General Health Problems among Oncology Nurses Handling Antineoplastic Agents: A Comparative Study

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Abstract:

Background: The antineoplastic drugs pose an occupational hazard to nurses. The General Health problems have not been addressed in the literature although they might provide early indicators for safety of nurses. **Aim:** to compare general health problems among oncology nurses handling antineoplastic agents and those in other departments not dealing with these hazardous exposures. **Setting & sample:** Retrospective study was conducted on 50 nurses in the oncology department at the nuclear medicine centre, and 50 control nurses from the departments of ophthalmology and orthopedic at El-kasr El Aini hospital. **Tool:** A self-administered questionnaire covering personal data, menstrual and reproductive history, and general health problems, and assessment of exposure to antineoplastic agents in exposed nurses was used for data collection. **Results:** More exposed nurses suffered dysfunctional bleeding (p=0.006), and menorrhagia (p=0.005), especially with no identified causes. The Odds Ratios (ORs) ranged between 2.7 for irregularity to 7.4 for dysfunctional bleeding. They had more dysuria (p=0.03), dermatitis (p=0.01), and stomatitis (p<0.001), with ORs 2.5 to 4.9. Menstrual problems increased with the duration of exposure, with ORs 4.3 for bleeding and 16.7 for menorrhagia, and significant positive correlations. **Conclusion:** The study confirms the hazardous effects of nurses' occupational exposure to antineoplastic agents on general health. **Recommendations:** The findings corroborate the need of health education program to maintain safety measures, medical examinations for nursing staff prior to their appointment and Periodic screening for early detection of any deviations from normal, with prompt occupational health intervention.

Key words: Oncology nurse, antineoplastic, occupational exposure, general health problems

Introduction:

The global burden of cancer continues to increase largely because of the aging and growth of the world population alongside an increasing adoption of cancer-causing behaviors, particularly smoking, in economically developing countries. Based on the GLOBOCAN 2008 estimates, about 12.7 million cancer cases and 7.6 million cancer deaths are estimated to have occurred in 2008; of these, 56% of the cases and 64% of the deaths occurred in the economically developing world.[1]

Approximately 60% of cancer patients will receive chemotherapy as part of their treatment.[2] The antineoplastic drugs pose an occupational hazard to nurses with potential short and long-term consequences due to their carcinogenic, mutagenic, and teratogenic effects. This hazard is becoming of significant importance given the increasing numbers of exposed nurses who are not properly trained in the safe handling of these medications despite the guidelines set to mitigate occupational exposure.[3]

The occupational exposure to chemotherapeutic agents may be through inhalation, ingestion, or skin contact. The risk of exposure is higher for injectable purging air bubbles,

connecting or disconnecting infusions, or changing continuous infusion bags.[4] Another possible route of exposure among nurses is through inadvertent ingestion or contamination of food and drink.[5] Moreover, aerosolization, vaporization or leakage during reconstitution, mixing or spill clean up can easily reaching distant locations. The outer surfaces of Iv bags and syringes may also be contaminated.[6] Therefore, the potentials of occupational exposures to these hazards should not be underestimated.[7]

The nursing role is integral in the provision of chemotherapy services with set standards to ensure the delivery of high quality care. [8] This role necessitates that the oncology nurses must have good knowledge of the pharmacology and administration of chemotherapeutic agents, and possible adverse effects. This is both for the benefit of the patients and the nurses, and has been emphasized in the NIOSH Alert published in 2004 for workers protection. [9]

Significance of the study:
Most of the studies investigating the effects of occupational exposure to antineoplastic agents among healthcare providers, particularly nurses, were focused on the reproductive problems,[10,11] as well as the associated genetic disorders.[12-15] The menstrual and general health problems have not been addressed in the literature although they might provide early indicators for safety of nurses. This is of importance since despite the alerts and guidelines, oncology nurses may still be exposed to the hazards of antineoplastic agents due to lack of awareness of the risks of exposure to these drugs and of the required safety equipment and their use.[16]

Aim of the study:
The aim of this study was to: compare general health problems among oncology nurses handling antineoplastic agents and those in other departments not dealing with these hazardous exposures.

