaces, bathroom floors (Hedmer et al., 2008; Connor et al., 2010; Sugiura et al., 2011; Kopp et al., 2013b; Janes et al., 2015). Biomonitoring data support these findings (Suspiro and Prista, 2011; Connor et al., 2014; Hon et al., 2014). Moreover, exposure of persons not directly handling ADs such as unit clerks or housekeepers in healthcare settings (Hon et al., 2015), and also nurses and laundry workers have been reported related to skin contact while cleaning tasks (e.g.; cleaning toilets and washing patients, handling contaminated bed sheets) even outside the hospital environment (Fransman et al., 2005; Meijster et al., 2006). Spillage of drug-containing body fluids in toilet rooms and bathrooms can endanger persons who come in contact with the contaminated surfaces at home of chemotherapy patients. However, studies on surface contamination inside

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the homes of ambulant chemotherapy patients are scarce. Only Yuki et al. (2013, 2015) in two studies quantified the contamination by ADs (CP, 5-FU) in the home environment of cancer patients receiving chemotherapy (Yuki et al., 2013) and also the urinary AD concentrations for both patients (Yuki et al., 2013, 2015) and family members (Yuki et al., 2015), but with comparably small sample numbers. Nevertheless, they found considerable CP residues on toilet surfaces and in the urine of the family members living in the same apartment postulating an exposure risk for family members in close contact with patients receiving chemotherapy. The aim of the present study was to identify potential surface contamination by three antineoplastic drugs inside 13 homes of ambulant chemotherapy patients using wipe samples and to quantify the urinary drug concentration of patients and their family members during three days in parallel. Thus, the potential exposure risk for persons at home of ambulant chemotherapy patients to ADs could be assessed and corrective interventions may be targeted.

2. Material and methods

2.1. Study design

The potential exposure to ADs at homes of chemotherapy patients who received outpatient treatment was investigated by environmental and biological monitoring. Wipe samples and urine samples were collected/quantified in order to determine the actual contamination situation within the private rooms of chemotherapy patients. Wipe and urine samples were analyzed for the presence of cyclophosphamide, 5-fluorouracil (urine: alpha-fluoro-beta-alanine) and platinum (as marker of the platinum-drugs cisplatin, carboplatin and oxaliplatin) which belong to the most commonly used ADs in outpatient cancer chemotherapy in Germany. The individual results were provided to the participants not before all wipe and urine analyses were completed. This study was conducted with the approval of the ethical committee of the Ludwig Maximilians University in Munich, Germany. Participation was voluntary and confidential. All potential participants were informed that privacy would be strictly respected and that they could withdraw of the study at any time. It was also possible to only participate in the wipe sampling. Samples were collected between October 2014 and May 2015.

2.2. Antineoplastic drugs under study

Only patients treated with chemotherapies containing 5-fluorouracil (5-FU), cyclophosphamide (CP) and/or platinum (PT) compounds (cis-, carbo-, oxaliplatin) were enrolled in this study. These ADs are substances which are administered frequently and in high amounts and numbers for the therapy of a variety of cancer types (e.g.; breast cancer, colon cancer). Moreover, reliable sensitive and validated analytical methods have been established for PT (as marker of cis, carbo- and oxaliplatin), FU and CP in environmental and biological monitoring in hospitals and pharmacies. CP is an alkylating drug classified (by the IARC) as "human genotoxic carcinogen" (group 1) (IARC, 2012) with a half-life between 1.3 and 6.8 h after oral administration (Popeau et al., 2016), of which 5–25% is excreted unchanged in the urine. FU is listed as antineoplastic drug "not classifiable as to its carcinogenicity to humans" (group 3) with a half-life around 10–20 min. Its metabolites are eliminated within 9–10 h, of which alpha-fluoro-beta-alanine (FBAL) represents 60–90% of the overall metabolites and is excreted via urine (Ndaw et al., 2010). Within the platinum-group, Cisplatin is defined as "probably carcinogenic to humans" (group 2A). The pharmacokinetics of the PT-drugs are characterized by a triphase elimination with a short initial distribution phase (half-life of total PT around

Table 1
Characteristics of participants and number of wipe and urine samples.

Patient	Sex	Age	Drug administered	Dose/cycle (mg)	Actual cycle/total cycles	Number of wipe samples			Number of urine samples		Analyzed drug in urine
						PT	FU	CP	Patient	Family member	
1	Female	42	Cisplatin	90	6/6	20	–	–	2	0	PT
2	Female	57	Carboplatin	650	5/6	15	–	–	3	3	PT
3	Male	71	5-FU/Oxaliplatin	5000/180	2/6	30	10	–	3	3	PT/FBAL
4	Male	52	Cisplatin	225	3/4	20	–	–	3	3	PT
5	Female	56	Carboplatin	350	2/5	20	–	–	3	3	PT
6	Female	37	Carboplatin	320	6/6	20	–	–	3	3	PT
7	Female	76	5-FU	3400	2/6	–	20	–	3	3	FU
8	Male	75	Cycloposphamide	1444	1/8	–	–	20	3	3	CP
9	Female	45	Cycloposphamide	1000	3/6	–	–	20	3	0	CP
10	Male	64	5-FU/Oxaliplatin	5590/182.75	2/9	20	20	–	3	6[a]	PT/FBAL
11	Female	70	5-FU	2500	3/7	–	6	–	0	0	FBAL
12	Female	69	Carboplatin	600	2/6	12	–	–	3	3	PT
13	Female	73	Cycloposphamide	1200	3/3	–	–	12	0	0	CP

[a] 3 urine samples per 2 participating family members.