



## REVISIONES

### **Antineoplastic and occupational risks for nurses: an integrative review**

*Antineoplásicos e os riscos ocupacionais para os enfermeiros: uma revisão integrativa*

*Antineoplásicos y riesgos laborales para los enfermeros: una revisión integral*

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Palavras chave: Riscos Ocupacionais; Exposição Ocupacional; Antineoplásicos; Enfermeiros; Enfermagem do Trabalho

Palabras clave: Riesgos laborales; exposición ocupacional; antineoplásicos; enfermeros; Enfermería del Trabajo

### **ABSTRACT**

**Introduction:** There are countless occupational hazards to which health workers who handle chemotherapeutic substances are exposed.

**Objectives:** To identify and describe the short-, medium- and long-term damages that are caused in the bodies of nurses and other health professionals who are exposed to antineoplastic drugs in the workplace.

**Methodology:** To study an integrative literature review, with data collection in the Virtual Health Library in the months from September to October 2013, the database of the Scientific Electronic Library Online,

and in the databases of the Latin American and Caribbean Health Sciences, the Database of Nursing and the Medical Literature Analysis and Retrieval System Online, with the keywords: "Antineoplásticos and Risco Ocupacional and Enfermagem", "Antineoplastic and Occupational Risk" and "Antineoplastic and Nursing."

**Results:** Damage to genetic material, increased frequency of micronuclei in lymphocytes, increased exchange of sister chromatids, increased levels of antineoplastic urinary excretion, increased cases of cancer, increased incidence of congenital anomalies in offspring and miscarriages in the first trimester of pregnancy are some of the results found in this study.

**Conclusion:** The most frequent damage occurred in the deoxyribonucleic acid, and predominated in medium and long terms, with the exposure time being crucial to increasing damage. In short and long term predominated damage linked to pregnancy and the developing fetus, with increase in congenital abnormalities and abortion. Genetic monitoring as well as Personal Protective Equipment are essential to minimize damage.

## RESUMO

**Introdução:** São inúmeros os riscos ocupacionais aos quais os trabalhadores de saúde que manipulam quimioterápicos são expostos.

**Objetivos:** Identificar e descrever os danos em curto, médio e longo prazo, causados ao organismo dos enfermeiros, e demais profissionais da saúde, que são expostos à antineoplásticos no ambiente de trabalho.

**Metodologia:** Estudo de revisão integrativa da literatura, com coleta de dados na Biblioteca Virtual da Saúde, nos meses de setembro a outubro de 2013, nas bases de dados da biblioteca eletrônica *Scientific Electronic Library Online* e nas bases de dados da Literatura Latino-Americana e do Caribe em Ciências da Saúde, da Base de Dados de Enfermagem e da *Medical Literature Analysis and Retrieval System Online*, tendo como descritores: "Antineoplásticos and Risco Ocupacional and Enfermagem", "Antineoplastic and Occupational Risk" e "Antineoplastic and Nursing".

**Resultados:** Danos ao material genético, aumento da frequência de micronúcleos em linfócitos, aumento da troca das cromátides irmãs, aumento do nível de antineoplásticos na excreção urinária, aumento dos casos de câncer, aumento da incidência de anomalias congênitas na prole e aborto no primeiro trimestre da gravidez são alguns dos resultados encontrados por este estudo.

**Conclusão:** O dano mais frequente ocorreu ao ácido desoxirribonucleico, e predominou em médio e longo prazo, com o tempo de exposição sendo decisivo ao aumento dos prejuízos. Em curto e longo prazo predominaram danos ligados à gestação e ao desenvolvimento do feto, com aumento das anomalias congênitas e aborto. Acompanhamento genético, bem como Equipamentos de Proteção Individual são fundamentais para minimizar os danos.

## RESUMEN

**Introducción:** Son muchos los riesgos laborales a los que están expuestos los trabajadores de salud que manipulan quimioterápicos.

**Objetivos:** Identificar y describir los daños a corto, medio y largo plazo, causados en el organismo de los enfermeros y otros profesionales de la salud, que están expuestos a los fármacos antineoplásticos en el lugar de trabajo.

**Metodología:** Estudio de revisión integradora de la literatura, con la recogida de datos en la Biblioteca Virtual en Salud, en los meses de septiembre a octubre de 2013, en las bases de datos de biblioteca electrónica *Scientific Electronic Library Online* y en las bases de datos de la Literatura Latino Americana y Caribeña Ciencias de la Salud, la Base de Datos de Enfermería y el Análisis de la Literatura Médica y Recuperación del Sistema en Línea, con las palabras: "Antineoplásticos and Risco Ocupacional and Enfermagem", "Antineoplastic and Occupational Risk" y "Antineoplastic and Nursing".

