NHSJ Nursing and Health Sciences Journal

Volume 2, Number 4 (December 2022)
e-ISSN: 2798-5067
p-ISSN: 2798-5059

Implementation and Evaluation of Safe Handling Precautions Training for Oncology Nurses: An Experimental Design

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Article Info:
Submitted:
22-10-2022
Revised:
15-11-2022
Accepted:
18-11-2022

DOI:
https://doi.org/10.53713/nhs.v2i4.215

ABSTRACT

Health workers may be exposed to antineoplastic drugs by inhalation, ingestion, or direct skin contact during the preparation, transport, administration, storage, and disposal of antineoplastic drugs. The use of guidelines which have been published in order to protect healthcare workers from possible exposure to ADs has been still not widespread. The study aims to evaluate the impacts of the training on the safe handling precautions and oxidative stress parameters for oncology nurses. The study which was an experimental study without a control group included 23 oncology nurses. Training effectiveness was evaluated with the safe handling precautions questionnaire and blood samples of oncology nurses. After the training, the frequency of using the closed system transfer devices and changing the chemotherapy glove every 30 min in preparation of antineoplastic drugs significantly increased in the post-test. The post-test 8-hydroxy-2'-deoxyguanosine mean of the nurses was found to be significantly lower than pre-test and follow-up. The safe handling precautions training program increased the use of safe handling precautions and reduced oxidative damage among oncology nurses. Institutions should evaluate nurses' adaptation to safety programs, and problems in adaptation to programs on a regular basis and regularly provide safe handling precautions training.

Keywords: occupational health; antineoplastic drugs; oncology nurses; safe handling precautions

INTRODUCTION

In humans or animals, drugs that can show one or more of properties (e.g., carcinogenicity, teratogenicity, genotoxicity, toxicity in the reproductive system, and organ toxicity at low doses) are called hazardous drugs (NIOSH, 2016). Moreover, antineoplastic drugs (ADs) are defined as hazardous drugs by The National Institute for Occupational Safety and Health (NIOSH) and are a hazard for both patients and healthcare workers (NIOSH, 2004). Healthcare workers may be exposed to ADs by inhalation, ingestion or direct skin contact during the preparation, transport, administration, storage and disposal of ADs (NIOSH, 2004; OSHA, 2016). Also, nurses may be more exposed to ADs because they spend more time with cancer patients than any other health worker (Khattab & Aljeesh, 2022).

Occupational exposure to ADs may cause acute side effects (e.g., skin rash, nausea, vomiting, diarrhea, constipation, alopecia, nail hyperpigmentation, dysuria, insomnia) (Riley, 2009) or chronic side effects (e.g., infertility, miscarriage, and damage in the fetus and embryo) (Dranitsaris et al., 2005; Rekhadevi et al., 2007), leukemia (Blair et al., 2001), and breast cancer (Ratner et al., 2010). The exposure level of healthcare workers to ADs should be determined to prevent these side effects. In several studies, occupational exposure of healthcare workers to ADs has been reported by measuring different biological indicators such as sister chromatid exchange, chromosomal abnormalities, micronucleus (MN) testing in lymphocytes and buccal cells and oxidative stress parameters (Mahboob et al., 2012; Rekhadevi et al., 2007). These studies found that DNA damage (Rekhadevi et al., 2007), chromosomal anomalies and micronucleus frequency (Ladeira et al., 2014; Mahmoodi et al., 2017) were high in nurses working with ADs, and nurses were sensitive to oxidative stress (Gómez-Oliván et al., 2014).

The Centers for Disease Control and Prevention (CDC) state that DNA damage is a sensitive and relevant endpoint to study because most antineoplastic agents target DNA (CDC, 2019). One of the useful markers for the

Volume 2, Number 4 (December 2022)
e-ISSN: 2798-5067
p-ISSN: 2798-5059

evaluation of oxidative DNA damage is 8-hydroxy-2'-deoxyguanosine (8-OHdG). Several studies showed that the 8-OHdG levels are increased in cancer patients after chemotherapy (Honda, Yamada, Tomonaga, Ichinose, & Kamihira, 2000; Tagesson, Källberg, Klintenberg, & Starkhammar, 1995).