Research question:
Is there any differences in general health problems among oncology nurses handling antineoplastic agents and those in other departments not dealing with these hazardous exposures?

Subjects and methods:
Design and setting:
Retrospective research design was used in this study. The study was carried out at the nuclear medicine centre and the ophthalmology and orthopedics departments in El-kasr El Aini hospital, affiliated to Cairo University. The nuclear medicine centre provides chemotherapy services to cancer patients at outpatient and inpatient (42 beds) levels. The departments of ophthalmology and orthopedic provided the control group members.

Study sample:
The study populations consisted of two groups of nurses. The study (exposed) group consisted of all the nurses working in the oncology department at the nuclear medicine centre. The control (unexposed) group included the nurses working in the ophthalmology and orthopedic departments. The selection criteria for inclusion in the study sample were being female in the child bearing period, working in the study setting for at least two years, and accepting to participate in the study. The sample size was calculated to detect any difference in menstrual problems between the two groups with a

prevalence of 25% or higher, and a prevalence Odds Ratio (OR) 2.0 at 95% level of confidence and 80% power. Using the Epi-Info statistical software package, the required sample size was 48 per group. This was increased to 50 to compensate for a dropout rate of 5%. A consecutive sampling technique was used to recruit nurses according to the inclusion criteria in the two groups to fulfill the sample size.

Data collection tool:

The researchers developed a self-administered questionnaire for data collection. It included a section for respondents' personal data such as the age, nursing qualification, experience years, marital status, and smoking. This was followed by a section for menstrual (dysfunctional bleeding, menorrhagia, irregular menses, and severe menstrual pain) and reproductive (marriage duration, number of children, infertility, abortion, low birth weight, premature labor, stillbirth, and fetal death) history. For each problem, a probe question asked about any obvious/diagnosed cause of the problem. The section asking for general health problems included questions about various body systems such as gastrointestinal, cardio-respiratory, urinary, with emphasis on the dermatological symptoms. For the study group, there was section of assessment of occupational exposure to antineoplastic agents which covered the duration of exposure, number of doses prepared per week, regular use of gloves, gowns and masks, and exposure to splashes.

The developed tool was reviewed by a group of experts in medical and nursing oncology for face and content validation. The tool was finalized after modifications were done

based on experts' suggestions. These included adding some probing questions, and re-wording of some phrases.

Administrative and ethical considerations:

The study protocol was approved by the department counsel. Official letters to conduct the study were addressed from the Dean of the Faculty of Nursing to the Director of El-kasr El Aini hospital, and the heads of the departments to be included in the study. Their official approvals were secured before beginning the study. The researchers met with each of the selected nurses to explain to her the purpose of the study and to obtain her verbal consent to participate after informing her about the rights to refuse or withdraw from the study with no untoward consequences. Participants were reassured about the confidentiality of the information collected, and that it would be used only for the purpose of scientific research. The study maneuvers could not entail any harm on participants.

Pilot study:

A pilot study was conducted on ten nurses (five from each group) representing 10% of sample to evaluate the clarity and applicability of the tool, as well as to estimate the time needed for data collection. Few modifications were done, namely rephrasing and utilizing simpler semantic for the statements. Those nurses were not included in the main study sample.

Field work:

After obtaining official approvals, the researchers started the process of selection of the participants according to the previously set criteria. Each potential participant was given the self-administered questionnaire upon consenting to participate in the

study. The researchers were present all the time for any clarification. The fieldwork lasted for three months, during the period lasted from January to April 2012.

Statistical Design:

Data entry and statistical analysis was done using SPSS 16.0 statistical software package. Categorical variables were compared using chi-square test. Whenever the expected values in one or more of the cells in a 2x2 tables was less than 5, Fisher exact test was used instead. Cornfield 95% confidence intervals were computed for significant findings. Pearson correlation analysis was used for assessment of the inter-relationships among quantitative variables, and Spearman rank correlation for ranked ones. Statistical significance was considered at p-value <0.05.