**Resultados:** Daño en el material genético, aumento de la frecuencia de micronúcleos en linfocitos, aumento de intercambio de cromátidas hermanas, un mayor nivel de la excreción urinaria antineoplásica, aumento de casos de cáncer, mayor incidencia de anomalías congénitas en la descendencia y aborto en el primer trimestre del embarazo son algunos de los resultados encontrados en este estudio.

**Conclusión:** El daño más frecuente ocurre al ácido desoxirribonucleico, el predominio a medio y largo plazo, siendo el tiempo de exposición fundamental para aumentar el daño. A corto y largo plazo predominaron daños relacionado con el embarazo y el desarrollo fetal, con aumento de anomalías congénitas y aborto. Acompañamiento genético, así como equipos de protección individual son esenciales para minimizar los daños.

## INTRODUCTION

The occupational risks and hazards to which health workers are exposed are the most varied ones, as well as their consequences to the body. Danger is defined as the source or situation that has potential for harm in terms of injury and damage to the human body, health, property or the working environment, and risk is the combination of the probability of a hazardous event or exposure occurring that can cause serious injury or disease<sup>1</sup>.

According to Ordinance No. 3214 of the Ministry of Labor of Brazil, as of 1978 through its Regulatory Standard No. 5 (NR-5), risks in the workplace can be classified as: risk of accidents, or ergonomic, physical, chemical and biologic risks<sup>2</sup>. In order for them to be minimized, there needs to be a systematic action, with classification, level of acceptance, an action plan and a review of the suitability thereof<sup>3</sup>.

There are several specialized committees, programs and services that are responsible, among other functions, for preventing occupational harm that is caused for workers, and one can cite the Internal Commissions for Accident Prevention (CIPA), Specialized service of Safety Engineering and Occupational Medicine (SESMT), the Environmental Risk Prevention Program (PPRA) and Occupational Health Control Program (PCMSO), besides required documentation, such as Technical Reports of Environmental Working Conditions (LTCAT) and the Professional Social Security Profile (PPP), which guarantee workers legal support related to future benefits that are their right and which may be required.

The National Institute for Occupational Safety and Health (NIOSH)<sup>4</sup> states that health professionals who are exposed to chemotherapeutic agents as part of their professional practice should take the due precautions to eliminate or reduce exposure whenever possible. This includes the use of Personal Protection Equipment (PPE), such as gowns, gloves, masks and goggles.

Pharmacists, who prepare medications, and nurses who can both prepare as well as administer them, are the two professional groups that have the greatest potential for exposure to antineoplastic agents<sup>4</sup>. Furthermore, the harm done to nurses is greater and more significant than that caused to pharmacists<sup>5-7</sup>.

These exposures can cause health effects in the short, medium and long terms. Chromosomal aberrations<sup>8-9</sup>, damage to deoxyribonucleic acid (DNA)<sup>6</sup>, increased micronucleus frequency in lymphocytes<sup>6</sup>, increased exchange of sister chromatids<sup>9</sup>, increased level of antineoplastic drugs in urinary excretion<sup>7</sup>, an increase in cases of

cancer<sup>10</sup>, increased incidence of congenital anomalies in offspring<sup>10</sup>, and miscarriages in the first trimester of pregnancy<sup>11</sup> are some of the effects described in the literature. In order to intervene in the outcome, it is essential that all this be well known. Thus, the objective was to identify and describe the short, medium, and long term damages which are caused to the bodies of nurses and other health professionals who are exposed to antineoplastic drugs in the workplace.

## **METHODOLOGY**

This is an integrative review about the occupational risks to which nurses and other health professionals are exposed upon handling antineoplastic substances.

In this study, six stages were used: identifying the issue and selecting the hypothesis for the preparation of the review, fixing criteria for inclusion and exclusion of studies, defining information that was extracted and categorizing the studies, evaluating the studies that were included, interpreting the results, and presenting the synthesis of the findings<sup>12</sup>.

A search was conducted in the Virtual Health Library (BVS, or *Biblioteca Virtual da Saúde*), in the months from September to October of 2013, by using the databases of the Scientific Electronic Library Online (SCIELO), the Latin American and Caribbean Health Sciences (LILACS), the Nursing Database (BDENF, or *Base de Dados de Enfermagem*) and the Medical Literature Analysis and Retrieval System Online (MEDLINE), and the keywords: "antineoplastics and Occupational Risk and Nursing ", "Antineoplastic and Occupational Risk" and "Antineoplastic and Nursing", in the respective order.

The criteria for inclusion was established as being original articles that have been made available in their entirety and in online form, which were published in Portuguese, English or Spanish in the period between 2009 and 2013 containing nurses in their samples. The criteria for exclusion were established as being articles of bibliographical research and reflection, theses, dissertations and articles that have been repeated in different databases.

To select the articles, three Relevance Tests were used. In Relevance Test 1, the publication period of the studies and language were considered. In Test 2, the productions were selected by considering the suitability of the title and the abstract in relation to the topic. In Test 3, the studies in their entirety were evaluated by considering the aforementioned issues as well as other inclusion and exclusion criteria. At that stage the articles were thoroughly analyzed by three reviewers, and the most relevant data for the study were briefly summarized and described. They are shown in Table 1, entitled "Identification and description of the main findings."

