

Health Hazards among Oncology Nurses Exposed to Chemotherapy Drugs

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ABSTRACT

AIM To determine the health hazards among nurses exposed to chemotherapy drugs; identify potential risk factors that may predispose nurses to chemotherapy hazards; and evaluate available protective measures used in clinical practice.

METHODS This was an analytical cross sectional study carried out during six months from February 2006 to July 2006 at Mansoura University hospitals. A study group of 35 oncology nurses and a control group of 29 non-oncology nurses were compared for safe behavior, use of protective measures while dealing with drugs, complaints due to drug exposure and mutagens in urine. Three tools were used in the study: a self administered questionnaire, a performance checklist to assess the practice of nurses, and Ames test for the detection of mutagens in urine.

RESULTS Health hazards among the study group and controls were: abortions (31.4% vs 10.3%), infertility & sub-fertility (14.3% vs 3.4%), premature labour (14.3% vs 17.2%), soft tissue injuries due to spills & splashes (14.3% vs 0.0%), and developmental and behavioral abnormalities among the children of the nurses (8.6% vs 3.4%). Urine samples from study nurses were more mutagenic than controls (40% vs 10.3%). Risky behaviour among study nurses included: eating food in drug handling areas (45.7%), use of improper place for preparing and handling cytotoxic drugs, expelling air from syringes filled with drugs, needle stick injuries, unsafe handling of contaminated material and unsafe cleaning of spills. Only 22.9% of the study nurses attended a training program about occupational health and safety and 8.6% of them mentioned that there are nursing care guidelines for procedures for dealing with patients receiving cytotoxic drugs as well as presence of in-service training programs. There was poor use of protective equipment in the study group.

CONCLUSION This study revealed poor safety and significant adverse events among nurses handling cytotoxic drugs. There is, therefore, a need to improve the safety of the work environment; make available protective equipment; develop standard practice guidelines for oncology nurses; implement good planning and design of the workplace; provide adequate specialized equipment (such as cytotoxic drug safety cabinets) and personal protective equipment; establish clinical pharmacy practice; and integrate health monitoring programs that include the assessment and counseling of prospective nurses before they commence any work involving cytotoxic drugs and related waste.

Keywords: Health hazards; Medical oncology; Nurses; Cytotoxic agents; Mutagens

INTRODUCTION

Drugs have a successful history in treating illnesses, and they are responsible for many of our medical advances. However, virtually all drugs have side effects associated with their use by patients, and both patients and nurses who handle them are at risk of suffering these effects that might result from exposure to even very small concentrations of certain hazardous drugs.¹ Many antineoplastic drugs are known to be carcinogenic, teratogenic and mutagenic to humans. There is thus a potential occupational exposure risk to cytotoxic drugs (CDs). Nurses are among the main groups of professionals that are exposed to these drugs in patient care settings.¹

Although the potential therapeutic benefits of hazardous drugs outweigh the risks of side effects for ill patients, exposed nurses risk these same side effects with no therapeutic benefit.² Among the possible chronic effects of CDs are cancer, fertility problems, and long term genetic changes in offsprings, abortion and abnormalities in the fetus.³

Today cancer patients are diagnosed earlier than before, and many receive multiple courses of chemotherapy for a longer period of time.³ Awareness of toxic effects of cancer chemotherapeutic drugs typically influences treatment plans for patients undergoing cancer therapy to prevent or mitigate adverse outcomes. However, beyond the patient safety concerns arising from the necessary therapeutic use of these drugs, occupational risks to health care workers handling these drugs in the course of their duties still need to be fully addressed.⁴⁻⁵

Exposures to hazardous drugs may occur through inhalation, skin contact, ingestion, or injection. Inhalation and skin contact, inappropriate hygienic behaviors such as eating, drinking or smoking during preparation, administration, or disposal of CDs⁶ are wrong behaviours that increase the risk of exposure.