Guidelines have been published since the late 1980s in order to protect healthcare workers from possible exposure, but studies have reported that the use of these guidelines has not been widespread (Ben-Ami, Shaham, Rabin, Melzer & Ribak, 2001; Power, Coyne, 2018; Rızalar, Tural & Altay, 2012). Therefore, all the healthcare workers involved in the handling of ADs should be provided with suitable, sufficient, and regular information and training relevant to their work (OSHA, 2016; Sessink, Sewell & Vandenbroucke, 2015). The training should include health risks arising from exposure to ADs, policies, and procedures for the protection and safe handling precautions (NIOSH, 2004). Moreover, the effect of training on safe handling precautions and oxidative stress parameters has not been commonly used according to the literature. There is a gap in the literature regarding cost-effective, easily implemented interventions to address safe handling precautions and oxidative damage among oncology nurses. Thus, this study aims to evaluate the impacts of the training on the safe handling precautions and oxidative stress parameters for the nurses handling the ADs.

METHOD

Setting and Participants: The study was an experimental study with a pre–post-test design. The sample of the study consisted of 32 oncology nurses involved in the preparation and administration of ADs. This study included oncology nurses who were non-smokers, without chronic disease, were not exposed to radiation, and who agreed to participate in the study. The study was conducted in three clinics (two pediatric oncology clinics and one chemotherapy center) at two hospitals. Nine nurses who didn't meet the inclusion criteria were not included in this study. Moreover, this study was conducted with 23 nurses who met the inclusion criteria in these three clinics. In addition, 14 nurses who worked in pediatric oncology clinics have both day and night shifts. No nurses in pediatric oncology clinics work on the night shift only. Nine nurses who worked in the oncology center just had daytime shifts. The power of the study was evaluated using the G Power 3.1.9.2 program. The 8-OHdG mean was used as the primary outcome variable in calculating the power of the research Given 23 sample size, 0.4 effect size, and a 0.05 alpha, this study's power of 0.99 was estimated.

Instruments: Three instruments which consist of general information questionnaire, safe handling precautions questionnaire and blood samples were used in this study.

General Information Questionnaire: The general information questionnaire contains questions about the socio-demographic characteristics (age, gender, education, and so on), occupational characteristics (working time as a nurse, oncology nurse, and so on), and medical history (current disease situation, gynecologic and obstetric history, and so on) of oncology nurses

Safe Handling Precautions Questionnaire: The safe handling precautions questionnaire consists of three parts i.e., the institution's safety program, the use of safe handling precautions during the preparation of ADs (this part cover questions which comprise preparing of ADs in the Biological Safety Cabinet), and the use of safe handling precautions during the administration of ADs (this part consists of questions about applying of ADs to the patients). This questionnaire was prepared by the researchers following the safe handling precautions guidelines (Connor, McLauchlan, Vandenbroucke, 2007; NIOSH, 2004; NIOSH, 2016; Oncology Nursing Association, 2009; Power, 1990). For the questionnaire, expert opinions were obtained from 10 people consisting of the president and vice president of the Oncology Nursing Association (Turkey), six oncology nurses, and two professors specializing in the field of oncology nursing.

Blood Samples: Blood samples from the nurses were collected to evaluate the oxidative damage. 8-OHdG and total antioxidant capacity (TAC) levels were used as oxidative stress parameters. Moreover, 8-OHdG is one of the oxidative bases formed as a result of free oxygen radicals attacking the DNA and is one of the most studied materials indicating oxidative DNA damage. Furthermore, 8-OHdG is a DNA lesion whose mutagenic properties have been identified, and can be measured with high precision (Valavanidis, Vlachogianni & Fiotakis, 2009). Several studies showed that oxidative stress plays an important role in the pathophysiology of diseases (e.g., cardiovascular diseases, diabetes, cancer, Alzheimer's, and so on) (Di Minno et al., 2016; Abudawood, Tabassum, Almaarik, & Aljohi, 2020). Also, 8-OHdG is recommended for detecting oxidative damage in healthcare workers working with ADs (Moretti et el., 2011). Thus, 8-OHdG was preferred as a biomarker of oxidative damage evaluating DNA damage for these reasons.