**Table 1. Identification and description of the main findings. Vitória, 2014.**

| IDENTIFICATION AND DESCRIPTION OF THE MAIN FINDINGS  |                               |      |                |   |   |  |  |
|--|-------------------------------|------|----------------|---|---|--|--|
| Identification of the Article  | Periodical                    | Year | Study Location | Objectives  | Methodology   | Population   | Main Conclusions   |
| <p><b>Cancer incidence and adverse pregnancy outcome in registered nurses potentially exposed to antineoplastic drugs</b></p> <p>Ratner <i>et al.</i><sup>10</sup></p>             | BMC Nursing                   | 2010 | Canada         | To determine if nurses who have been exposed to antineoplastic drugs have a higher risk of developing cancer, and if their children are more likely to be born with congenital anomalies. | Those who participated were nurses that had been registered in a professional organization for over a year, with their registrations going from 1974 to 2000. They had to have worked in oncology. Their contact with antineoplastic drugs was evaluated according to the number of years they had worked and their level of exposure. A cohort group of babies born in 1986 was evaluated. Exposure during pregnancy was considered as follows: Estimated exposure in the first trimester of pregnancy; and cumulative exposure over a 10 year period preceding the child's birth. | 56,213 nurses<br><br>22,491 children, born alive.                                  | Nurses who have worked in cancer centers or oncology units had a higher risk of getting breast cancer. The children of nurses exposed to chemotherapy drugs during pregnancy were significantly susceptible to congenital abnormalities in the eye. The risk of cleft palate and/or cleft lip was significantly higher among those born to women who had a cumulative exposure of 10 years prior to their pregnancy. Nurses with higher exposure had higher risk of rectal cancer  |
| <p><b>Evaluation of genotoxicity induced by exposure to antineoplastic drugs in lymphocytes of oncology nurses and pharmacists.</b></p> <p>El-Ebiary <i>et al.</i><sup>5</sup></p> | Journal of Applied Toxicology | 2013 | Egypt          | To assess the damage in the genome associated with the handling of antineoplastic drugs to oncology nurses and pharmacists working in a major cancer center in Egypt                      | A questionnaire about socio-demographics, health, habits of living and working. The subjects were neither smokers nor alcoholics. The subjects of the case study had worked with antineoplastic drugs for 2 to 20 years. Blood samples were taken. Lymphocytes were isolated. Genotoxic effects were evaluated for chromosome aberrations, and tests were performed with manganese. Cells in metaphase and binucleate lymphocytes were evaluated for the presence of micronuclei  | 20 nurses and 18 pharmacists as the case group; and 30 nurses as the control group | There was a difference regarding the years of exposure between pharmacists and nurses, being higher for the latter group, which also had higher levels of chromosome damage and aberrant lymphocytes. Aberrations such as deletions, gaps, and ruptures were found. The age of the individuals showed a positive correlation to chromosomal damage. The control group showed significantly less damage to the genome. The study infers that the reason for the difference between nurses and pharmacists is due to the fact that the latter adopt stricter protection when handling antineoplastic drugs, with gloves, masks, and gowns, while the nurses would only don gloves. |

**IDENTIFICATION AND DESCRIPTION OF THE MAIN FINDINGS (Part 2)**

| Identification of the Article  | Periodical                                       | Year | Study Location | Objectives  | Methodology  | Population  | Main Conclusions  |
|--|--|------|----------------|---|--|---|---|
| <p><b>Assessment of chromosomal aberrations, micronuclei and proliferation rate index in peripheral lymphocytes from Tunisian nurses handling cytotoxic drugs.</b><br/>Bouraoui S. <i>et al.</i><sup>8</sup></p> | <p>Environmental Toxicology and Pharmacology</p> | 2011 | Tunisia        | <p>To verify the genotoxicity of the exposure to antineoplastic drugs among nurses.</p>                     | <p>A questionnaire was filled out regarding socioeconomic status and lifestyle habits. Blood samples were collected for posterior testing for chromosomal aberrations and cells with binucleated micronuclei.</p>  | <p>20 nurses (4 men and 16 women) who had been exposed and 20 matched controls.</p>                     | <p>Among those who had been exposed, chromosomal damage was assessed as being 5.7 times higher than in the control group. Chromosomal aberration was 3.75 times higher in chromatids and 5 times higher in chromosomes in the case group. No associations were found between exposure time and genetic changes. The index of the lymphocyte proliferation rate was significantly lower in the case group.</p>   |
| <p><b>Occupational risk assessment of genotoxicity and oxidative stress in workers handling anti-neoplastic drugs during a working week.</b><br/>Rombaldi, F. <i>et al.</i><sup>6</sup></p>                      | Mutagenesis                                      | 2009 | Brazil         | <p>To assess oxidative parameters and genotoxicity in hospital workers who handle antineoplastic drugs.</p> | <p>The three oxidative stress parameters used were the concentration of catalase, the antioxidant enzyme superoxide dismutase and substances that are reactive to thiobarbituric acid. Genotoxicity was evaluated by comet assay and by the frequency of micronuclei in lymphocytes. All participants answered a questionnaire on health. Protective equipment use was also evaluated. There was blood collection, which underwent a clinical trial, and the slides were coded for blind analysis. The damage index (DI) to the DNA was ranked 0-4 in ascending order.</p> | <p>20 nurses and pharmacists in the case group, and 20 nurses and pharmacists in the control group.</p> | <p>The DI of the DNA of exposed workers, as well as the concentration of manganese and catalase, increased significantly compared to those in the control group. Nurses who handled antineoplastic drugs had a higher frequency of micronuclei as compared to the other groups. Alcohol consumption was associated with higher DI of the DNA. The frequency of micronuclei increased with the working time and age. Contact with antineoplastic substances led to the breaking down, cross-linking disruptions, and intercalation of the DNA.</p> |



