

# Protective Measures to Minimize Cyclophosphamide-Induced Surface Contamination Risk in Breast Cancer Patients

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## Abstract

**Background:** Cancer chemotherapy has shifted from inpatient to outpatient settings where exposure of family members to hazardous drug is a serious concern.

**Methods:** We enrolled 5 female Japanese patients (age:  $38.0 \pm 20.5$ ) who were administered cyclophosphamide (CPA) and thereafter immediately introduced to the bathroom. After urination, the lid of the toilet seat was closed, and excreta were drained twice. Sampling sheets on the surface and back of the toilet seat were collected and analyzed for CPA. The ability of wiping to eliminate experimental contamination was evaluated in a biological safety cabinet using 4 commercially available materials (10 squares of toilet tissue, 10 squares of toilet tissue soaked with 1 mL of water, thin and thick disposable cloths). CPA was added to a sampling sheet (Addition site) and another sampling sheet was set next to the addition site (Diffusion site). A wiper to test wiping effectiveness was placed 10 cm to the left of the additional site, a weight of 500 g was put on the wiper, and the weight was moved in 3 different wiping patterns (one direction (once and twice), outward and back (once)) at a speed of 1 cm/sec. The residual CPA in the addition and diffusion sites were analyzed.

**Results:** Average CPA on the surface and back side of the toilet seat for the five subjects was 15.2 and 121.2 ng, respectively. At the addition site, the residual CPA was less than 5 ng after wiping in one direction (once) with all materials. Recontamination with CPA was detected after wiping in one direction (twice) with the thin cloth and after wiping outward and back (once) with the thin and thick cloths. At the diffusion site, migration of CPA was detected after wiping in one direction (once) with the thin cloth.

**Conclusion:** These findings show that wiping off the back of the toilet seat is necessary after use of the restroom. When cleaning, protective measures are necessary to minimize exposure risk for family members, and wiping using 10 squares of toilet tissues soaked with water in one direction (once) is as an easy and simple method.

## Background

Cancer chemotherapy or radiation therapy has shifted from inpatient to outpatient settings. Effective home-based medical care for breast cancer survivors has placed ever-greater emphasis on survivorship care to maximize women's quality of life and the relief of family members [1]. Exposure of hospital workers to anti-neoplastic drugs in the work environment has been described [2-4]. Thus, exposure of family members to anticancer drugs is a serious concern. However, surface contamination on toilet surfaces and removal methods are not clear.

Breast cancer is the cancer that has the largest effect on procreation in women of reproductive age, and its incidence is increasing at an alarming rate. In the US, 1 in every 8 women will develop breast cancer during her life [5]. Chemotherapy plays an important role in breast cancer treatment, and the most recommended chemotherapy treatments for breast cancer in the current guidelines include cyclophosphamide (CPA). CPA is classified as a group 1 agent (carcinogenic to humans) by the International Agency for Research on Cancer and in pregnancy category D by the US Food and Drug Administration Center for Drug Evaluation and Research [6].

CPA was detected in saliva immediately after the chemotherapy and exponentially reduced with the passage of time (half-life of  $6.51 \pm 1.48$  h) [7]. CPA was detected at levels of 0.03-7.34 ng/cm<sup>2</sup> in 8 of the 12 wipe samples obtained from the homes of the patients administered CPA [8].

## Publication History:

Received: June 20, 2022

Accepted: July 02, 2022

Published: July 04, 2022

## Keywords:

Hazardous drugs, Drug exposure, Home excretion environment, Surface contamination

This study provides an insight into the biological contamination with CPA in the excretion environment within the hospital and at home. Another aim is to document protective measures to minimize CPA-induced surface contamination risk using toilet tissues and commercial wipes.

## Materials and Methods

### Wiping materials

Ten squares of the toilet tissue, 10 squares of the toilet tissue soaked with water, a thin commercial cloth toilet wipe (0.0625 mm) containing ethyl alcohol, isopropyl alcohol and benzalkonium chloride (Kobayashi Pharmaceutical Co., Osaka, Japan) and a thick commercial cloth toilet wipe (0.425 mm) containing alkylglycoside, glycoethers and an anti-bacterial agent (Kao Co., Tokyo, Japan) were used, with a size of 10 cm x 10 cm.

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**Citation:** Hasegawa N, Makino T, Nakajima K, Matsumoto C, Takizawa R, et al. (2022) Protective Measures to Minimize Cyclophosphamide-Induced Surface Contamination Risk in Breast Cancer Patients. Int J Nurs Clin Pract 9: 361. doi: <https://doi.org/10.15344/2394-4978/2022/361>

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### CPA on the surface and back side of the toilet seat

Five patients (age:  $38.0 \pm 20.5$ ) whose ages suggested the possibility of the childcare were administered CPA (560-700mg) and thereafter immediately introduced to the bathroom in the hospital. After urination, the lid of the toilet seat was closed, and excreta were drained twice according to the Japanese guideline [9]. The sampling sheets that were preliminarily affixed on the surface and back of the toilet seat for 5 patients were collected using a disposable plastic glove and analyzed for CPA using LC-MS/MS after the extraction with acetic acid (Shionogi Analysis Centre Co., Ltd., Japan).