The mechanisms that protect the body from oxidative damage are called antioxidant systems. These systems allow free radicals to be reduced, allowing the cell to maintain its oxidation reduction state. A balance between the rate of formation of free radicals in the organism and the rate at which they are eliminated was noted, which is called

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e-ISSN: 2798-5067
p-ISSN: 2798-5059

oxidative balance. As long as the oxidative balance is maintained, the organism is not affected by free radicals. If a decrease in the rate at which free radicals are eliminated is noted, this will cause the deterioration of oxidative balance. Moreover, antioxidant capacity can be defined as the ability of a compound to reduce oxidant activity (Özcan, Erdal, Çakırca & Yöndem, 2015; Serafini & Del Rio, 2004). Therefore, the evaluation of antioxidant capacity in biological systems is important.

Blood samples from the nurses were taken at the end of the 5-day study (40 h) to ensure standardization of blood samples. Blood samples for the chemotherapy centers were taken at the end of the 5-day (40 h) study. Moreover, blood samples for the pediatric clinics were collected at the end of the 40 h by calculating night shifts and daytime working hours. The pre–post test design was used to check the effect of variables (polycyclic aromatic hydrocarbons, air pollution, and so on) that may affect the 8-OHdG levels. Nurses served as their own control. Also, one follow-up before post-test was done in this study for result reliability.

After blood collection, samples that were centrifuged for 10 min at 3,000 rpm were kept at -80 ºC until analyzed. Plasma 8-OHdG level was measured in the study using Human 8-Hydroxy-Desoxyguanosine ELISA Kit (Cat No: YHB0050Hu; Shanghai Yehua Biological Technology, Shanghai, China). Plasma TAC level was measured using Total Antioxidant Status ELISA Kit (Cat.No:YHB3515Hu, Shanghai Yehua Biological Technology).

Safety Handling Precautions Training: The attitudes, opinions, and experiences of the nurses working with ADs on safe handling precautions were determined in the first phase of the study which was performed qualitatively (Topçu & Beşer, 2017). The Health Belief Model (HBM)was used to evaluate the factors that affect the use of safe handling precautions of nurses. The Health Belief Model (HBM) was developed in the 1950s to describe why some people who are free of illness will take actions to prevent illness, whereas others fail to do so. The model has potentially useful to predict individuals who would or would not use preventive measures and to suggest interventions that might increase the willingness of resistant individuals to engage in preventive behaviors (Pender, Murdaugh & Parsons, 2015). The basic HBM concepts that explained protective health behaviors are perceived susceptibility, perceived seriousness, perceived benefits, perceived barriers, cues to action, and self-efficacy (Pender, Murdaugh & Parsons, 2015). The most important factors about safe handling precautions were perceived barriers and cues to action determined based on experiences, viewpoints, and attitudes emphasized by most nurses (Topçu & Beşer, 2017). The training was planned in this direction (Topçu & Beşer, 2017).

Pre-tests were applied to the nurses at the first interview and blood samples were taken at the end of 5-day (40-h) study (Figure 1.). After pre-tests and blood samples were collected, training were carried out. Training time were determined following the work intensities of the nurses. The training was held for 40-60 min for the groups with at least one nurse or a maximum of three nurses. For oncology clinics, training was mostly performed during the night shift where nurses were more suitable, and, at times, of low intensity for chemotherapy centers. Brochures that included safe handling precautions were given to all nurses after the training. Magnets that demonstrated the safe handling precautions were pasted on the Biological Safety Cabinet (BSCs). Reminders that explained safe handling precautions for preparation, administration, and spillage of ADs were hanged to be easily visible in clinics and chemotherapy centers. Blood samples were collected again at the end of the 5-day (40-hour) study in the first (follow-up) and third months (post-test) after the training. Questionnaires were applied in both follow-up and post-test.

Data analysis: The data were evaluated in SPSS 21 program. Descriptive statistics were used to assess sociodemographic information. Cochran's Q test was used to compare the frequency of safe handling precautions before and after training. Moreover, the Friedman test was used to compare 8-OHdG and TAC levels before and after training.

