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Research Article

Occupational Exposure Reducing Remedies in Oncology Units

Metin Deniz Karakoc[1], Burcu Yapar Taskoylu[2]

[1]Department of Cytotoxic Drug Preparation, Denizli Public Hospital, Zafer Goksin Oncology Centre, Denizli, Turkey
[2]Department of Medical Oncology, Pamukkale University, Faculty of Medicine, Denizli, Turkey

Abstract

Objectives: The aim of our study is reducing the healthcare workers' duration of exposure to the cytotoxic agents without increasing the unused dose wasting during preparation by making changes in vial sizes of cytotoxic drugs.

Methods: Wasted doses and preparation time (potential exposure time) of the selected antineoplastic drugs were measured for six months. The usage of small dose vials which causes prolongation in preparation time has been avoided and larger dosage forms were preferred in last trimester. Wasted drug dose amounts and preparation periods were recorded. Subsequently, the data compared between the trimesters.

Results: The total preparation period in the first trimester was 1407 minutes while it was 1058 minutes in the second trimester. There was no significant changes between the first and the last trimester of the study in terms of patients numbers that receiving chemotherapy and the rate of unused drug doses extermination ($p>0.05$). On the other hand, drug preparation time, in other words the health employee's exposure period to cytotoxic drugs was reduced 24.81%.

Conclusion: In the study, it has been shown that by making rational choices about drug usage can reduce the healthcare workers duration of exposure to the cytotoxic agents.

Keywords: Cytotoxic, healthcare worker, occupational exposure, toxicity

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Among antineoplastic agents, cytotoxic drugs display nonspecific activity towards both tumor and the healthy cells which is responsible for their numerous side effects. The toxicity of antineoplastic agents are related to several parameters like their intrinsic carcinogenic character, concentration in tissues and their length of contact with the same tissue. In case of recurring contamination of healthy people, cytotoxic agents may lead to acute and/or delayed toxicity. The most common side effects include renal, hepatic, cardiac, haematopoietic, pulmonary and reproductive system toxicity, ototoxicity, immunotoxicity, dermal toxicity, and particular injury to tissues with rapid turnover rate.[1, 2]

In last two decades, governments and researchers have been issued to improve safety standards and protect health care workers. In cytotoxic drug preparation, most important measures for preventing exposure in health care workers are centralizing the cytotoxic drug preparation units, establishing specific guidelines, determining appropriate organizational measures and specialized technical equipments such as vertical laminar air flow Class IIB2 biosafety cabinets in negative pressurized clean rooms and making the usage of personal protective equipments as a compulsory.[3] Despite the implementation of these detailed guidelines and regulations, many recent studies reveals that nurses and cytotoxic drug preparation unit personnel (pharmacists and pharmacy technicians) are still being exposed to these cytotoxic substances.[4-6] Although these guidelines are advanced to reduce workers' exposure, studies have shown that recommendations were not always applied and that workplace contamination and occupational exposure have decreased but are still present.[4, 7-9]

Address for correspondence: Metin Deniz Karakoc, MD. Denizli Devlet Hastanesi, Zafer Goksin Onkoloji Merkezi, Denizli, Turkey
Phone: +90 258 263 93 11 (4502) **E-mail:** mdkarakoc@gmail.com

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Exposure of cytotoxics to the health care workers have been investigated by studies of biological markers. Early DNA damage elicited with single-cell gel electrophoresis (Comet-Assay, Trevigen Inc, Gaithersburg, Maryland) were shown in health care workers handling antineoplastic drugs. Cytogenetic effects, such as mutagenic activity in urine, chromosomal aberrations, micronucleus induction, and sister-chromatid exchanges, were reported.[7, 10, 11] Moreover, potential various acute and chronic (eg, cancer) effects of residual exposure to hazardous drugs have been described in several epidemiologic studies.[12-15] This situation suggests that there is a requirement to develop exposure reducing strategies for healthcare workers. The aim of our study is reducing the healthcare workers' duration of exposure to the cytotoxic agents without increasing the unused dose wasting during preparation by avoiding the use of small size vials of five different drugs that frequently used in oncology centres.

Methods

The study was conducted in a public hospital's oncology centre. First, a written permission (20.07.2017-49349904) was obtained from the hospital management for the study. All antineoplastic agents are prepared in negative pressurized clean rooms with using Class IIB2 biosafety cabinets and closed system transfer devices throughout the study. Initially, we identified the most frequently used antineoplastics in our hospital which have different dosage sizes on the market. We decided that carboplatin, cisplatin, doxorubicin, epirubicin, and oxaliplatin were the appropriate drugs for the study. Doxorubicin (10 and 50 mg), epirubicin (10 and 50 mg), cisplatin (10, 50 and 100 mg), oxaliplatin (50, 100 and 200 mg), and carboplatin (50, 150 and 450 mg) wasted doses and preparation time (potential exposure time) were measured for six months. The usage of small dose vials which causes prolongation in preparation time has been avoided and larger dosage forms were preferred as much as possible in last trimester. Amount of wasted drug doses and the preparation periods were recorded. Subsequently, the data compared between the first and the last trimesters. Data analyzed with Statistical Package for the Social Sciences (SPSS) version 22 (SPSS Inc., Chicago, IL, USA). The differences between the trimesters were analyzed with descriptive statistics. Chi-square (χ^2) test was used for analyzing the relations between the exposure time with wasted drug amounts and patient numbers.

