



Safe Handling of Cytotoxic Drugs and Risks of Occupational Exposure to Nursing Staffs

Somayeh Hanafi¹, Hassan Torkamandi¹, Sahar Bagheri², Maria Tavakoli³, Naser Hadavand⁴, Mohammadreza Javadi^{5*}

¹Pharmaceutical Care Department, Dr.Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran.

²School of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran.

³Clinical Pharmacy Department, School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

⁴Rajaie Cardiovascular Medical and Research Center, Iran University of Medical Sciences, Tehran, Iran.

⁵Pharmaceutical Care Department, Dr.Shariati Hospital and Research Center for Rational Use of Drugs, Tehran University of Medical Sciences, Tehran, Iran.

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ABSTRACT

Background: Inherent toxicity of cytotoxic drugs is the basis for their potential adverse risks from occupational exposure to the nursing staff. In Iran, chemotherapy regimens are prescribed and administered according to the world updated protocols. But little is done regarding the protective standards in this field.

Methods: An observational cross-sectional survey was conducted among nurses who work in three tertiary care teaching hospitals in Tehran, Iran in 2012. All participants worked in one of the hospital wards handling cytotoxic drugs (preparation and administration). A questionnaire was used for interviewing all subjects, and observing them preparing and administering the drugs. We examined all adverse effects associated with handling of antineoplastic drugs.

Results: Totally 270 adverse reactions were reported. The most frequently reported adverse effects included headache and vertigo (40 cases), hair loss (36 cases), skin rashes and itching (31 cases), and burning sensation in eyes (31 cases). In all hospital wards, the standards were met in not more than 50% of the items.

Conclusion: Monitoring the personnel who are directly involved in handling of cytotoxic drugs is of great importance. Furthermore, educating the personnel in the field of standards of cytotoxic drugs handling could increase the nursing staff's knowledge regarding these drugs' adverse reactions.

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Introduction

Cytotoxic is often used to refer to any agent that may be hazardous to the cells in any way. Cytotoxic drugs are therapeutic agents mostly used for the treatment of

cancer (1). Side effects of cytotoxic drugs (e.g. immune suppression, nausea, and hair loss) are due to damage to these cells (2). Inherent toxicity of these drugs is the basis for their potential adverse risks from occupational exposure to them. If employees are exposed to these drugs, even the therapeutic doses which patients receive could cause the same effects. Cytotoxic drugs are genotoxic, carcinogenic, teratogenic and could cause developmental toxicity (3, 4). Related studies found the relationship between exposure

* Corresponding Author: Dr Mohammadreza Javadi

Address: Pharmaceutical Care Department, Dr. Shariati Hospital, Kargar St., Tehran, Iran, Tel: +982184902364, Fax: +982188220025.

Email: mrjavadi@sina.tums.ac.ir

to cytotoxic drugs and acute adverse reactions: urine mutagenicity (5); skin disorders (6); fetal loss during the first trimester of pregnancy (7); spontaneous abortion (8); malformations (9) and genotoxicity (10).

The routes of exposure with cytotoxic drugs may include inhalation of aerosols, particulates and droplets; skin or eye contact through splash of liquids; ingestion through poor personal hygiene or splash of liquid and injection resulting from injuries from sharps (5). High risk activities related to cytotoxic drugs may include preparation, administration, cleaning spills of drugs, and handling patients' liquid discharges (11).

In 1983, the Occupational Safety and Health Administration (OSHA) and American Society of Health System Pharmacists (ASHP) released recommendations on preventing accidental contacts with cytotoxic drugs (5). For the first time in 1990, ASHP published its revised technical assistance bulletin on handling cytotoxic and hazardous drugs (12). In most hospitals in Iran, there are not any national guidelines and usually specific instructions have been made by using other countries' drug leaflets and published guidelines regarding safe handling of cytotoxic drugs. In addition pharmacists in Iran do not monitor the process of cytotoxic drugs preparation in the hospitals officially. Evaluation of standard procedures implementation in hospital wards involved in cytotoxic drugs handling, and assessment of adverse drug reactions of these drugs is the main goal of this study.

Methods

An observational cross-sectional survey was conducted among nurses working in three tertiary care teaching hospitals in Tehran, Iran in 2012. Of 86 nurses working in cancer care wards in these hospitals and are involved in handling of antineoplastic agents, who were asked to participate in this survey, 78 nurses were included in our study and 77 of them completed the questionnaires, giving a response rate of 98.7%.