Ethical considerations: The study was approved by the Institutional Review Board. Written informed consent was obtained from the nurses who agreed to participate in the study.

Volume 2, Number 4 (December 2022)
e-ISSN: 2798-5067
p-ISSN: 2798-5059

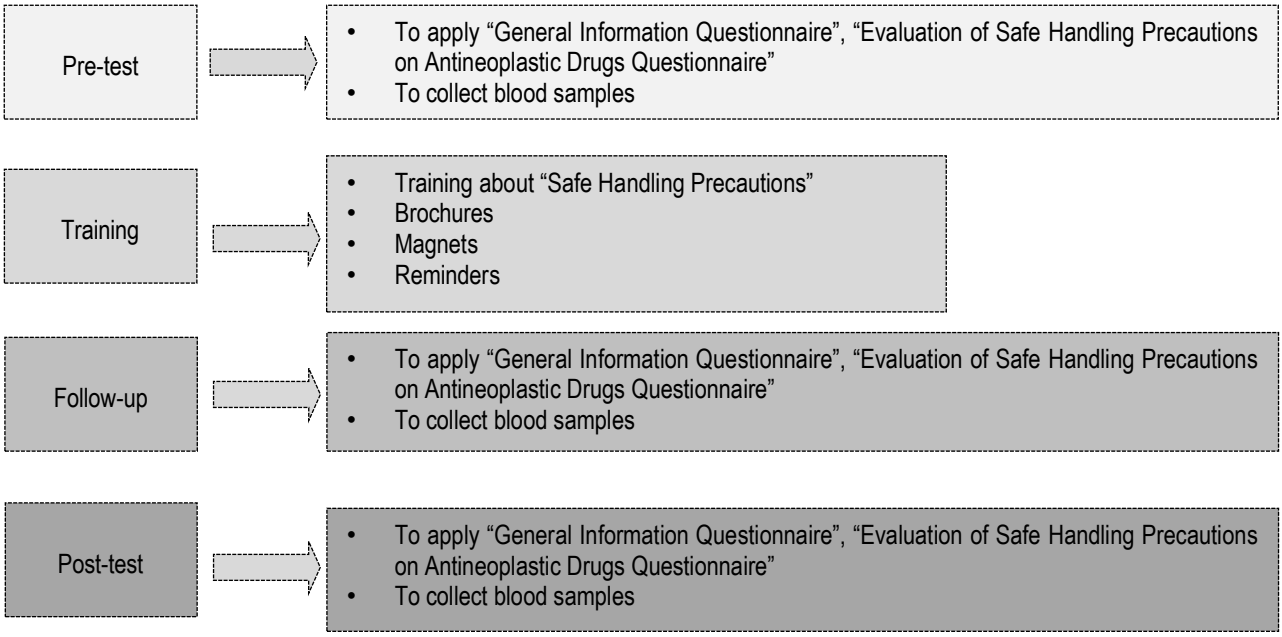

Figure 1. Intervention Plan

RESULT

The mean age of the nurses was 34.78 ± 4.93 years. In addition, 82.6% of the nurses are married and 78.3% of them had a baccalaureate degree (Table 1). All clinics (100%) had class II BSC and a safety program to minimize exposure to ADs, which were prepared in a separated room. The pre-test, follow-up, and post-test evaluated the availability of materials (written or visual) that explained safe handling precautions in an easily accessible and visible place during the preparation and administration of ADs. Nurses reported be found materials in the pre-test, follow-up, and post-test 60.9%, 100%, and 100%, respectively. Pre-test, follow-up, and post-test found that 69.6% of nurses were given in-service training about the safe handling precautions for ADs by their institutions.