Studies have demonstrated an increase in the potential risks due to occupational exposure to CDs. Despite current work practice guidelines, nurses exposed to hazardous drugs still experience serious side effects that are influenced by: drug handling

circumstances (preparation, administration, or disposal), amount of drug prepared, frequency and duration of drug handling, potential for absorption, use of ventilated cabinets, personal protective equipment (PPE) and work practices.^{3,7-8} Compliance with guidelines for handling CDs has been reported to be sporadic.⁹⁻¹⁰ In addition, measurable concentrations of some hazardous drugs have been documented in the urine of health care workers who prepared or administered them, even after safety precautions had been employed.¹¹⁻¹² Environmental studies of patient-care facilities have documented measurable concentrations of drug contamination, even in settings thought to be following recommended handling guidelines.¹¹⁻¹⁴ An oncology nursing station is the site where drugs are administered to the patient. Although the primary function of the oncology nurse is to administer the drugs, in some instances drugs may also be prepared at this site due to absence of clinical pharmacy facilities. Most drugs are given to the patient through an intravenous (IV) drip, but some drugs are “pushed” via a syringe. In either case, drug administration poses a risk to the nurse from a spill or release from the IV bag or through a pressured release during the drug “push”. Drug administration to patients requires the same personal protective wear as used by pharmacists in the event of a spill or other unplanned release.

Although there has been an increased awareness and concern regarding the issue of safe handling of CDs, many nurses may still not follow the guidelines and procedures in the hospital settings and may not use the recommended safety equipment.^{3-5,7-8,15} In our hospital nurses are especially exposed while preparing and administering CDs. For that reason the need to provide nurses with information about possible toxicities and required protection measures is very high.

This study set out to determine health hazards among nurses exposed to CDs, identify potential risk factors, and evaluate available protective measures used in clinical practice.

METHODS

This was an analytical cross sectional study carried

out during six months from February 2006 to July 2006 at Mansoura University hospitals. A study group and a control group of nurses were recruited. The study group included 35 oncology nurses who were involved in direct patient care and were exposed to CDs during their preparation and administration. This was composed of 19 nurses from an adult oncology center and 16 from a paediatric oncology department. Nurses who worked for less than 10 years in oncology departments and those who refused to give consent for the study were excluded. The control group consisted of a convenience sampling of nurses of the same sex and within the same age brackets of the study group. It included 29 nurses, 10 from a surgical department; 11 from a general medical department and 8 from a chest medicine department. These nurses were involved in direct patient care without being exposed to CDs. Both groups were in the same hospital management structure and had more than 10 years experience, without change in position over the past 10 years. All participants signed an informed consent.

Three tools were used in the study: a self administered questionnaire, a performance checklist to assess the practice of nurses, and Ames test for the detection of mutagens in urine. The self administered questionnaire included: general information on the subject's demographic characteristics such as age, education, and marital status. It also included number of years in the nursing profession; personal, occupational and exposure history; safe behavior while dealing with CDs; complaints due to CDs exposure and the source of information on CDs. The questionnaire also covered experience in chemotherapy handling, level of current activity, relevant training and organisation concerns, nursing risky behavior and risky practice. Participants were asked to report their use of protective measures during exposure to CDs, health hazards due to unsafe practice of CDs and level of accidents over the past year. The performance checklist was developed to assess the practice of the study group and validate their application of knowledge gained in actual practice and use of protective measures while being exposed to CDs. The tools were constructed and developed by the researchers after reviewing related literature. The questionnaire sheet was tested

for content validity and discussed in a specialists panel and some of the unclear and ambiguous questions were modified according to the results.

Permission to carry out the study was obtained from the hospital research and ethics committee. The researchers emphasized that the participation was absolutely voluntary and confidential, and ensured anonymity, privacy, and safety of the subjects throughout the study. Participants had the right to withdraw at any time from the study. A pilot study was carried out on 9 nurses, not included in the main study to test the feasibility and applicability of the questionnaire sheet.