**IDENTIFICATION AND DESCRIPTION OF THE MAIN FINDINGS (Part 3)**

| Identification of the Article   | Periodical   | Year | Study Location | Objectives   | Methodology  | Population   | Main Conclusions  |
|---|--|------|----------------|--|--|--|---|
| <p><b>Occupational exposures to antineoplastic drugs in an Oncology-Hematology Department.</b> –</p> <p>Derry Stover<br/>Chandran<br/>Achutan<sup>15</sup></p>                          | Journal of Occupational and Environmental Hygiene  | 2011 | Nebraska (USA) | To evaluate the occupational hazards of exposure to antineoplastic drugs in the hematology department of an oncology hospital; as well as complying with guidelines set forth in the document of the <i>National Institute for Occupational Safety and Health</i> (NIOSH). | The questionnaire was applied for four days at the beginning of the morning and night shifts. Demographic variables, level of exposure to chemotherapy, level of training and the use of personal protective equipment were evaluated. Samples from the surfaces of the nursing staff's workplaces, as well as from the rooms of patients, were collected with sterile gauze and sodium hydroxide to measure the level of contamination by antineoplastic drugs. All samples were stored at -20 °C.  | 40 nurses and 10 nursing technicians and/or nurse aids   | The average time they had been employed was 3.66 years. The handling of the medications occurred only at the time of administration. The drugs that were handled the most were cytarabine, cyclophosphamide, etoposide, methotrexate, and ifosfamide. More than 65% of the sample handled the drug at least once a month, 46% had a certificate from the institution for administering chemotherapeutic drugs, and 82% had received training to handle these drugs safely. About 96% of nurses wore a pair of gloves that are resistant to chemotherapeutic drugs when handling them, 49% wore two pairs, and did so often or always, and 51% rarely or never wore two pairs. To remove the plastic in which the medication is placed, 69% reported wearing gloves, 86% usually wore protective gowns, and 18.9% would reuse this equipment. Less than 3% always used all the PPE that exists and is recommended, and 87% washed their hands after contact with the chemotherapeutic drugs. There was no association between the amount of training and the use of PPE. Seven of the 13 samples collected contained chemotherapeutic drugs. |
| <p><b>The genotoxic risk in health care workers occupationally exposed to cytotoxic drugs--a comprehensive evaluation by the SCE assay.</b></p> <p>Kopjar <i>et al.</i><sup>9</sup></p> | Journal of Environmental Science and Health Part A | 2009 | Croatia        | To evaluate the frequency of sister chromatid exchange in health care workers who had been exposed to cytotoxic drugs.   | A study carried out in health-care workers who had been exposed in 22 hospitals in Croatia. During the regular check-up, during the years from 1997 to 2007, tests were performed on the samples and analyses of sister chromatid exchange (TCI) in circulating lymphocytes. Blood samples were collected, the lymphocytes were cultured and analyzed in accordance with a standard protocol. Exchanges in the middle of the chromosomes, the chromatids, were recorded as 2 events, while the exchanges on the tips were counted as only 1 event. | Nurses and Nursing Technicians (376)<br>Doctors (26)<br>402 individuals (392 women and 10 men) | Nurses and technicians manipulated 96% of the antineoplastic drugs; only 2% were by pharmacists and the other 2% were by technicians in a pharmacy. Different PPE were used, the most used were gloves. Age, smoking, and being a woman influenced to increase the amount of TCI and high-frequency cells (HFC). Having other types of exposure to carcinogens such as radiation and ultrasound (which could be considered a confounding factor), significantly increased the number of TCI. The duration of exposure to antineoplastic drugs increased TCI and HFC events  |