Table 1. Sample Characteristics (N=23)

Variables	Nurses (N=23)	
Age (x±SD)	34.78±4.93	
Gender (%)		
Female	23	100.0
Male	0	0.0
Marital Status (%)		
Married	19	82.6
Single	4	17.4
Education (%)		
High School of Health	1	4.3
Associate Degree	3	13.0
Baccalaureate	18	78.3
Masters	1	4.3

Safe Handling Precautions in Preparation of ADs

The frequency of using nurses' safe handling precautions in preparation of ADs was presented in Table 2. A significant difference in frequency of using closed-system transfer devices (*Cochran's Q*=6.50, *p*=0.03), changing chemotherapy gloves every 30 min (*Cochran's Q*=14.00, *p*=0.00), and using chemotherapy pads (*Cochran's Q*=7.60, *p*=0.05) was noted between pre-test, follow-up, and post-test. The nurses' use frequency of closed-system transfer devices in follow-up and post-test was determined to be significantly higher than the pre-test. In the post-test, the

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e-ISSN: 2798-5067
p-ISSN: 2798-5059

frequency of changing the chemotherapy glove of the nurses every 30 min was found to be statistically higher than follow-up and pre-test.

Table 2. Comparison of Safe Handling Precautions Between Pre-test, Follow-up, and Post-test in Preparation of ADs (N=23)

Safe Handling Precautions	Pre-Test		Follow-up		Post-Test		Cochran's Q	p
	n	%	n	%	n	%		
Closed-system transfer devices								
Yes	19	82.6	22	95.7	23	100	6.50	0.03*
No	4	17.4	1	4.3	0	0		
Chemotherapy glove								
Yes	21	91.3	22	95.7	22	95.7	2.00	0.36
No	2	8.7	1	4.3	1	4.3		
Changing chemotherapy glove every 30 min								
Yes	0	0	0	0	7	30.4	14.00	0.00*
No	23	100	23	100	16	69.6		
Double chemotherapy glove								
Yes	3	13	7	30.4	6	26.1	2.00	0.36
No	20	87	16	69.6	17	73.9		
Chemotherapy gown								
Yes	20	87	21	91.3	21	91.3	2.00	0.36
No	3	13	2	8.7	2	8.7		
Changing chemotherapy gown every three hours								
Yes	18	78.3	20	87	20	87	2.66	0.26
No	5	21.7	3	13	3	13		
Disposable head/hair cover								
Yes	2	8.7	3	13	2	8.7	0.66	0.71
No	21	91.3	20	87	21	91.3		
Disposable shoe covers								
Yes	2	8.7	2	8.7	3	13	2.00	0.36
No	21	91.3	21	91.3	20	87		
Chemotherapy Pads								
Yes	13	56.5	15	65.2	18	78.3	7.60	0.02*
No	10	43.5	8	34.8	5	21.7		

*p<0.05

No significant difference in frequency of using a chemotherapy gloves (Cochran's Q=2.00, p=0.36), double chemotherapy gloves (Cochran's Q=2.00, p=0.36), chemotherapy gown every three hours (Cochran's Q=.2.66, p=0.26), and head/hair covers (Cochran's Q=0.66, p=0.71), and shoe covers (Cochran's Q=2.00, p=0.36) was noted between pre-test, follow-up, and post-test.

Safe Handling Precautions in Administration of ADs

The frequency of using nurses' safe handling precautions in the administration of ADs is presented in Table 3. A significant difference was noted in the frequency of using closed-system transfer devices (Cochran's Q=16.00, p=0.00), using chemotherapy gloves (Cochran's Q=13.00, p=0.00), using chemotherapy gown (Cochran's Q=16.53, p=0.00), and changing chemotherapy gown every three hours (Cochran's Q=7.60, p=0.05), and wearing eye protection (if there is a risk of splashing; Cochran's Q=9.33, p=0.00) between pre-test, follow-up, and post-test.