The practice of study group nurses was observed over a period of half a day during morning and afternoon shifts in different clinical settings for one week to evaluate their application of knowledge gained in actual work practice and use of protective measures while being exposed to CDs. Both groups were asked to collect a 24-hour urine sample for detection of mutagens in urine by Ames test. Urine mutagenicity was tested using amino acid-dependent strains of salmonella typhimurium. Two strains were used TA 98, TA 102 (histidine).¹⁸⁻²⁰

Variables studied were categorical and were represented as percentages. Comparisons between the study group and control group were achieved using the chi square test with continuity correction if indicated. Comparisons within groups were done by McNemar test. The threshold of significance was fixed at the 5% level.

RESULTS

Sixty four nurses participated in this study; 35 as a study group and 29 as controls. More than half of the nurses in the study group were in the age group 30-40 (54.3%) compared to 51.7% in the control group. The majority of the study group nurses (85.7%) had diploma degrees compared to 86.2% in the control group. Seventy one point four percent of the study group nurses worked in the profession more than 20 years compared to 75.9% of the control group. More than three quarters (88.6%) of the study group nurses were married compared to 93.1% among the control

group. Fifty seven point one percent of the study group nurses dealt with CDs every shift and 42.9% of them dealt with CDs every day. The two groups showed no statistical differences between them in relevant characteristic variables (Table 1).

Abortions were the most common health hazard among the study group nurses (22.6%) compared to 10.3% among the control group nurses. This was followed by infertility & sub-fertility (14.3% and 3.4%) and represented 2.9% before exposure to CDs among the study group nurses. Other health hazards were premature labour (11.4% vs 5.7%) and soft tissue injuries due to spills & splashes (14.3% vs 0.0%). The least common health hazard was developmental and behavioral abnormalities among children of the study nurses (5.7% vs 0.0%), Table 2. All differences between the 2 groups were statistically significant ($p < 0.05$) with the exception of low birth weight and menstrual disturbances that were higher among the study group nurses but not statistically significant. Some of these side effects also occurred before exposure but at lower rates that were comparable to rates among the control group.

A total of 14 (40%) urine samples were mutagenic being positive for either strain among study group nurses compared to 3 (10.3%) in controls ($P < 0.001$). Positivity for each strain was significantly higher among study group nurses compared to the control group ($p < 0.001$). Positivity for tester strain TA 98 was detected in 28.6% of study group nurses compared to 6.9% of control group nurses. Positivity for tester strain TA 102 was detected in 11.4% of samples of study group nurses compared to 3.4% for non exposed nurses, Table 3.

Eating food in drug handling areas was the most common risky behaviour among study group nurses (45.7%), followed by drinking beverages (37.1%). Improper place for preparing and handling CDs as well as expelling air from syringes filled with CDs were the commonest risky nursing activity while preparing and administering CDs, representing 71.4% followed by needle stick injuries 54.3% and contaminated hands and poor hand washing (51.4%). The least risky nursing activities were counting uncoated oral tablets from multi-dose bottles, collection of blood, urine and stool samples

and crushing or breaking tablets to make oral liquid preparations, 14.3% each. Handling contaminated material generated during the preparation and administration process and cleaning spills were also common risky nursing activities (40%) as were handling body fluids or body-fluid-contaminated clothing, dressings, linens, and other materials (11.4%), Table 4.

Few study group nurses attended training programs about occupational health and safety (22.9 %). Only 8.6% of the study group nurses mentioned that there is nursing care standard guideline for procedures for CDs as well as presence of in-service training programs, Table 5.

Gloves were used when handling patient waste by 42.9% of study group nurses and 25.7% of them used gloves while cleaning up spills. Thirty one point four percent of the nurses used gowns when handling patients' waste. Mask and eye protection were not used during nursing care activity, Table 6.

