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Original article

Exposure to cytotoxic drugs threatens the health of staff in oncology wards

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Abstract: *Background* — Cancer is one of the leading causes of death worldwide. Using cytotoxic drugs for cancer treatment is increased. The hazardous effects of occupational exposure to cytotoxic drugs are challenging.
Objective — This study aimed to compare the frequency of adverse effects and using personal protective equipment (PPE) between the staff of oncology wards and other hospital wards staff in Iran.
Methods — A cross-sectional study with a control group was conducted on female staff members in educational hospitals, selected through convenience sampling. A data collection form was designed for this study. It includes demographic data, acute complications (allergic and neurologic reactions), chronic complications (infertility, menstrual disorders, malignancy, and congenital malformations), and use of PPE. Data analysis was performed using SPSS software through Chi-square and Mann-Whitney tests.
Results — The frequencies of chronic complications were not statistically different between the two groups. The frequency of itching (P=0.001), hair loss (P=0.003), itchy eyes (P=0.001), watery eyes (P=0.001), runny nose (P=0.003), headache (P=0.001), vertigo (P=0.007), and nausea (P=0.008) were significantly higher in oncology wards nurses. Among different PPE, only the frequency of using the mask (P= 0.001), and glasses (P=0.027) were significantly higher in the staff of oncology wards.
Conclusion — Despite the frequency of acute complications of exposure to cytotoxic drugs, oncology staff does not fully adhere to the standard precautions. Providing effective training and emphasis on implementing accreditation laws can improve the existing situation.

Keywords: occupational exposure, nurses, chemotherapy, neoplasms, personal protective equipment.

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Introduction

Nowadays, considering the advances in health science, somecancers are diagnosed at an earlier stage, and patients receive multiple chemotherapy agents for an extended length of time [1]. Cytotoxic drugs are therapeutic agents that affect cancerous and non-cancerous cells simultaneously. due to the teratogenic, mutagenic and carcinogenic effects of cytotoxic drugs, long-term exposure to them in the workplace is associated with adverse outcomes [2]. According to the International Agency for Research on Cancer (IARC), ten cytotoxic drugs are classified as carcinogenic agents for humans (Group 1), and ten cytotoxic drugs are classified as probable carcinogenic agents for humans (Group 2A) [3].

The frequency of adverse effects of occupational exposure to cytotoxic drugs varies between different staff members depending the duration and frequency of exposure to cytotoxic drugs, the toxicity of different drugs, and the vulnerability of each staff member [4-6]. Nurses who work in wards where cytotoxic drugs are used are at risk for the adverse effects of these drugs, including headache, nausea, vomiting, abdominal pain, skin irritation and dermatitis, hair loss, blood count decline, damage in peripheral lymphocytes, liver damage, reproductive disorders, congenital abnormalities, fetal loss, miscarriage, sub-fertility, low birth weight, and breast and rectal cancer [1, 6-9].

Most exposure to cytotoxic drugs in nurses is through inhalation and skin absorption [10]. On the other hand, several studies have demonstrated that work surfaces are contaminated with cytotoxic drugs even after they are cleaned [3]. Protecting health care workers from the adverse effects of cytotoxic drugs is challenging. International and national guidelines are provided to minimize the adverse occupational effects of cytotoxic drugs, but adherence to these guidelines is insufficient in developing countries, including Iran [9, 11, 12].

Some studies have demonstrated different signs and symptoms of adverse effects of cytotoxic drugs among nurses [13, 14]. Due to the importance of occupational safety, this study was conducted in Kerman, Iran, comparing the frequency of adverse effects of cytotoxic drugs among the oncology staff and staff who worked in other hospital wards. We also asked the staff about their safety behaviors.

Material and Methods

This cross-sectional study with a control group was conducted in Kerman, Iran, in 2019. All 37 female staff members, who worked

in the oncology wards of different public hospitals, including Afzalipour Hospital, Shahid Bahonar Hospital, and Javadolaemeh Clinic, were recruited for the study. Among other different wards of Afzalipour and Shahid Bahonar hospitals, 42 female staff members were selected as the control group using the convenience sampling method. Staff members with a history of chronic or mental disorders, those with a history of cytotoxic drug consumption, and staff who did not give consent to take part in the survey were excluded from the study. Also, staff with a history of working in the oncology wards were excluded from the control group. Due to the low number of male nurses, only female staff were included in the study.