**IDENTIFICATION AND DESCRIPTION OF THE MAIN FINDINGS (Part 4)**

| Identification of the Article   | Periodical  | Year | Study Location | Objectives   | Methodology  | Population  | Main Conclusions  |
|---|---|------|----------------|--|--|---|---|
| Assessment of genotoxic risks in Croatian health care workers occupationally exposed to cytotoxic drugs: a multi-biomarker approach. Kopjar N <i>et al.</i> <sup>11</sup> | International Journal of Hygiene and Environmental Health | 2009 | Croatia        | To evaluate the genome damage induced in the lymphocytes of peripheral blood of health care workers who are exposed to cytotoxic drugs | A standardized, socio-cultural questionnaire was applied to know the additional data handling and manipulation of antineoplastic drugs. In groups, 25 smokers and 25 nonsmokers were selected. Blood samples were taken from those in the case study group at their annual check-up, whereas those in the control group donated spontaneously. The samples were treated equally. For assessing damage to DNA, cytogenetic analysis and alkaline comet assay were used. The slides were microscopically analyzed at 250X. Two slides per individual were replicated and analyzed at 50-100 comets. The measurement of the tail length was used to assess DNA damage, as well as the frequency of the nuclei with long tails. There was culture of lymphocytes, an aberration test, and a micronucleus count | 100 female volunteers (50 female workers who had been exposed to chemotherapeutic drugs and 50 in the control group, all of whom were matched regarding gender, age and smoking habits) | Regarding the use of PPE, many stated that they only wear gloves (40%) or gloves and other safety devices (60%), gloves, gowns and vertical air flow (38%), gloves and masks (16%) and all of the aforementioned simultaneously (6%). Older nurses were less likely to use PPE. Using PPE greatly reduced the primary DNA damage. In the case group four types of chromosomal aberrations were observed: chromatid breaks, acentric fragments, chromosome breakage and dicentric chromosomes. In the control group, only the first three aberrations were present. Also in the case group, all values except the breakage of chromosomes were statistically higher than in the control group. Among non-smokers, age significantly influenced the DNA damage. In the population that had been exposed, smokers had higher frequencies of sister chromatid exchange and high-frequency cells. There were miscarriages. The study confirmed that handling these drugs without the proper safety precautions provides various genotoxic risks. Cytogenetic vigilance is recommended. |

**IDENTIFICATION AND DESCRIPTION OF THE MAIN FINDINGS (Part 5)**

| Identification of the Article   | Periodical | Year | Study Location | Objectives  | Methodology  | Population  | Main Conclusions  |
|---|------------|------|----------------|---|--|---|---|
| Evaluation of antineoplastic drug exposure of health care workers at three university-based US cancer centers. Cannon <i>et al.</i> <sup>24</sup> | JOEM       | 2010 | USA            | To evaluate the multiple factors that can result in contamination of the working environment and of workers exposed to a group of antineoplastic drugs. | Inclusion criteria: exposure to antineoplastic drugs for at least six months, and having worked with the handling of chemotherapeutic drugs for at least 24 hours during the week before the evaluation. Unexposed group: individuals with a similar job, but without any contact with antineoplastic drugs. Workers who currently smoked, who had received chemotherapy and/or radiation therapy, | 80 nurses; 21 pharmacists; 10 pharmacy technicians; 10 nursing technicians. 68 Cases that had been exposed and that had handled | During the six weeks, 9762 events of handling antineoplastic drugs were reported. Samples of antineoplastic drugs on the floor were probably underestimated, due to the low recovery of those agents. The number of events of handling was linked to the increase of some antineoplastic drugs in the areas investigated. Paclitaxel was the most manipulated antineoplastic, but it was only found in 16% of samples collected. Ifosfamide was the drug with the lowest rate of handling, however it was found in 26% of the |



or who were using antineoplastic drugs, and men who had undergone hormone therapy for less than 6 months were excluded from the study. A socio-cultural questionnaire was applied, information on the use of PPE and a daily description of the frequency of handling antineoplastic drugs were also collected. The drug measurement method took into account samples from the surface, location, air samples and the breathing zone of the persons. A measurement was taken of the drugs in the urine of workers and genetic damage biomarkers (comet assay). All the subjects wrote information regarding the handling of antineoplastic drugs in a diary for 6 weeks. The nursing technicians were not included in the individual analyses of handling because it was not possible to measure their exposure to antineoplastic drugs due to the variability of their tasks.

antineoplastic drugs  
53 in the control group who had not handled nor had been exposed.

samples. Cyclophosphamide was found in 46% of the cleaning samples. Pharmacy areas showed high levels of contamination, since the nursing areas had low concentrations as compared to the pharmacy area. Most of the air samples showed low concentrations of the drugs, and in the control group most were without any of the agents studied. Only 3 of the urine samples showed the substances that were investigated. The DNA changes were not different for the case group and the control group.