In 1990, ASHP published its technical assistance bulletin on handling cytotoxic and hazardous drugs. Also OSHA issued new guidelines on controlling occupational exposure to hazardous drugs in 1995. The questionnaire in our study was designed according to the recent guidelines of OSHA and ASHP to evaluate the knowledge, attitudes and safe behaviors of nurses' handling cytotoxic drugs. The questionnaire was translated from English to Persian. The validity of the questionnaire was assessed through feedback from a panel of experts who reviewed the questionnaire and confirmed it.

The first part of the questionnaire included participants' socio demographic information such as age, gender, marital status, education, years of working experience as an oncology nurse, type of activity in the ward (drug preparation, administration, NG tube replacement,...), pregnancy history, infertility history, cancer family

history and history of suspected adverse drug reactions due to chemotherapeutic exposure.

The second part included 18 questions (first goal) regarding knowledge about protection against hazardous drugs. The second goal included 16 questions about education in the field of standard procedures regarding preparation and administration of cytotoxic drugs and protection protocols against their toxic effects. The third to sixth goals of the questionnaire were respectively related to these issues: prevention of accidental contacts with cytotoxic drugs (32 items), discarding cytotoxic drugs (15 items), handling the spillage of cytotoxic drugs (18 items), and clean room (18 items).

The questionnaires were filled in by interviewing all subjects, observing them preparing and administering the cytotoxic drugs and also asking the patients' caregivers. Each correct answer in Yes/No/Not Available items and multiple-choice items received one score. Confidentiality was ensured by anonymity of the participants.

The knowledge of nurses toward cytotoxic handling was determined through another questionnaire. The questions were about standards of working such as garbing, safe compounding, spills, side effects and wastes. For number of 15 questions, each nurse was interviewed for 30 minutes personally. All questions were multiple choices (2 or 4 choices).

Statistical analysis

For presenting the results, both descriptive and analytical statistics were used. Data were analyzed using the Statistical Package for Social Sciences 17.0 (SPSS). Independent sample t-tests and chi-square tests were used to compare differences in safe practices as a result of their knowledge. The level of significance was considered at 0.05.

Results

This survey was conducted in three tertiary care teaching hospitals in Tehran which had clinic, oncology and hematology wards. Eighty three percent of the nurses were female, and 88.3% of them had Bachelor degrees in Nursing. The mean age of the participants was 35 years and their mean working experience was more than six years. All the participants worked in one of the hospital wards handling cytotoxic drugs (preparation and/or administration). Table 1 shows the characteristics of these three hospitals. The most frequent cancer types in participants' family history of different cancers were colorectal cancers (51.7%), lymphoma and leukemia (8 cases), ovarian and uterine cancers (4 cases), and breast cancer (3 cases).

We examined all adverse effects associated with handling of antineoplastic drugs. Totally 270 adverse reactions were reported. The most frequently reported adverse effects included headache and vertigo (40 cases),

Table 1. Characteristics of the hospitals.

Hospital	Wards No.	Beds No.	Nurses No.	Cytotoxic regimens
Hospital No.1	3	36	24	Busulfan, Melphalan, Paclitaxol, Methotrexate, Cytarabine
Hospital No.2	3	60	20	Methotrexate, Cytarabine, 5-FU
Hospital No.3	4	87	33	5-FU, Oxaliplatin, Rituximab, Cisplatin, Docetaxel, Taxol, Gemcitabine

Table 2. The situation of standards for each goal in the hospitals.

Standards of the goals	Hospital No.3	Hospital No.2	Hospital No.1
First goal (18 questions)	E	E	E
Second goal (16 questions)	B	C	C
Third goal (32 questions)	C	C	C
Fourth goal (15 questions)	C	D	D
Fifth goal (18 questions)	E	E	E
Sixth goal (18 questions)	E	E	E

A. Meet 80-100% of the total items (excellent)

B. Meet 60-80% of the total items (good)

C. Meet 40-60% of the total items (acceptable)

D. Meet 20-40% of the total items (bad)

E. Meet 0-20% of the total items (very bad)

hair loss (36 cases), skin rashes and itching (31 cases), and burning sensation in eyes (31 cases). Figure 1 shows the frequency of the adverse drug reactions due to handling of cytotoxic drugs in three hospitals.