Results:

Nurses in the study (exposed) and control (unexposed) groups had similar personal characteristics, with no statistically significant differences. The means of their age were respectively 31.7 and 30.1 years, with more than half of them having diploma nursing qualification (64.0% vs 54.0%), being married (62.0% in both), and having children (83.9% vs 93.5%). Only 3 (6.0%) of the exposed and 4 (8.0%) of the control groups were smoking. The mean experience years was higher in the exposed (10.3) compared to the control (7.1) group (p<0.001).

The duration of exposure to antineoplastic agents among nurses in the study group ranged between two and twelve years (mean±SD 0.8±1.6), while the number of doses prepared by each nurse ranged between 20 and 115 per week (mean±SD 47.2±23.6 doses). Approximately half (46.0%) of them reported not using personal protective measure as gowns, gloves and masks, and almost all of them (98.0%) have been exposed to splashes.

Comparison of the menstrual history between the study and control groups revealed a number of statistically significant differences (Table 1). It is evident that most nurses in the study group suffered from dysfunctional bleeding (p=0.006), and menorrhagia (p=0.005). The differences were even more obvious when only the cases with no identified causes of the problem were compared, especially regarding irregular menses (p=0.016). The prevalence ORs ranged between 2.7 for irregularity to 7.4 for dysfunctional bleeding. As for reproductive problems, the table indicates higher frequency of most of the problems with no identified cause among exposed nurses. The only exceptions were related to premature labor and low birth weight. However, due to the low frequencies, no statistically significant differences could be revealed.

Table (2) shows that nurses in the study group have significantly higher frequency of symptoms of dysuria (p=0.03), skin inflammation (p=0.01), and stomatitis (p<0.001). The ORs ranged between 2.5 and 4.9. Meanwhile, no significant differences were detected in other body systems.

As regards the effect of the duration of exposure on menstrual and reproductive problems, table (3) indicates a higher frequency of all menstrual problems, except menstrual pain, among the nurses with longer duration of exposure (3+ years). This was evident regardless whether the problem had an identified cause or not. The ORs ranged from 4.3 for bleeding with no identified cause, to 16.7 for menorrhagia with identified cause.

Similarly, the frequency of reproductive problems was higher in the longer exposure group, but the differences could not reach statistical significance.

Table (4) points to statistically significant positive correlations between the number of menstrual and menstrual and/or reproductive symptoms with or without identified cause and the duration of exposure to antineoplastic agents. However, these were not correlated to the number of doses prepared weekly or the number of personal protective equipment (PPE) used. Meanwhile, the number of reproductive problems correlated negatively to the duration of marriage.

Discussion:
The present study findings indicated a significant association between occupation exposure to antineoplastic agents among nurses and the frequency of menstrual disorders, as well as dysuria and skin problems. The findings are consistent with the generally known hazards of exposure to these agents. However, if the side effects of these medications might be tolerated in the therapy of cancer patients, they should not occur among health care providers in the course of their duties. [7]

The current study results of the association between menstrual disorders and exposure to antineoplastic agents among nurses are further confirmed by a kind of dose response with the duration of exposure. In fact, such problems were more frequent among those with longer duration of exposure, with a significant positive correlation. Furthermore, after analysis excluding the menstrual disorders with identified causes, the relation was still present. These findings provide more evidence of the

possible effect of occupational exposure to antineoplastic agents on menstruation. Thyroid dysfunction might be implied in this effect. [17] In agreement with the present study finding, Fransman et al. and Wu et al. [18,19] reported that occupational exposure to chemotherapy drugs may have the potential of menstrual abnormalities. On the same line, although in another context, patients on cancer chemotherapy are prone to ovarian problems that led to programs for fertility preservation. [20, 21]

The current study could not achieve the secondary objective concerned with the reproductive problems. According to the study results, such problems were more frequent in the exposed group compared to the unexposed, and also among those with longer duration of exposure. In fact, this objective has been previously addressed in many studies, which showed that occupational exposure to antineoplastic agents was associated with higher rates of fetal loss, congenital malformations, low birth weight, congenital abnormalities, [22] infertility and sub-fertility, [13] abortions, [11] as well as other genotoxic effects. [23]