DISCUSSION

Today cancer patients are diagnosed earlier than in the past, and many receive multiple courses of chemotherapy for a longer period of time.¹⁶ The toxic effects of anticancer chemotherapy are well known to oncology specialists and to primary care clinicians. Awareness of these effects typically influences treatment plans for patients undergoing cancer therapy to prevent or mitigate adverse outcomes. However, beyond the patient safety concerns arising from the necessary therapeutic use of these drugs, there is evidence to show that nurses who prepare and administer antineoplastic drugs suffer these effects and have higher indicators of mutagenic substances in their urine compared with non exposed workers.¹⁷

The present study was carried out to determine the health hazards among nurses exposed to chemotherapy drugs, identify potential risk factors that may predispose nurses to chemotherapy hazards, and to evaluate available protective measures used in clinical practice.

The findings indicate a higher frequency of several health hazards among exposed nurses compared to

Table 1: Characteristics of Participants

Characteristic	Study group n= 35		Control group n= 29	
	No.	%	No.	%
Age group (years)				
20-30	11	31.4	10	34.5
30-40	19	54.3	15	51.7
40-45	5	14.3	4	13.8
Position				
Supervisor	6	17.1	4	13.8
Staff nurse	29	82.9	25	86.2
Qualification				
BSc nursing	5	14.3	4	13.8
Diploma	30	85.7	25	86.2
Marital status				
Married	31	88.6	27	93.1
Single	3	8.6	2	6.9
Divorced	1	2.9	-	-
Duration in the profession (years)				
10-20	10	28.6	7	24.1
more than 20	25	77.1	22	75.9

controls. These include abortions, infertility & sub-fertility, premature labour, soft tissue injuries due to spills & splashes, fetal loss as well as congenital malformations, and developmental and behavioural abnormalities in offsprings. Many surveys have associated workplace exposures to antineoplastic drugs with adverse reproductive outcomes including infertility, spontaneous abortions, and congenital malformations.^{9,11-14,16-22}

A meta-analysis of 14 studies performed from 1966 to 2004 in the United States and Europe described an association between exposure to antineoplastic drugs and adverse reproductive effects in female health care workers.²³ The most common reproductive effects found in these studies are increased fetal loss, (21.2%) congenital malformations (23%), low birth weight and congenital abnormalities (24%) and infertility (25%). In this meta-analysis, no significant association was detected between exposure to antineoplastic drugs and congenital malformations and stillbirths. However, a significant association was identified between exposure and spontaneous abortions. A number of other endpoints has elevated

Table 2: Health Hazards among Participants

Hazard	Study group n=35		Control group n=29	
	No.	%	No.	%
Abortions				
Before exposure	3	8.6	1	3.4
After exposure	8	22.6	3	10.3
Infertility & sub-fertility				
Before exposure	1	2.9	1	3.4
After exposure	4	11.4	1	3.4
Premature labour				
Before exposure	-	-	-	-
After exposure	4	11.4	1	3.4
Soft tissue injury due to spills & splashes				
Before exposure	-	-	-	-
After exposure	4	11.4	-	-
Menstrual changes				
Before exposure	-	-	-	-
After exposure	3	8.6	2	6.9
Fetal loss				
Before exposure	1	2.9	-	-
After exposure	3	8.6	1	3.4
Congenital malformation				
Before exposure	-	-	-	-
After exposure	3	8.6	1	3.4
Low birth weight				
Before exposure	-	-	-	-
After exposure	3	8.6	2	6.9
Developmental & behavioral abnormalities				
Before exposure	-	-	-	-
After exposure	2	5.7	-	-

Before exposure = before exposure to cytotoxic drugs (CDs) for exposed group and before employment condition for non exposed group; After exposure = after exposure to CDs for exposed group and after employment condition for non exposed group.

responses, but are not statistically significant. A study from China that was not included in the meta-analysis reported a significant decrease in full-

Table 3: Results of Ames test for urine mutagens

Parameters	Study group n= 35		Control group n= 29	
	No.	%	No.	%
Mutagenic strain				
TA 98 + ve	10	28.6	2	6.9
TA 102 + ve	4	11.4	1	3.4
Total	14	40.0	3	10.3

Differences are significant at $p < 0.001$

term births and significant increases in premature birth, spontaneous abortion, and congenital malformations in nursing personnel who were exposed to antineoplastic drugs.²⁴ A study by Martin²⁵ documented learning disabilities in the children of nurses who had handled antineoplastic drugs during the course of their employment.