After obtaining the ethical code (IR.KMU.AH.REC.1397.2742) from the Ethics Committee of Kerman University of Medical Sciences, the data collection process began. The data collecting form included the socio-demographic characteristics of staff (gender, marital status, educational level, work experience, type of employment, duration of working in the ward under study, income satisfaction, and job satisfaction), information about the skin disorders (itching, skin lesions, and hair loss), allergic reactions (itchy eyes, watery eyes, runny nose, sneezing, and chronic cough), neurologic reactions (headache, dizziness, nausea, and vomiting), and reproductive disorders (spontaneous abortion, stillbirth, congenital anomalies, infertility, low birth weight, irregular menstrual cycles, and abnormal uterine bleeding). Income satisfaction and job satisfaction were assessed with a 5-point Likert scale ranging from very low to very high. The survey also asked about the frequency of utilization of personal protective equipment (PPE), including gloves, gown, glasses, and masks by nurses.

The data were entered into the IBM SPSS software (version 20). The chi-square test, Fisher- exact test and the Mann-Whitney U test were used for analysis. The significance level was set at less than 0.05.

Table 1. Comparison of demographic variables between two groups of participants

Demographic Variable	Oncology wards		Other wards		P-value
	Median	IQR	Median	IQR	
Age (year)	28	11	28	10	0.755
work experience (year)	5	8	4.5	8	0.985
work experience in current ward (year)	2	7.5	2	2	0.297
	Frequency	Percent	Frequency	Percent	
Educational status					
≤16 years	5	14.3	2	3.9	0.086
>17 Years	30	85.7	49	96.1	
Marital status					
Married	26	74.3	32	37.3	0.262
Unmarried	9	25.7	19	62.7	
Job					
Nurse	31	88.6	37	72.5	0.073
Others	4	11.4	14	27.5	
Employment status					
Recruitment	16	47.1	28	54.9	0.478
Un recruitment	18	52.9	23	45.1	
Job satisfaction					
Yes	16	45.7	22	44.9	0.941
No	19	54.3	27	55.1	
Income satisfaction					
Yes	7	20	11	22.4	0.787
No	28	80	38	77.6	

Table 2. Comparison frequency of acute side effects between two groups of participants

Acute Side effects	*Oncology wards*		*Other wards*		*P-value*
	Frequency (%)	Percent	Frequency (%)	Percent	
Skin itching					
Yes	27	73	20	38.5	0.001
No	10	27	32	61.5	
Skin lesions					
Yes	18	48.6	16	30.8	0.087
No	19	51.4	36	69.2	
Hair loss					
Yes	17	45.9	9	17.3	0.003
No	20	54.1	43	82.7	
Eyes itching					
Yes	20	54.1	9	17.3	0.001
No	17	45.9	43	82.7	
Tearing					
Yes	20	54.1	8	15.4	0.001
No	17	45.9	44	84.6	
Nose discharge					
Yes	19	51.4	11	21.2	0.003
No	18	48.6	41	78.8	
Chronic Sneezing and coughing					
Yes	13	35.1	11	21.2	0.143
No	24	64.9	41	78.8	
Headache					
Yes	25	67.6	14	26.9	0.001
No	12	32.4	38	73.1	
Vertigo					
Yes	13	35.1	6	11.5	0.007
No	24	64.9	46	88.5	
Nausea					
Yes	14	37.8	7	13.5	0.008
No	23	62.2	45	86.5	
Vomiting					
Yes	7	18.9	5	9.6	0.225
No	30	81.1	47	90.4	

Results

In this study, 89 staff members were studied in two oncology wards (n=37) and other wards (n=52). There was no significant difference between the two groups in the median of age (P=0.755), work experience (P=0.985), and work experience in the current ward (P=0.297) (*Table* 1). The results also showed that demographic variables and other probable confounders, including educational status, marital status, job income satisfaction, job satisfaction, and employment status, were not significantly different between the two groups (*Table* 1).