Concerning the general health effects, the present study findings showed higher frequencies of symptoms of dysuria, stomatitis, and dermatitis among exposed nurses. Martin [24] stated that the skin and mucous membranes symptoms might be explained by the direct contact or spills, which mostly irritant. This is confirmed by the fact that almost all exposed nurses reported having been exposed to spills of these toxic agents, with low rate of using personal protective equipments. Similar findings were shown by Terui et al. [25] in study on Japanese nurses, where the

spills of antineoplastic agents posed an occupational health problem. Furthermore, another study in Japan Yoshida et al. [26], demonstrated similarly low rates of use of personal protective equipment, which led to incidents at work such as drugs adherence to skin and mucous membranes, with associated problems.

The lack of effect of use of personal protective equipment on the studied health problems among exposed nurses might be explained by the high rate of non-compliance to these protective measures. Another explanation is that these personal measures are not effective in dealing with environmental contamination with these hazardous agents. In congruence with this explanation, Sottani et al.[27] found that despite the adherence to the recommended safety practices by Italian pharmacists and nurses, residue contamination on surfaces and floors continued to pose an important source of the hazard. Therefore, Yoshida et al., [28] recommended negative pressure in these settings to protect healthcare providers.

Conclusion and recommendations:
The study findings lead to further confirmation of the hazardous effects of occupational exposure to antineoplastic agents on general health among nurses. These effects are correlated to the duration of exposure. However, these findings should be cautiously interpreted in the light of the study limitations of non-probability sampling, and high non-response of blood testing. Additionally, the assessment of health problems depended only on self-reporting, which might be exaggerated among those exposed. The findings corroborate the need of health education program to maintain safety measures and promote the use of personal protection to avoid

exposure during the handling of antineoplastic drug. Periodic screening of these symptoms may help in early detection of any deviations from normal, with prompt occupational health intervention. The high frequency of dysuria symptom needs further research. Finally, the need to conduct medical examinations for nursing staff prior to their appointment in the departments of oncology.

Table (1): Menstrual and reproductive history of nurses in the study and control groups

History of problems:	Group Study (n=50)	Control (n=50)	X^2 Test	p-value	OR (95% CI)
Menstrual:					
Dysfunctional bleeding:					
▪ Total	19	7	7.48	0.006*	3.8(1.3-11.4
▪ No identified cause	16	3	10.98	<0.001	7.4(1.8-34.8)
Irregularity:					
▪ Total	32	36	0.74	0.39	
▪ No identified cause	30	18	5.77	0.016*	2.7 (1.1-6.5)
Menorrhagia:	34	20	7.89	0.005*	3.2(1.3-7.9)
▪ Total					
▪ No identified cause	29	14	9.18	0.002*	3.6(1.4-8.9)
Menstrual pain:					
▪ Total	32	35	0.41	0.52	
▪ No identified cause	32	27	1.03	0.31	
Reproductive:					
Abortion:					
▪ Total	6	8	0.33	0.56	
▪ No identified cause	6	4	0.44	0.51	
Premature labor:					
▪ Total	0	5	Fisher	0.06	
▪ No identified cause	0	3	Fisher	0.24	
Low birth weight:					
▪ Total	2	6	Fisher	0.29	
▪ No identified cause	2	1	Fisher	1.00	
Stillbirth:					
▪ Total	3	0	Fisher	0.24	
▪ No identified cause	3	0	Fisher	0.24	
Fetal death:					
▪ Total	4	0	Fisher	0.12	
▪ No identified cause	2	0	Fisher	0.49	
Low birth weight:					
▪ Total	1	5	Fisher	0.20	
▪ No identified cause	1	2	Fisher	1.00	
Infertility:					
▪ Total	2	1	Fisher	1.00	
▪ No identified cause	2	0	Fisher	0.49	
Congenital anomalies:					
▪ Total	2	0	Fisher	0.49	
▪ No identified cause	1	0	Fisher	1.00	