### Ethical approval

Ethical approval for this study was obtained from Ishikawa Nursing University (No. 561).

### Wiping ability to eliminate experimental contamination

The ability of wiping to eliminate experimental contamination was evaluated in a biological safety cabinet using 4 commercially available materials (Figure 1). CPA (Endoxan<sup>TM</sup> for injection, Shionogi & Co., Ltd., Osaka, Japan) was diluted with saline and 50  $\mu$ L (1  $\mu$ g) was added to a circle with a radius of 2 cm and spread on a 10 cm x 10 cm sampling sheet (Addition site). Another sampling sheet was set next to the additional site (Diffusion site). A wiper to test wiping effectiveness was placed 10 cm to the left of the addition site and a weight of 500 g was put on the wiping material and the weight was moved in 3 different wiping patterns at speed of 1cm/sec so that the wiping material was not torn. The residual CPA in the addition and diffusion sites were analyzed (Shionogi Analysis Centre Co., Ltd., Japan).

### Statistical analysis

Results are expressed as the mean  $\pm$  SD. The differences between wiping effectiveness were evaluated using a one-way analysis of variance. A p-value of  $< 0.05$  was considered to be statistically significant. Analyses were carried out using SPSS 21 for Windows (IBM, Japan).

### Results and Discussion

#### Surface wipe testing on the surface and back side of the toilet seat

Average CPA on the surface and back side of the toilet seat for the five subjects was 15.2 and 121.2 ng, respectively. A previous study found that the total amount of CPA excreted in the urine during the 48 h post-administration period was 24.3% of the total administered dose in breast cancer patients [11]. Patients and their family members also need to be careful of contamination of the toilet environment. Wiping off the back of the toilet seat is necessary after the use of the restroom, and makes it possible to reduce the risk of exposure to CPA for patients, their family members and healthcare workers.

#### Wiping effectiveness with experimental contamination

At the addition site, the residual CPA was less than 5ng after wiping in one direction (once) with all materials (Figure 2A). With the toilet paper soaked with water and the thick cloth, it was lower than the detection limit (0.04ng/mL). After wiping in one direction (twice) with the thin cloth and after wiping of outward and back (once) with the thin and thick cloths, recontamination of CPA was detected. In the diffusion site, the residual CPA was less than 10 ng except when using the thin cloth after wiping in one direction (once) (Figure 2B).

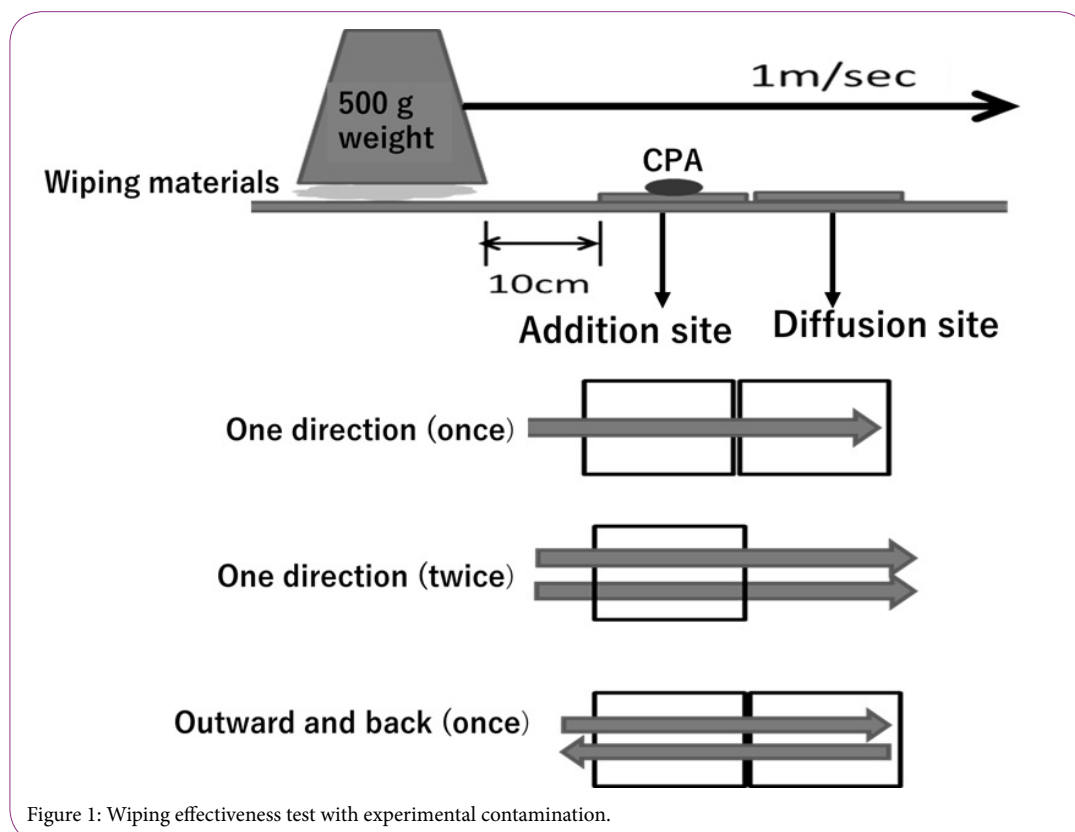


Figure 1: Wiping effectiveness test with experimental contamination.