Volume 2, Number 4 (December 2022)
e-ISSN: 2798-5067
p-ISSN: 2798-5059

Table 3. Comparison of Safe Handling Precautions Between Pre-test, Follow-up, Post-test in Administration of ADs (N=23)

Safe Handling Precautions	Pre-Test		Follow-up		Post-Test		Cochran's Q	p
	n	%	n	%	n	%		
Closed-system transfer devices								
Yes	13	56.5	21	91.3	21	91.3	16.00	0.00*
No	10	43.5	2	8.7	2	8.7		
Chemotherapy glove								
Yes	10	43.5	12	52.2	18	78.3	13.00	0.00*
No	13	56.5	11	47.8	5	21.7		
Changing chemotherapy glove every 30 min								
Yes	15	65.2	17	73.9	18	78.3	4.66	0.09
No	8	34.8	6	26.1	5	21.7		
Double chemotherapy glove								
Yes	7	30.4	8	34.8	8	34.8	0.50	0.77
No	16	69.6	15	65.2	15	65.2		
Chemotherapy gown								
Yes	7	30.4	17	73.9	19	82.6	16.53	0.00*
No	16	69.6	6	26.1	4	17.4		
Changing chemotherapy gown every three hours								
Yes	10	43.5	10	43.5	15	65.2	10.00	0.00*
No	13	56.5	13	56.5	8	34.8		
Eye protection								
Yes	2	8.7	6	26.1	8	34.8	9.33	0.00*
No	21	91.3	17	73.9	15	65.2		

*p<0.05

The nurses' frequency of using closed-system transfer devices and chemotherapy gown in follow-up and post-test were higher than the pre-test. The nurses' frequency of using chemotherapy gloves and changing the chemotherapy gown every three hours in the post-test were significantly higher than pre-test and follow-up. No significant difference was noted in the frequency of changing chemotherapy gloves every 30 min (Cochran's Q=4.66, p=0.99), using double chemotherapy gloves (Cochran's Q=0.50, p=0.77), between pre-test, follow-up, and post-test.

Parameters of Oxidative Stress

The 8-OHdG mean of nurses in the pre-test, follow-up, and post-test was found in 818.92 ng/ml±238.64, 754.43 ng/ml±370.78, 535,74 ng/ml±298,11, respectively (Table 4.). The post-test 8-OHdG mean of the nurses was found to be significantly lower than pre-test and follow-up (χ^2=10.17, p=0.00). The TAC mean of nurses in pre-test, follow-up, and post-test was found 33.86 ng/ml±19.11, 36.83 ng/ml±16.17, 47.26 ng/ml±21,40, respectively. Moreover, a significant difference in the TAC means was noted between pre-test, follow-up, and post-test (χ^2=16.35, p=0.00). TAC means of nurses in post-test was found to be significantly higher than pre-test and follow-up.

Table 4. Comparison of Oxidative Stress Parameters Between Pre-test, Follow-up, and Post-test (N=23)

Oxidative stress parameters	Pre-Test	Follow-up	Post-test	X^2	p
	x±SD	x±SD	x±SD		
8-OHdG	818.92±238.64	754.43±370.78	535.74±298.11	10.17†	0.00*
TAC	33.86±19.11	36.83±16.17	47.26±21.40	16.35†	0.00*

*p<0.05, †Friedman test

Volume 2, Number 4 (December 2022)
e-ISSN: 2798-5067
p-ISSN: 2798-5059

DISCUSSION

The study by Al-Azzam et al. (2015) found that 58.7% of nurses reported BSC in the working area. In a study by Polovich and Clark (2012), 89% of nurses stated that written protocols about safe handling precautions of ADs are available in their institutions but did not reflect current guidelines. Engineering controls and administrative controls are part of the hierarchy of controls that can lower worker occupational exposures and reduce the risk of illness/injury (Leli, Kundaryanti & Novelia, 2022). When compared with the literature, the institutions involved in this study were considered to be at a very good level in terms of engineering controls (BSC) and administrative controls (written policy and guidelines). Moreover, all clinics have the materials provided by the researcher as part of the initiative also contributing to the development of administrative controls of the institutions.

Safe Handling Precautions in Preparation of ADs

During the preparation and administration of ADs, closed-system transfer devices which are defined as a means to prevent or reduce drug escape from the system are part of the additional engineering controls. NIOSH (2004) proposed the use of closed-system transfer devices together with engineering controls and personal protective equipment (PPE). This study found that the use frequency of closed-system transfer devices in follow-up and post-test was significantly higher than pre-test. In particular, the use of closed-system transfer devices by all nurses in post-test was thought to be due to the increased perceived benefits of nurses due to education.