#### IDENTIFICATION AND DESCRIPTION OF THE MAIN FINDINGS (Part 6)

| Identification of the Article   | Periodical  | Year | Study Location | Objectives   | Methodology  | Population  | Main Conclusions   |
|---|-------------|------|----------------|--|--|---|--|
| Assessment of primary, oxidative and excision repaired DNA damage in hospital personnel handling antineoplastic drugs. Villarini M <i>et al.</i> <sup>7</sup> | Mutagenesis | 2011 | Itália         | To evaluate the contamination of the working environment by antineoplastic drugs in a hospital in Italy, and assess the risks associated with handling these genotoxic drugs | A sociocultural questionnaire was applied. Swabs were used to replace the skin, assessing its exposure to antineoplastic drugs. Each of the workers who had been exposed used 6 swabs, three from the inside of his work clothes, and three from the outside. The model compound (fluorouracil and cytarabine) was determined by using the liquid chromatography method for detecting ultraviolet rays. The actual exposure was assessed by urinary excretion of cyclophosphamide which was determined by gas chromatography/mass spectrometry. The alkaline comet assay measured DNA damage in peripheral blood lymphocytes. The study subjects were genotyped. | 52 Cases (6 pharmacy technicians, 16 nurses from the day hospital, 22 nurses from wards and 8 attendants) and 52 controls who were matched as to gender, age and lifestyle. | The prevalence of GSTM1 genotype was 63 individuals. The null count of GSTT1 was 9, whereas of GSTP1 it was 56 subjects, and polymorphism of the TP53 gene was found in 54 participants. Environmental monitoring showed different concentrations of antineoplastic drugs in the locations of administration and preparation, and the latter had the highest concentration of medications. There was contamination in the clothing of the cases. In some urine samples it was possible to detect the markers. There were obvious changes in the genetic material of those who had been exposed. The DNA damage was higher in the nurses who had exposed, as compared to the control group and pharmacists. The use of PPE was associated with a decreased in data of the genetic material. |

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## RESULTS

A total of 408 articles were found in the databases searched, of which 376 were in MEDLINE, 14 were in LILACS, 12 were in BDNF, and 6 were in SCIELO. Of these, only 10 met all of the criteria for eligibility, and they were used.

They showed results that were in compliance with the objective of the study, and all of them somehow evaluated the effects of antineoplastic drugs in short, medium or long terms, not only in the bodies but also in the quality of life of workers that handled them. Much of this was in the form of case-control studies. There was a higher frequency when using the keywords "Antineoplastic and Nursing", with 358 articles.

In Relevance Test 1, when using the keywords "antineoplastic and Occupational Nursing and Risk," 10 articles were found. After reading the abstracts (Relevance Test 2), only one article remained, and it was excluded after Relevance Test 3, which evaluated the full content of the study.

By using the keywords "Antineoplastic and Occupational Risk" in Relevance Test 1, 40 articles were found; while in Relevance Test 2, 10 articles remained; and at the end, in Relevance Test 3, eight articles met all the criteria for eligibility.

By using the keywords "Antineoplastic and Nursing", 358 works were found, of which four remained after performing Relevance Test 2, and at the end, 2 articles were selected.

The reasons for excluding articles from Relevance Test 2 and putting them in Relevance Test 3 were: Repetition in different databases (2), not presenting results nor conclusions, articles that were not yet completed (1), or a qualitative study, which did not present results (1). The total is 5 exclusions.

After performing the analysis, significant occupational impact on the workers was noticed. In the short term, workers who manipulated antineoplastic drugs during pregnancy had significantly higher rates of congenital abnormalities in the eyes of their offspring<sup>10</sup>, and they were more likely to have miscarriages, even in the first three months of pregnancy<sup>11</sup>. In the medium term there was chromosome damage<sup>5,6,8,11,7</sup>, aberrant lymphocytes, deletions, gaps and ruptures<sup>5</sup>, aberrations in chromatids<sup>8,11</sup>, decreased production of lymphocytes<sup>8</sup>, and increased frequency of micronuclei<sup>6,14</sup>. Over the long term, nurses who handled chemotherapeutical substances had a higher risk of their children being born with a cleft lip/cleft palate, as well as a higher risk of breast cancer and rectal cancer<sup>10</sup>.

The most common risk factors for increasing occupational harm were: being a nurse<sup>5,6,7,10</sup>, the workplace<sup>10</sup>, the amount of time in being exposed to antineoplastics<sup>5,9,10</sup>, idade<sup>5,9,11</sup>, not using or misusing PPE<sup>5,11,15</sup>, and consuming alcohol<sup>6</sup> and tobacco<sup>9,11</sup>.

In Table 1, the 10 articles that met all inclusion criteria and were approved in all of the relevant tests are identified and described. The details that are described succinctly and objectively include the Article Identification, stating the title and author of each article, the journal in which it was published, the year of publication, the study location,

the objectives thereof, the methodology used, the population that was studied, and finally, the Main Conclusions.

## DISCUSSION

There have not been many studies with satisfactory methodological quality that analyze the occupational risks to which nurses and health staff are exposed upon handling antineoplastic substances.