Nurses reported that adverse reactions happened mostly due to preparation of cytotoxic drugs rather than the nurses' presence in the wards. Skin rashes, itching and burning sensation in eyes were reported after direct contact with cytotoxic drugs. All of the adverse reactions except hair loss and anemia were temporary. Fortunately the majority of the adverse reactions were resolved during 1 to 7 days. The only exception was "hair loss" untreatable in more than 80% of the afflicted cases (29 cases out of 36). The incidence of adverse reactions related to reproduction was less than 3 percent (2.6%). Since preparation of all cytotoxic drugs was done simultaneously under the laminar airflow, no relationship was found between the type of cytotoxic drug and adverse reaction type. Table 1 also shows which cytotoxic drugs in each of the three hospitals were suspicious of causing the reported adverse reactions.

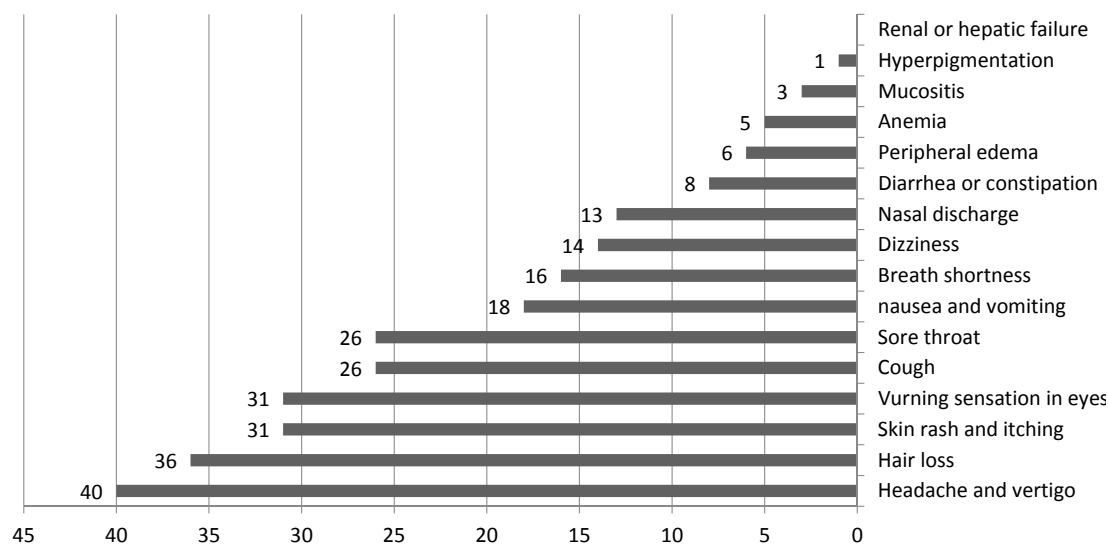
Only 52% of the standards of education were met in our settings, and the knowledge level of the nursing staff was about 65%. Total number of 117 items was assessed in 6 main goals. Tables 2 shows how many standards for each goal are met in each of the hospital wards.

As the results show, in all hospital wards, the standards were met in not more than 50% of the items. Regarding the first goal (protect and secure packages of

hazardous drugs), since the patients procure packages of drugs themselves, it would be impossible to meet the standards of this goal in our settings. Furthermore, in most of the cases since the administered dose is different from the available dosage forms, adjusting the dose of the drug would be problematic for the nursing staff because nurses would be exposed to the drugs more. Considering the second goal (inform and educate all involved personnel about hazardous drugs and train them in the safe handling procedures relevant to their responsibilities), no nurse was educated before starting her work in one of the chemotherapy related wards. Generally, new nurses are unofficially educated by the experienced nursing staff. In all three hospitals, some patient education leaflets were prepared for patients receiving chemotherapy regimens. Regarding the third goal (prevent accidental contamination of health-care professionals and patients with hazardous substances), protective measures were not fully available in the wards, and in the cases where they were available the personnel didn't use them regularly. In other words, some standards like wearing a disposable closed-front gown and disposable latex gloves were met, but hair and shoes coverings, and special materials for absorbing the spills were not available in the wards. Regarding the fourth goal (preparing the hazardous drugs for disposal), in all three hospitals, although there is theoretically an emphasis on separate disposal of these substances' waste, the standards are not met at all. There were no

Table 3. The knowledge of nurses toward cytotoxic drugs handling.