Ben-Ami et al. (2001) found that 58% and 32% of nurses wore latex and surgical gloves (PVC) in the preparing of Ads, respectively. The study by Polovich and Martin (2011) reported that of the nurses who used the gloves, 91% used chemotherapy gloves. The nurses' use of chemotherapy gloves gradually increased in the preparation of the ADs (Polovich & Martin, 2011). Similarly, the nurses' use of chemotherapy gloves in the preparation of ADs was quite high in this study. Moreover, Rızalar, Tural, Altay (2012) reported that 100% of the nurses used gloves in preparation and administration of ADs, but only 36% changed gloves every 30 min. In the present study, although nurses' use of chemotherapy gloves was very high, none of the nurses changed the chemotherapy gloves in every 30 min in pre-test and follow-up. Despite the training having a positive effect on the changing of chemotherapy gloves every 30 min, it was not at the desired level. Polovich & Martin (2011) reported that, 96% of nurses used gloves in preparation of ADs, but only 11% used double gloves. Furthermore, Topçu & Beşer (2017) found that nurses did not use double chemotherapy gloves because of not being able to move comfortably with double gloves. The results of the current study suggest that the use of double chemotherapy gloves was quite low in pre-test, follow-up and post-test. Even though an increase in the use of double chemotherapy gloves was noted due to the decrease in the perceived barriers of nurses after training, it was thought that it was still not at the desired level. Kosgeroglu, Ayranci, Özerdogan & Demirustu (2006) reported that only 5.5% of nurses have used the gown. Polovich and Martin (2011) found that 80% of the nurses used a chemotherapy gown while most of the nurses got out of their gowns at the end of the day. Contrary to the findings of other studies, the use of chemotherapy gown and the changing of the chemotherapy gowns every three hours was very high in nurses in the present study. Most of the studies found that PPEs, which were the least used by nurses, were shoe and head/hair covers (Momeni et al. 2013; Olgun and Şimşek, 2010). Similarly, this study found that nurses used the least shoe and head/hair covers in preparing of ADs. After the training, the behavioral changes could not be realized because the perceived benefits of the nurses on this issue could not be increased. Chemotherapy pads are materials used to absorb ADs leaks and spills, covering the work surfaces of engineering controls. Moreover, NIOSH (2016) recommends the use of chemotherapy pads in BSCs. This study found a significant difference in the frequency of using chemotherapy pad between pre-test, follow-up, and post-test.

After the training, the frequency of using the closed system transfer devices, changing the chemotherapy glove every 30 min, and using the chemotherapy pad in the preparation of ADs significantly increased in the post-test. The most used safe handling precautions by nurses in preparing ADs were that closed system transfer device, chemotherapy glove, chemotherapy gown, replacement of chemotherapy gown every three hours, and chemotherapy pad respectively. According to these results, safe handling precautions training contributed to increasing using safe handling precautions among oncology nurses. Institutions should regularly provide oncology nurses with safe use standards training and structure this training according to their necessities.

Safe Handling Precautions in Administration of ADs

One of the most evaluated PPEs in nurses handling ADs is gloves. Topçu & Beşer (2017) reported that although 100% of nurses used gloves, the type of glove used changed. He, Mendelsohn-Victor, McCullagh, & Friese (2017) found that oncology nurses wore only one pair of chemotherapy-tested gloves at least 75% of the time during routine administration/preparation activities. This study found that the use of chemotherapy gloves in post-test was significantly

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e-ISSN: 2798-5067
p-ISSN: 2798-5059

higher than pre-test and follow-up ($p<0.05$). After the training, a significant increase was noted in the use of chemotherapy gloves due to the increase in the perceived susceptibility of nurses.