A case controlled study examined the relationship between fetal loss and occupational exposure to antineoplastic drugs in nurses in 17 Finnish hospitals. A statistically significant association was observed between fetal loss and occupational exposure to antineoplastic drugs during the first trimester of pregnancy (odds ratio 2.30, 95% confidence interval 1.20-4.39).^{17,26}

Table 5: Study group relevant training and organizational aspects

Aspect	No	%
Attended training program		
Occupational health and safety	8	22.9
Hazards of exposure to CDs and relevant safety measures	7	20.0
Organizational aspects		
Presence of written nursing care guidelines for procedures for dealing with patients receiving CDs	3	8.6
Presence of in-services training program	3	8.6

Table 4: Study group risky nursing activities

Activity	No.	%
Risky behaviour in handling areas		
Eating food	16	45.7
Drinking beverages	13	37.1
Storing food and beverages & using cosmetics	6	17.1
Risky nursing activity: Preparing and administering CDs		
Improper place for preparing and handling CDs	20	57.1
Expelling air from syringes filled with CDs	20	57.1
Needle stick injury during preparation and administration of CDs	19	54.3
Contaminated hands and poor hand washing	18	51.4
Priming the IV set with a drug-containing solution at the patient bedside (this procedure should be done in the pharmacy)	16	45.7
Administering CDs by intramuscular, subcutaneous, or IV routes	12	34.3
Generating aerosols during the administration of drugs, either by direct IV push or by IV infusion	8	22.9
Counting uncoated oral tablets from multi-dose bottles	5	14.3
Collection of blood, urine and stool samples	5	14.3
Crushing or breaking tablets to make oral liquid preparations	5	14.3
Risky nursing activity: Handling contaminated material		
Handling contaminated material generated during preparation and administration process and cleaning spills	14	40.0
Handling contaminated linens and clothing of patients treated with CDs	7	20.0
Handling contaminated wastes generated at any step of the preparation or administration process	6	17.1
Changing bed sheets	5	14.3
Handling body fluids or body-fluid-contaminated clothing, dressings, linens, and other materials	4	11.4

IV, intravenous; CDs, cytotoxic drugs

Table 6: Use of Personal Protective Equipment

Activity	Gloves		Gowns		Mask		Eye†	
	No.	%	No.	%	No.	%	No.	%
When handling patients' waste	15	42.9	11	31.4	0	0	0	0
When caring for patients	13	37.1	8	22.9	0	0	0	0
During preparation & administration of CDs	10	28.6	7	0.2	0	0	0	0
While cleaning up spills	9	25.7	5	14.3	0	0	0	0

†Eye protection

Urine mutagenicity of the study nurses was higher than that of controls. In a study conducted by Falck et al., nurses who prepared and administered antineoplastic drugs had higher indicators of mutagenic substances in their urine compared with nonexposed workers.¹⁹ Benhamou S et al., in 1986 studied a cohort of 29 nurses who extensively handled cytotoxic drugs, and 29 controls matched on sex and age, and 7 patients under chemotherapy. Urinary mutagenicity assays performed with the Ames test towards *Salmonella typhimurium* TA 98 with and without S9 mix, gave an increased mutagenic activity, although not statistically significant as compared to controls.^{20,22}

As an indicator of internal worker exposure to antineoplastic drugs, 19 studies have measured some of the same marker drugs used in environmental sampling in the urine of health care workers. All but two of the studies detected one or more of the drugs in the urine. Four studies reported the presence of antineoplastic drugs in the urine of workers who were not preparing the drugs, indicating secondary exposure from environmental contamination.²⁷⁻²⁸

Our results about the nurses' safety behaviour showed that eating food in handling areas was the most common risky behaviour among exposed nurses, followed by drinking beverages. Improper place for preparing and handling CDs as well as expelling air from syringes filled with CDs were common risky nursing activities. Others included needle stick injuries, contamination of hands, poor hand washing, counting uncoated oral tablets from multi-dose bottles, collection of blood, urine and stool samples and crushing or breaking tablets

to make oral liquid preparations, cleaning spills, and handling body fluids or contaminated materials. Few study nurses attended training programs about occupational health and safety and even fewer mentioned that there are nursing care guidelines for procedures for dealing with patients receiving CDs as well as presence of in-service training programs. These findings show that the working place was not a safe environment for these nurses.