Score of knowledge	Hospital No.3	Hospital No.2	Hospital No.1	p-value
	64.5%	67.1%	65.3%	0.66

**Figure 1.** Frequency of the adverse drug reactions in three hospitals.

thick sealable plastic bags in the wards for disposal of cytotoxic drugs and the waste materials were not transferred to a hazardous waste dump site. Considering the fifth goal (prevention of accidental spills), there was no special material to clean up spills of hazardous drugs and personnel were not trained in their proper use. In other words, no standard cleanup protocol was established in the wards. According to the sixth goal's standards, all cytotoxic drugs should be prepared under class II laminar air-flow in a cleanroom. Since there was no cleanroom in the wards, none of the standards was met and all drugs were prepared under class II vertical laminar airflows in the wards' treatment rooms.

The results showed that the level of nurses' knowledge in three hospitals was the same approximately (Mean=65%, $p>0.05$). Score of knowledge was entered in the regression model with independent variables and none of the variables (such as demographic variables and job related variables) influenced on nurses' knowledge. (Table 3)

Discussion

The results of our study showed that most of the reported adverse reactions were due to drug preparation procedures.

One of the most prevalent adverse reactions of cytotoxic drugs handling in nursing staff was burning sensation in the eyes, while most of the nurses don't wear protective goggles during preparing the drugs. Also the majority of the experienced nurses mentioned inflammation in their mouth which shows that simple 3-layered masks are not as protective as surgical masks.

Although in our study, only nursing staff are involved in preparation, handling, and administration of the cytotoxic drugs, according to recommendations released by the OSHA, preparation, handling, and administration of the cytotoxic drugs should be done by health-care personnel including physicians and nursing staff (5). In a study by Ishii and Dakeishi in Japan, it was shown that 88% of the personnel who were involved in handling, preparation and administration of cytotoxic drugs were nurses, and the remaining 12% were physicians and pharmacists (13). While guidelines for safe handling of chemotherapy drugs and their occupational risks have been available for more than 30 years, evidence for worker exposure is still being reported (14). Literature shows that nursing staff are still unable to implement the safety standard guidelines for handling cytotoxic drugs (15). Similarly, Ben-Ami showed that there is a gap between nurses' knowledge

and real practice towards safe handling of cytotoxic drugs (16). Turk and Davas in 2004 showed that nurses' knowledge of chemotherapy drugs' adverse reactions is not at an acceptable level. They recommended educational programs to increase their knowledge regarding this issue (17). Likewise, the results of our study also showed that the average of knowledge score about cytotoxic drugs handling, preparation and administration was 65.5 out of 100. Also in all wards, each standard was met in less than 50% of its items. Considering the environmental contamination of cytotoxic drugs, educating the personnel about the standard protocols for handling these drugs could be considered a high priority necessity which could decrease their adverse reactions among personnel involved in their preparation and administration (18). OSHA in 2004 showed that standard protective measures against chemotherapy drugs are implemented limitedly (19). Also the results of a study on nurses working in a medical university of Nepal showed that chemotherapy drugs were prepared in nursing stations where there were no laminar airflow hoods (20). Similarly, the results of our study showed that only less than 50% of the whole standards are met.

Monjamed and Parsayekta in 2000 evaluated the quality of care for patients in chemotherapy wards of hospitals affiliated to Tehran University of Medical Sciences. The results showed that the physical structures of the wards, preparation (45.18%), administration (7.7%), and disposal (26.03%) of cytotoxic drugs were less than standard levels (21). It has also been shown that the personnel involved in cytotoxic drugs handling, are not precautious enough when exposed to these drugs. This would be due to their lack of knowledge and being uneducated in this regard (21). The cornerstone of all guidelines for cytotoxic drugs preparation, storage, transport, administration, and waste disposal is the training and education of health care providers (22).

There are some limitations in our study. The first one is unconformity of data gathering sources with interviewers' observations. The second limitation is related to the cytotoxic drugs simultaneous preparation under the laminar air flow. Consequently, it is impossible to pinpoint which drug is directly responsible for causing which adverse reaction.

In conclusion, availability of necessary devices for meeting the standards and educating the personnel for using these devices are two important issues in the field of cytotoxic drugs handling. Monitoring the personnel who are directly involved in handling of cytotoxic drugs by national standard guidelines is of great importance. Furthermore, educating the personnel in the field of standards of cytotoxic drugs handling could increase the nursing staff's knowledge regarding these drugs'

adverse reactions.

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