There is scientific evidence that they exist, and the damages to workers' health are unquestionable<sup>5,8,10-11,16-17</sup>. A study conducted in Croatia brought together 100 women, half of whom had had contact with chemotherapeutic drugs. Of these, 7, or more than 10% of the case group, stated they had suffered a miscarriage at least once<sup>11</sup>, so it is clear that antineoplastic substances cause a major interference in fetal formation. Another study, which was conducted in Canada<sup>10</sup>, evaluated a cohort group of babies who were born as of 1986, and it revealed that the children of nurses who had been exposed to these drugs during gestation had a significantly higher risk of abnormalities in their eyes. When a cumulative exposure over 10 years was taken into account, their children had higher rates of occurrence of cleft lip and cleft palate. These same women had a higher risk of developing cancer. It is a fact that handling chemotherapy drugs, whether it is over the short, medium or long term, irreversibly alters human genes.

Damage to genetic material is something that has already been well established. In Egypt<sup>5</sup>, in Brazil<sup>6</sup>, in Tunisia<sup>8</sup>, in Croatia<sup>11</sup>, and in Italy<sup>7</sup> studies have shown damage to chromosomes, most of which was evaluated by comet assay. In Egypt, the subjects of the case studies had worked with chemotherapy for 2-20 years. The damage to DNA was directly proportional to the time for which they had worked<sup>5</sup>.

It is clear that the use of devices which can reduce the workers' exposure are fundamental<sup>18-19</sup>. In many cases, concern about reducing the contamination of the environment<sup>19,20</sup>, coupled with the use of high-quality PPE<sup>21-22</sup>, has resulted in decreasing the harm caused by antineoplastic drugs<sup>5,7,11</sup>.

It is not enough just to provide PPE for workers, but it is also necessary to provide continuing education so that they can be used correctly<sup>22</sup>, since the incorrect usage of them has contributed to the increased contamination of workers and damage to their bodies<sup>5,11</sup>.

The fact that nurses represent the professional class with the highest rate of occupational injuries among those studied<sup>5-7</sup>, may be due to less stringent measures adopted by them at the time of handling antineoplastic drugs<sup>5</sup>.

Studies have shown that cytogenetic vigilance<sup>11,23</sup> along with periodic monitoring of the health status of these workers are forms of control, and consistent attitudes, in relation to the risks that have been shown<sup>11</sup>, may modify the course of the changes, thus minimizing [negative] outcomes.

## CONCLUSION

This study shows that health care workers who have been exposed to chemotherapeutic agents suffer innumerable adverse effects on the body in the short, medium and long terms.

Nurses are those who are the most affected when compared to other professional groups.

The most frequent damage is that which is done to the DNA, and it was predominant in the medium and long terms. The amount of exposure time was crucial for the increase of such damages.

What stood out in the short and long terms were the damages related to the development of the fetus, thus increasing congenital anomalies.

There are many risks to which the nursing staff that handles antineoplastic drugs is exposed, with deleterious effects to one's health. Educating about, encouraging and requiring the correct usage of PPE can be a good way to start improving these indicators.

Studies should be conducted to determine the most significant risk factors among these types of exposure, and proposals should be made so that the risks and dangers can be minimized, since the benefits to cancer patients who receive chemotherapy are even greater than the risks offered to the staff that administers it.

This study brings forth contributions to nursing and all the staff that handles these medications, whereas it shows evidence that there is much to be done for the occupational safety of these workers.

## REFERENCES

- 1 OHSAS 18001:2007. Sistemas de gestão da segurança e saúde no trabalho: requisitos. São Paulo: Risk tecnologia, 2007.
- 2 Brasil. Ministério do Trabalho [internet]. Portaria n° 3.214, 08 de junho de 1978. [acesso 2013 ago 03]. Disponível em: <<http://portal.mte.gov.br/legislacao/portaria-n-3-214-de-08-06-1978-1.htm>>.
- 3 FUNDACENTRO (2005). Diretrizes sobre Sistemas de Gestão da Segurança e Saúde no Trabalho. Versão Brasileira das Diretrizes da OIT (ILO-OSH 2001). Fundacentro, Brasil, 2005.
- 4 The National Institute for Occupational Safety and Health (NIOSH). [internet] Occupational Exposure to Antineoplastic Agents. [acesso 2013 out 12]. Disponível em: <<http://www.cdc.gov/niosh/topics/antineoplastic/>>.
- 5 El-Ebiary AA, Abuelfadl AA, Sarhan NI. Evaluation of genotoxicity induced by exposure to antineoplastic drugs in lymphocytes of oncology nurses and pharmacists. *J Appl Toxicol.* 2013 Mar; 33(3): 196-201.
- 6 Rombaldi F, Cassini C, Salvador M, Saffi J, Erdtmann B. Occupational risk assessment of genotoxicity and oxidative stress in workers handling anti- neoplastic drugs during a working week. *Mutagenesis.* 2009 Sep; 24(2): 143-8.
- 7 Villarini et al. Assessment of primary, oxidative and excision repaired DNA damage in hospital personnel handling antineoplastic drugs. *Mutagenesis.* 2011 May; 26(3): 359-69.
- 8 Bouraoui S, Brahem A, Tabka F, Mrizek N, Saad A, Elghezal H. Assessment of chromosomal aberrations, micronuclei and proliferation rate index in peripheral lymphocytes from Tunisian nurses handling cytotoxic drugs. *Environ Toxicol Pharmacol.* 2011 Jan; 31(1): 250-7.
- 9 Kopjar et al. Assessment of genotoxic risks in Croatian health care workers occupationally exposed to cytotoxic drugs: a multi-biomarker approach. *Int J Hyg Environ Health.* 2009 Jul; 212(4): 414-31.