Results

In the first trimester, the total preparation time of the selected antineoplastic agents with different size vials was 1407 minutes. On the other hand, preparation time was measured as 1058 minutes in the second trimester which avoided the small size vial usage as much as possible. There was no significant changes between the first and the last trimester of the study in terms of number of patients treated with chemotherapy (504 and 505 patients respectively) and the rate of unused drug doses extermination (totally 840 mg and 782 mg respectively) ($p>0.05$). On the other hand, drug preparation time, in other words the health employee's exposure period to cytotoxic drugs was reduced 24.81% (349 minutes). Details were shown in Table 1.

Discussion

In last decades, an increasing was observed both in the number of patients and the diversity of cytotoxic drugs used in the treatment of cancer. This situation is also causes an increasing in the cytotoxic drug exposure to the healthcare workers.[16, 17] In our study, an important data was achieved about reducing the occupational exposure to cy-

Table 1. The effects of dosage form changes to the wasted drug amount and exposure time

Dosage (mg)	Doxorubicin		Epirubicin		Cisplatin		Oxaliplatin		Carboplatin	
	before	after	before	after	before	after	before	after	before	after
10	210	18	249	15	90	-				
50	111	144	90	141	105	112	46	7	132	-
100					60	58	40	52		
150									110	122
200							29	30		
450									35	48
Total	7.650	7.380	6.990	7.200	12.150	11.400	12.100	11.200	38.850	39.900
Wasted amount (mg)	210	192	270	255	-	-	360	335	-	-
Number of patients	85	83	78	81	124	122	78	75	139	144
Exposure time (min.)	298	226	241	188	207	162	271	201	390	281

totoxic drugs. On the other hand, it was conducted only in a single-center and five frequently used drugs. Therefore, the results of the study can not be generalised for all hospitals and these were the limitations of our study.

The reduction of occupational exposure to the cytotoxic drugs become an important issue for many governments and researchers in recent years. The determination of occupational exposure may be performed by environmental monitoring of the workplace and biological monitoring of staff.[14] Biological monitoring of healthcare workers may be by performed using urinary mutagenicity and cytogenetic monitoring, or compound-selective methods, such as urinary monitoring of specific cytotoxic drugs. Urinary mutagenicity tests has been used as an important indicator of exposure to antineoplastic drugs. Ames test and thioether assay are the frequently used techniques for the determination of urinary mutagenicity. Cytogenetic monitoring is an effective way to detect DNA damages of the health employees who are working with cytotoxic drugs. The most common methods of cytogenetic monitoring are the analysis of sister chromatid exchanges, micronuclei tests, chromosomal aberrations, mutation tests, and COMET assay. Chromosomal aberrations is the most performed method to determine the exposure to cytotoxic agents via changes in chromosome numbers or chromosome structures, especially in blood lymphocytes.[18]

Demonstration of the healthcare workers' exposure to cytotoxic drugs via the biological and environmental monitoring, prompted the authorities to take measures for reducing the cytotoxic exposure. Publishing guidelines for safe handling of cytotoxics, preparing cytotoxics in Class IIB2 biosafety cabinets, the use of personal protection equipments such as chemotherapy gloves, FFP3 hepa filtered masks, chemo-protect gowns, and protective goggles were the first step measures. Subsequently, preparing the cytotoxics in centralised aseptic units, negative pressurized clean rooms and the use of closed system transfer devices were the second step measures. These measures not only reduced the likelihood of healthcare workers exposure to antineoplastic drugs, but also resulted in a reduction of the work place contamination.[19, 20] On the other hand, despite improving the conditions in practice and the introduction of various protective measures, contamination of both the working place and healthcare workers are still reported. Obviously, healthcare workers still at risk of routine exposure to low levels of cytotoxic agents. The clinical significance of low level exposure to cytotoxic agents is not fully identified, especially when workers are exposed to a combination of antineoplastic drugs over long periods of time.[21, 22]

Even though the use of newer and potentially less toxic antineoplastic drugs, such as monoclonal antibodies, has increased, the use of traditional cytotoxic drugs will continue in coming years. Therefore, further efforts to reduce exposure in the working environment is needed.[14] Taking measures to shorten the duration of the cytotoxic drug preparation period as much as possible may also reduce the amount of exposure by shortening the length of time which the staff stays in the clean room. In our study, we demonstrated that the time spent by the healthcare worker in the clean room can be reduced by 24.81% without increasing the unused dose wasting during preparation. The method we use in our study may provide a significant benefit in reducing the exposure of cytotoxic drugs to healthcare workers. Preferring large dose vials instead of small dose vials which causes prolongation in preparation time may be a solution for reducing the cytotoxic drug exposure.

Conclusion

In our study, it has been shown that by making rational choices about drug usage can reduce the healthcare workers duration of exposure to the cytotoxic agents without increasing the unused dose wasting during preparation. There are need for multi-center and long-term studies to demonstrate the exposure reducing ratio more precisely.

Disclosures

Ethics Committee Approval: Republic of Turkey Ministry of Health, Denizli Provincial Directorate of Health Local Ethics Committee 20.07.2017-49349904.

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