The comparison of the acute side effects between the two groups is presented in *Table* 2. The results showed that 73% of the oncology staff and 38.5% of the staff in the other sections had skin itching, with a significant difference (P=0.001). Also, 45.9% of oncology staff and 17.3% of staff in other wards had hair loss, which was significant (P=0.003). Nearly 54.1% of oncology staff and 17.3% of staff in other wards had eye itching, which was significant (P=0.001). Approximately 54.1% of oncology staff and 15.4% of staff in other wards reported experiencing tearing (P=0.001). Nose discharge was reported by 51.4% of oncology staff and 21.2% in staff of other wards (P=0.003). Nearly 67.6% of the oncology staff and 26.9% of the other staff members reported having headaches, which showed a significant difference (P=0.001). The frequency of dizziness reported was 35.1% in oncology staff and 11.5% in staff in other wards, which was statistically significant (P=0.007). Approximately 37.8% of oncology

staff and 13.5% of staff in other wards reported having nausea which was statistically significant (P=0.001).

Comparison of frequency of pregnancy-related chronic fetal and neonatal side effects, menstrual disorders, and malignancy in the two groups showed no significant difference between the two groups. However, except for infertility, other side effects were higher in oncology staff than in other wards (*Table* 3).

The results showed that gloves and masks were the most common protective equipment used by all participants. Nearly 89.2% of the oncology staff and 42.3% of staff in other wards used the mask, which showed a statistically significant difference (P=0.001). Nearly 40.5% of oncology staff and 19.2% of the staff in other wards wore glasses which showed a statistically significant difference (P=0.027). The results showed no significant difference between the frequency of use of gowns and gloves in the two groups (*Table* 4).

Table 3. Comparison frequency of chronic gynecologic, obstetric side effects between two groups of participants

Chronic Side effects	Oncology wards		Other wards		P-value
	Frequency (%)	Percent	Frequency (%)	Percent	
Abortion					
Yes	6	23.1	3	9.4	0.274
No	20	76.9	29	90.6	
Stillbirth					
Yes	1	3.8	1	3.1	0.881
No	25	96.2	31	96.9	
Congenital malformation					
Yes	1	3.8	1	3.1	0.881
No	25	96.2	31	96.9	
Infertility					
Yes	1	3.8	3	9.4	0.620
No	25	96.2	29	90.6	
Low birth weight					
Yes	7	26.9	7	21.9	0.655
No	19	73.1	25	78.1	
Malignancy					
Yes	1	2.7	0	0	0.416
No	36	97.3	52	100	
Oligomenorrhea /Polymenorrhea					
Yes	19	51.4	20	38.5	0.227
No	18	48.6	32	61.5	
Hypermenorrhea /Hypo menorrhea					
Yes	17	45.9	18	34.6	0.281
No	20	54.1	34	65.4	

Table 4. Comparison frequency of PPE use between two groups of participants

Personal protective equipment	Oncology wards		Other wards		P-value
	Frequency (%)	Percent	Frequency (%)	Percent	
Gown					
Yes	14	37.8	12	23.1	0.131
No	23	62.2	40	76.9	
Mask					
Yes	33	89.2	22	42.3	0.001
No	4	10.8	30	57.7	
Glasses					
Yes	15	40.5	10	19.2	0.027
No	22	59.5	42	80.8	
Gloves					
Yes	35	94.6	46	88.5	0.319
No	2	5.4	6	11.5	

Discussion

To consider the confounding factors, the present study, assessed the frequency of demographic factors, job and income satisfaction, and socioeconomic factors in the two study groups, revealing no significant difference between them. Comparing the frequency of acute side effects showed that the frequency of skin and allergic reactions (except for sneezing and chronic cough) and neurological reactions (except for vomiting) were significantly higher in oncology personnel than in others. Worthington (2000) showed that nurses who had been exposed to cytotoxic drugs for a long time without adequate protection experienced several side effects such as dizziness, headache, hair loss, allergic reactions, nausea, respiratory disorders, liver fibrosis, bladder cancer, leukemia, and reproductive system damage [15]. Also, other studies reported the experience of different acute side effects by nurses who worked in oncology wards, including headache, nausea, vomiting, abdominal pain, dermatitis, allergic symptoms, and hair loss [6-9, 13, 16]. Lack of a control group is a limitation of some cross-sectional studies on occupational exposure to cytotoxic drugs. The use of a control group and adjusting confounders in the present study enabled us to compare the frequency of acute side effects in oncology ward personnel with personnel of other wards. Considering these occupational hazards, the occupational health system of hospitals should monitor and evaluate the personnel of chemotherapy wards with more precision.