- 10 Ratner et al. Cancer incidence and adverse pregnancy outcome in registered nurses potentially exposed to antineoplastic drugs. *BMC Nurs.* 2010 Sep; 9(15): 1-11.
- 11 Kopjar et al. The genotoxic risk in health care workers occupationally exposed to cytotoxic drugs--a comprehensive evaluation by the SCE assay. *J Environ Sci Health A Tox Hazard Subst Environ Eng.* 2009 Apr; 44(5): 462-79.
- 12 Mendes KDS, Silveira RCCP, Galvão CM. Revisão integrativa: método de pesquisa para a incorporação de evidência na saúde e na enfermagem. *Texto & contexto enferm.* 2008 Oct./Dec; 17(4): 758-64.
- 13 Pereira AL, Bachion MM. Atualidades em revisão sistemática de literatura, critérios de força e grau de recomendação de evidência. *Rev gaúch enferm.* 2006 dez; 27(4): 491-8.
- 14 Stover D, Achutan C. Occupational exposures to antineoplastic drugs in an Oncology-Hematology Department. *J Occup Environ Hyg.* 2011 Jan; 8(1): D1-6.
- 15 Cavallo D, Ursini CL, Rondinone B, Iavicoli S. Evaluation of a suitable DNA damage biomarker for human biomonitoring of exposed workers. *Environ Mol Mutagen.* 2009 Dec; 50(9):781-90.
- 16 Huang YW, Jain L, Zhang MB, Zhou Q, Yan XF, Hua XD, Zhou Y and He JL. An investigation of oxidative DNA damage in pharmacy technicians exposed to antineoplastic drugs in two Chinese hospitals using the urinary 8-OHdG assay. *Biomed Environ Sci.* 2012 Feb; 25(1): 109-16.
- 17 Mrđanović J, Jungić S, Šolajić S, Bogdanović V and Jurišić V. Effects of orally administered antioxidants on micronuclei and sister chromatid exchange frequency in workers professionally exposed to antineoplastic agents. *Food Chem Toxicol.* 2012 Aug; 50(8): 2937-44.
- 18 Forges F, Simoens X and Chauvin F. Comparative parallel assessment of a transfer device in reducing 5-fluorouracil environmental contamination inside positive air pressure isolators. *J Oncol Pharm Practice.* 2011 Mar; 17(1): 61-7.
- 19 Clark BA and Sessink PJM. Use of a closed system drug-transfer device eliminates surface contamination with antineoplastic agents. *J Oncol Pharm Prac.* 2013 Jun; 19(2): 99-104.
- 20 Chu WC, Hon C-Y, Danyluk Q, Chua PPS and Astrakianakis G. Pilot assessment of the antineoplastic drug contamination levels in British Columbia hospitals pre- and post-cleaning. *J Oncol Pharm Practice.* 2012 Mar; 18(1): 46-51.
- 21 Capron A, Destree J, Jacobs P and Wallemacq P. Permeability of gloves to selected chemotherapeutic agents after treatment with alcohol or isopropyl alcohol. *Am J Health-Syst Pharm.* 2012 Oct; 1;69(19): 1665-70.
- 22 Gulten T, Evke E, Ercan I, Evrensel T, Kurt E and Manavoglu O. Lack of genotoxicity in medical oncology nurses handling antineoplastic drugs: effect of work environment and protective equipment. *Work.* 2011; 39(4): 485-9.
- 23 NIOSH. 2013. Workplace solutions: medical surveillance for health care workers exposed to hazardous drugs. [internet]. DHHS (NIOSH) Publication No. 2013-103. [acesso 2013 out 14]. Disponível em: <[www.cdc.gov/niosh/docs/wp-solutions/2013-103/pdfs/2013-103.pdf](http://www.cdc.gov/niosh/docs/wp-solutions/2013-103/pdfs/2013-103.pdf)>.
- 24 Connor et al. Evaluation of antineoplastic drug exposure of health care workers at three university-based US cancer centers. *J Occup Environ Med.* 2010 Oct; 52(10): 1019-27.

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