An analytical cross sectional study carried out in Ege University teaching hospital by Meral et al. (2004),²⁹ reported that 49.6% of the nurses were drinking beverages, 43.0% were storing food and beverages and 40.5% were eating food in the CDs handling area, and that 46.9% of the nurses have at least one risky behaviour in the working environment. Only 32.5% of the nurses declared that they prepare the CDs in proper preparation cabins. Only 45.1% of the nurses reported that their working environment had proper aspiration system. In a previous study, it was reported that 94% of the nurses drink and eat in the preparation area for CDs.^{3,16}

Although some of the previous studies report similar findings² some studies especially in the more developed countries report that the majority prepare CDs in a laminar air flow hood.¹⁸ Exposure of health care providers to antineoplastic drugs is varied, and the routes of exposure are typically inhalation, dermal, or oral. Workers may be exposed by inhalation via droplets, particulates, and vapors when they create aerosols, generate dust by crushing tablets, and clean up spills. Dermal exposure may occur when workers touch contaminated surfaces during the preparation, administration, or disposal of hazardous drugs, and oral

exposure may occur from hand-to-mouth contact. Accidental injection with an antineoplastic drug, although rare, has been documented.⁴

In a study by Mason in the United Kingdom, significant concentrations of several drugs in both personal and area air samples were reported. Drug particulates can become airborne after the drying of contaminated areas. Inadvertent ingestion may be an additional route of exposure. When food or beverages are prepared, stored, or consumed in work areas, they may easily become contaminated with airborne particles of antineoplastic drugs. Likewise, hands, cigarettes, cosmetics, and chewing gum can be contaminated. A potential source of exposure is direct skin contact when a spill or leak occurs and a large volume of drug is released to the environment.

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In this study there was poor use of gloves, gowns and personal protective equipment by study nurses when handling patient waste, and when cleaning up spills. When handling CDs, there was good use of gloves and surgical masks by study nurses but a very small number of them used all of the recommended protective equipment.

Results about the nurses' safety behaviour and usage of recommended health safety measures showed that, notwithstanding the rules and regulations pertaining to CDs, nurses did not comply to them fully. Valanis (1991) reported that beliefs about what protection is required have a stronger correlation with actual use than does policy content.³¹ This evidence highlights the critical need to reduce exposure to all hazardous drugs in the health care environment. Efforts must be made to reduce occupational exposure to concentrations as low as reasonably achievable. A combination of exposure control methods can be

applied to achieve this goal.

CONCLUSION

The level of awareness of the nurses handling CDs is of concern because it is important in raising standards of safety. In-service training is a very effective tool to increase the level of knowledge. This study also revealed the necessity of the improvement of the work environment and the need to make available protective equipment. As the primary prevention measure involves the least possible exposure to CDs, guidelines should be developed and information regarding these guidelines should be disseminated both at the practice and administrative levels. A safety committee in the hospital should ensure the appropriate implementation of safety policies, and keep the staff informed about the procedures for safety handling of CDs.

There should be good planning and design of the workplace to improve safety as well as best practice control measures, specialized equipment (such as cytotoxic drug safety cabinets), adequate personal protective equipment, establishment of clinical pharmacy practice and integrated health monitoring program that includes the assessment and counseling of prospective nurses before they commence any work involving CDs and related waste; and ensures employee confidentiality is maintained.

FOOTNOTES

Conflicts of interest: The authors declare no competing conflicts of interest

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