Comparing the frequency of chronic side effects between the two groups showed that none of these chronic side effects was significantly different between the two groups. However, except for infertility, other cases were more common in oncology staff than in other staff. Several studies have shown that occupational exposure to cytotoxic drugs has genotoxic effects, and is able to change genetic biomarkers [17-19]. The results of a systematic review showed an association between occupational exposure to cytotoxic drugs and spontaneous abortion [4]. Also, one review study showed that occupational exposure to cytotoxic drugs is associated with an increased risk of miscarriage, congenital malformations, and infertility [7]. The results of a cohort study showed an increased incidence of breast and rectal cancer in women with occupational exposure to cytotoxic drugs [20]. In this study, most of the chronic side effects were more common in oncology staff, but there was no significant difference. Some confounding factors, including the history of polycystic ovary syndrome and other factors affecting the menstrual process, could affect the significance of the results.

On the other hand, the average experience in the oncology ward in the study subjects was two years. Therefore, one reason for the insignificant difference in the frequency of these side effects betweeb the two groups was probably the relatively short exposure to cytotoxic drugs. In this study, a significant number of personnel were single, so they were not included in analyzing data on the frequency of side effects associated with neonatal and fetal malformations. During analysis, the low sample size can reduce the difference in the frequency of side effects between the two groups. Despite the differences in results, most studies emphasize the carcinogenic, teratogenic, and mutagenic effects of cytotoxic drugs. Therefore, it is vital for oncology ward health care workers to follow standard precautions.

The use of PPE by personnel was compared in the two study groups, which showed that oncology personnel were significantly

more likely to use masks and glasses than other personnel. The frequency of use of gowns and gloves were not significantly different between the two groups. Different principles and guidelines were developed to protect occupational contact with cytotoxic drugs by the Australian Oncology Society, the American Hospital Pharmacologists, and the American Oncology Nurses Association [21]. In the present study, among the oncology personnel, 37.8% used gowns, 89.2% used masks, 40.5% used glasses, and 94.6% used gloves. There were significant differences between oncology ward nurses and other nurses in relation to wearing a masks and glasses. Evaluating the oncology nurses at Shiraz University of Medical Sciences (2013) showed that the frequency of using gowns, masks, glasses, and gloves were 73%, 90%, 71%, and 95%, respectively (12). Evaluating the outpatient and office-based oncology nurses in the United States (2003) showed that nearly 94% of nurses usually wore gloves, but less than 6% of them usually used respiratory and face protection equipment [22]. One study among chemotherapy ward nurses in Isfahan, Iran, reported the frequency of using gowns, masks, glasses, and gloves as 58.9%, 79.5%, 58.9%, and 100%, respectively [23]. Comparing the frequency of using PPE in different oncology settings in Iran demonstrated that PPE compliance is not acceptable among Kerman hospital oncology ward nurses. Also, other nurses in Kerman hospitals did not comply with PPE use standards. Policy-makers should promote nurses' knowledge of and attitude to PPE use. Implementing and evaluating the efficacy of precaution regulations in hospitals is essential to protect personnel from occupational hazards.

One of the strengths of the present study is using a control group to evaluate the side effects of chemotherapy in oncology staff. However, the cross-sectional nature of this study, the need for prolonged exposure time for the occurrence of chronic side effects, lack of control over all confounding factors, and the small sample size were the limitations of this study. Future longitudinal studies with a larger sample size and follow-up period are recommended to investigate the long-term effects of exposure to chemotherapy drugs.

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Conflict of interest

None declared

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