Polovich & Martin (2011) reported that only 18% of nurses used double gloves in administration of ADs. DeJoy, et al. (2017) found that only 20% of oncology nurses always used double gloves. NIOSH (2004) suggest that the gloves should be replaced every 30-60 min and that double chemotherapy gloves should be used in all applications with ADs. No statistically significant difference in the changing of chemotherapy gloves every 30 min and the use of double chemotherapy gloves between pre-test, follow-up, and post-test was noted in the current study. Although the training increased nurses' use of gloves, the use of double chemotherapy gloves and the replacement of the gloves at appropriate intervals was limited and should be improved. Several studies found that the frequency of the use of gowns was varied between 31% and 77% in the ADs administration of ADs (Polovich & Martin, 2011; Rızalar, Tural, Altay, 2012). In the present study, pre-test results were similar to the literature. However, a significant increase in the use of chemotherapy gown due to the decrease in the perceived barriers of the nurses was noted after the training.

After the training, the frequency of using closed-system transfer device, using chemotherapy glove, using chemotherapy gown, changing the chemotherapy gown every three hours, wearing eye protection in the administration of ADs significantly increased in the post-test. These findings may result from the positive effect of the training program on the use of safe handling precautions.

Parameters of Oxidative Stress

In the literature, no study exists to evaluate 8-OHdG in plasma as an indicator of oxidative damage in nurses working with Ads. However, studies evaluating 8-OHdG levels in plasma or serum in different sample groups. Onbaşı, Noyan, Çebi, Kıroğlu (2011) reported that the mean of serum 8-OHdG was found to be 77.50 ng/ml±9.72 with the ELISA method in adults. Also, Turhan et al. (2012) reported that 8-OHdG levels were 3.8ng /ml±0.7 in the serum samples of healthy adult women. The results of the current study suggest that the nurses; means of 8-OHdG was higher than healthy individuals. In several studies, many different biomarkers were used as indicators of DNA damage in the assessment of occupational exposure to ADs. CDC (2019) state that DNA damage is a sensitive and relevant endpoint to study because most antineoplastic agents target DNA. In this study, oxidative damage was reduced accordingly to increase the use of safe handling precautions.

In the present study, nurses' mean of TAC in the post-test was found to be significantly higher than pre-test and follow-up. The decrease of the 8-OHdG level due to the increase in the frequency of using nurses' safe handling precautions contributed to the increase of post-test TAC level. Thus, the antioxidant capacity of nurses increased in the post-test.

Strenghts and Limitations

This study has several strengths. It is the first study that used biological materials for evaluating oncology nurses' occupational exposure before education and after. Therefore, this study not only enabled knowledge of oncology nurses' occupational exposure but also evaluated the effect of the training program on preventing occupational exposure. This study had several limitations. Male nurses couldn't be included in the study because no male nurse was available in two of the clinics and no male nurse met the criteria for sampling in the other clinic. Also, this study included three clinics that had different cancer types, number of patients and chemotherapy doses. This situation was one of the important limitations of the current study. Despite these limitations, the current study has several important strengths. The current study is the first to assess the effectiveness of training in oncology nurses who handle ADs. Indeed, current study indicates that oxidative stress is high in oncology nurses

CONCLUSION

The effect of the training on the use of safe handling precautions of oncology nurses and the parameters of oxidative stress were evaluated in this study. All of the institutions included in the study had a safety program to minimize exposure to ADs. After the training, the frequency of using safe handling precautions in the preparation and administration of ADs significantly increased in the post-test. The training program provided a positive contribution to increase the use of safe handling precautions and reduce oxidative damage. This study showed that this training program, which is very economical when evaluated in terms of cost-effectiveness, may provide a very high benefit in shaping the behavior of nurses, especially for institutions that do not have enough budget for biomarker studies.

According to the results of this study, training program can be used to develop protective health behaviors to reduce occupational exposure. To evaluate the level of the use of safety programs of oncology nurses, developing validity and reliability measurement tools is recommended. Institutions should evaluate nurses' adaptation to safety

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p-ISSN: 2798-5059

programs and problems in adaptation with programs on a regular basis. To reduce the occupational exposure of nurses to ADS, institutions creating their own hazardous drug lists, regularly update their guidelines, and provide employees with adequate PPE recommended.

ACKNOWLEDGEMENT

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This work was funded by The Scientific and Technological Research Council of Turkey (TUBITAK), 1002 - Short Term R&D Funding Program (Project No:315S083)

Declaration of conflicting interests

The authors declared no potential conflict of interest with respect to the research, authorship, and/or publication of this article.

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