(*) Statistically significant at p<0.05

Table (2): Systemic symptoms among nurses in the study and control groups

Health problems:	Study (n=50)		Control (n=50)		X^2 Test	p-value	OR (95% CI)
	No.	%	No.	%			
General (dizziness, headache, fatigue, aches)	49	98	50	100	Fisher	1.00	
Gastrointestinal (anorexia, nausea, vomiting, diarrhea)	43	86	45	90	0.38	0.54	
Respiratory (cough, dyspnea, palpitations)	29	58	30	60	0.04	0.84	
Urinary (dysuria)	32	64	21	42	4.86	0.03*	2.5(1.0-5.9)
Dermatological:							
▪ Allergy	25	50	16	32	3.35	0.07	
▪ Inflammation	19	38	8	16	6.14	0.01*	3.2(1.1-9.3)
▪ Stomatitis	30	60	4	8	30.12	<0.001*	4.9(17.3-67.0)
▪ Conjunctivitis	12	24	6	12	2.44	0.12	
▪ Hair fall	40	80	40	80	0.00	1.00	

(*) Statistically significant at p<0.05

Table (3): Relation between menstrual and reproductive problems and the duration of exposure to chemotherapeutic agents among nurses in the study group

History of Problems	Duration of exposure				X^2 Test	p-value	OR (95% CI)
	2 years (n=20)		3+ years (n=30)				
	No.	%	No.	%			
Menstrual:							
Bleeding:							
▪ Total	3	15.0	16	53.3	7.48	0.006*	6.5(1.4-35.2)
▪ No identified cause	3	15.0	13	43.3	4.43	0.035*	4.3 (1.1-23.5)
Irregularity:							
▪ Total	7	35.0	25	83.3	12.17	<0.001*	9.3(2.1-44.9)
▪ No identified cause	6	30.0	24	80.0	12.50	<0.001*	9.3(2.1-44.1)
Menorrhagia:							
▪ Total	7	35.0	27	90.0	16.68	<0.001*	16.7(3.1-103.6)
▪ No identified cause	5	25.0	24	80.0	14.90	<0.001*	12.0(2.6-60.3)
Menstrual pain:							
▪ Total	10	50.0	22	73.3	2.84	0.09	
▪ No identified cause	10	50.0	22	73.3	2.84	0.09	
Reproductive:							
Abortion:							
▪ Total	2	10.0	4	13.3	Fisher	1.00	
▪ No identified cause	2	10.0	4	13.3	Fisher	1.00	
Low birth weight: ▪ Total	0	0.0	2	6.7	Fisher	0.51	
▪ No identified cause	0	0.0	2	6.7	Fisher	0.51	
Stillbirth:							
▪ Total	0	0.0	3	10.0	Fisher	0.27	
▪ No identified cause	0	0.0	0	0.0	--	--	
Fetal death:							
▪ Total	0	0.0	4	13.3	Fisher	0.14	
▪ No identified cause	0	0.0	0	0.0	--	--	
Low birth weight:							
▪ Total	0	0.0	1	3.3	Fisher	1.00	
▪ No identified cause	0	0.0	1	3.3	Fisher	1.00	
Infertility:							
▪ Total	1	5.0	1	3.3	Fisher	1.00	
▪ No identified cause	1	5.0	1	3.3	Fisher	1.00	
Congenital anomalies:							
▪ Total	2	10.0	0	0.0	Fisher	0.16	
▪ No identified cause	1	10.0	0	0.0	Fisher	0.40	

(*) Statistically significant at p<0.05   (--) Test result not valid

Table (4): Correlation between menstrual, reproductive problems and some personal and exposure characteristics of nurses in the study group

No. of:	Pearson correlation coefficients				
	Age	Marriage years	Years of exposure	No. of doses prepared	No. of PPE used[@]
▪ Reproductive problems	-.02	-.47**	.21	-.13	-.16
▪ Menstrual problems	.09	-.11	.33*	-.14	-.05
▪ Reproductive/menstrual	.06	-.30	.37**	-.13	-.06
▪ Reproductive/menstrual with no identified cause	.02	-.48**	.35*	-.15	-.07

(*) Statistically significant at p<0.05   *(**) Statistically significant at p<0.01*
(PPE): personal protective equipment   *(@) Spearman rank correlation*

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