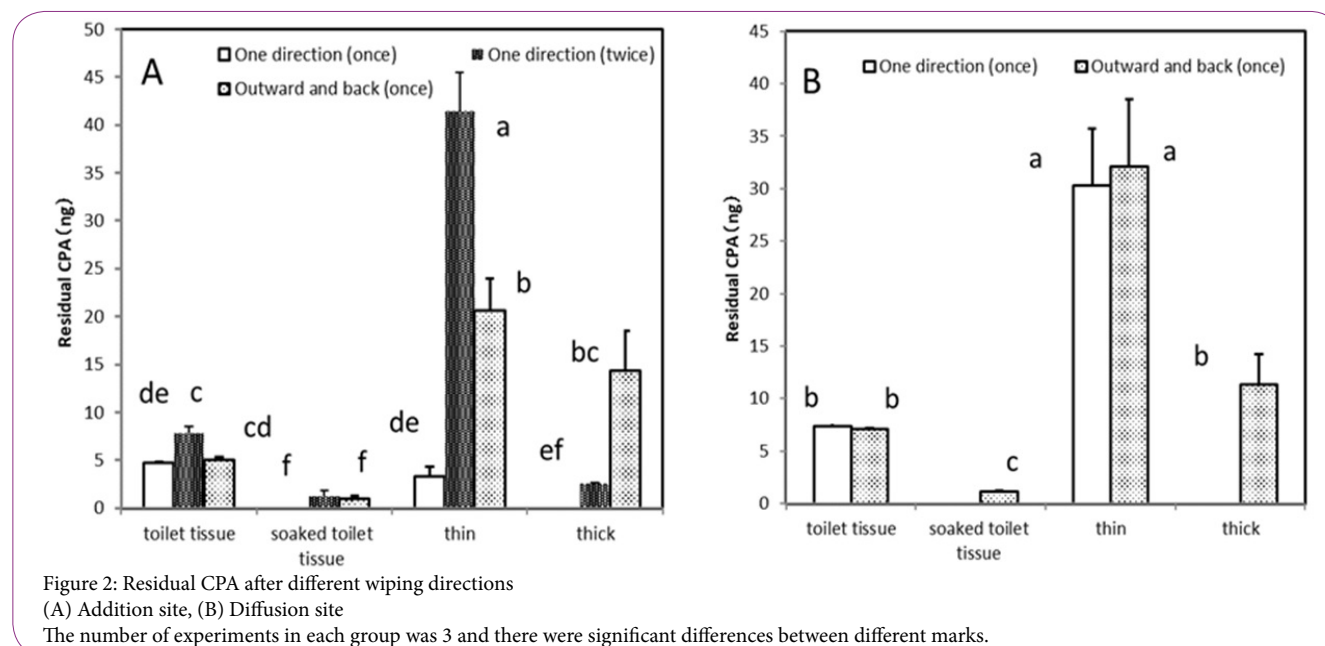


Figure 2: Residual CPA after different wiping directions (A) Addition site, (B) Diffusion site

The number of experiments in each group was 3 and there were significant differences between different marks.

Wiping in one direction (once) was effective with all materials, but CPA migrated to the neighbouring site when the commercial thin cloth was used. The high propensity for healthcare surfaces to be re-contaminated with bacteria following initial wiping suggests that a “One wipe, One surface, One direction, Dispose” policy should be implemented and rigorously enforced [10]. When cleaning, protective measures are necessary to minimize exposure risk for family members, and wiping using 10 squares of toilet tissue soaked with water in one direction is an easy and simple method.

Breast cancer is the most diagnosed cancer in women worldwide and it accounts for 29% of all new cancers in women. Its onset age is also younger than that of other cancers. It is important for patients and their family members to protect themselves from unaltered CPA.

## Conclusion

These findings show that the wiping off the back of the toilet seat is necessary after use of the restroom. When cleaning, protective measures are necessary to minimize exposure risk for family members, and wiping using 10 squares of toilet tissue soaked with water in one direction (once) is an easy and simple method.

## Competing Interests

The authors declare that they have no competing interests.

## Funding

This work was supported by JSPS KAKENHI Grant Number JP16K12069.

## Acknowledgements

Dr. Hasegawa was responsible for the study conception, design, and analysis, interpretation of data, and drafting of the manuscript.

Dr. Makino was responsible for the study conception, design, data acquisition and proof-reading of the manuscript.

Ms. Nakajima was responsible for data acquisition and proof-reading of the manuscript.

Ms. Matsumoto was responsible for data acquisition and proof-reading of the manuscript.

Ms. Takizawa was responsible for data acquisition and proof-reading of the manuscript.

Ms. Imakata was responsible for data acquisition and proof-reading of the manuscript

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