INTEGRATIVE REVIEW ARTICLE

NURSING CARE PROVIDED TO HEMATOLOGIC CANCER PATIENTS RECEIVING HIGH-DOSE CHEMOTHERAPY: AN INTEGRATIVE REVIEW

CUIDADOS DE ENFERMAGEM A PACIENTES ONCO-HEMATOLÓGICOS SUBMETIDOS A ALTAS DOSES DE QUIMIOTERAPIA: REVISÃO INTEGRATIVA

CUIDADOS DE ENFERMEIRIA A PACIENTES ONCO-HEMATOLÓGICOS SOMETIDOS A ALTAS DOSIS DE QUIMIOTERAPIA: REVISIÓN INTEGRADORA

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ABSTRACT
Objective: To identify in the Brazilian and international literature nursing care provided to adult hematologic cancer patients receiving high-dose chemotherapy. Method: integrative review conducted in six stages intended to answer the question: “What type of nursing care is provided to adult hematologic cancer patients receiving high-dose chemotherapy followed by HSCT or not?” The search strategy included the combination of the descriptors: nursing, hematologic diseases, bone marrow transplantation, hematopoietic stem cell transplantation, and neutropenia in the Cochrane/Central, Cinahl, Lilacs and Medline databases. The analysis and synthesis of data were described according to thematic categories. Results: the sample was composed of 13 primary studies divided into three thematic categories: Physical exercises and fatigue, Patient safety, and Mucositis care. Conclusion: synthesized evidence enables nurses to select and implement strategies intended to prevent or control conditions that limit patients during treatment. Descriptors: Nursing Care; Hematopoietic Stem Cell Transplantation; Drug Therapy; Hematologic Diseases.

RESUMO
Objetivo: avaliar a partir da literatura nacional e internacional os cuidados de enfermagem prestados aos pacientes onco-hematológicos adultos internados submetidos a altas doses de quimioterapia. Método: revisão integrativa conduzida em seis etapas, a fim de responder a pergunta norteadora: “Quais os cuidados de enfermagem prestados aos pacientes onco-hematológicos adultos internados submetidos a altas doses de quimioterapia seguida ou não de TCTH?” A estratégia de busca foi realizada utilizando a combinação dos descritores: enfermagem, doenças hematológicas, transplante de medula óssea, transplante de células-tronco hematopoéticas e neutropenia, na Cochrane/Central, Cinahl, Lilacs e Medline. A análise e síntese dos dados foram descritivas segundo as categorias temáticas identificadas. Resultados: a amostra foi constituída por 13 estudos primários divididos em três categorias temáticas: Atividade física e fadiga, Segurança do paciente e Cuidados com mucosite. Conclusão: as evidências sintetizadas contribuem para o enfermeiro selecionar e implementar estratégias que possam prevenir ou controlar as condições que sejam limitantes ao paciente durante o tratamento. Descriptores: Cuidados de Enfermagem; Transplante de Células-Tronco Hematopoéticas; Quimioterapia; Doenças Hematológicas.

RESUMEN
Objetivo: evaluar a partir de la literatura brasileña e internacional los cuidados de enfermería prestados a pacientes onco-hematológicos adultos internados sometidos a altas dosis de quimioterapia. Método: revisión integradora conducida en seis etapas para responder a la pregunta orientadora: ¿Cuáles los cuidados de enfermería prestados a los pacientes onco-hematológicos adultos internados sometidos a altas dosis de quimioterapia seguida o no de TCTH? La estrategia de búsqueda fue aplicada utilizando la combinación de los descritores: enfermería, enfermedades hematológicas, trasplante de médula ósea, trasplante de células-tronco hematopoyéticas y neutropenia, en la Cochrane/Central, Cinahl, Lilacs y Medline. El análisis y síntesis de los datos fueron descritivas según las categorías temáticas identificadas. Resultados: la muestra abarcó 13 estudios primarios divididos en tres categorías temáticas: Actividad física y fatiga, Seguridad del paciente y Cuidados con mucositis. Conclusion: las evidencias sintetizadas contribuyen para que los enfermeros selecciones e implementen estrategias capaces de prevenir o controlar las condiciones limitadoras al paciente durante el tratamiento. Descriptores: Atención de Enfermería; Trasplante de Células Madre Hematopoyéticas; Quimioterapia; Enfermedades Hematológicas.

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INTRODUCTION

Hematologic cancer diseases can compromise several lineages of blood cells, both lymphoid and myeloid cells. The main diseases include acute and chronic leukemia, Hodgkin and non-Hodgkin lymphomas.1

The strategic therapies used to treat these diseases have considerably evolved in recent years and the antineoplastic chemotherapy is among the most relevant and promising ones, however, the side effects arising by high-dose induction and/or consolidation protocols have the potential to compromise the success of treatment.2 Note that the hematopoietic Stem Cell Transplantation (HSCT), which demands high-dose chemotherapy aiming pre-transplant bone marrow aplasia and subsequent engraftment of hematopoietic stem cells, has presented the possibility of healing and improving the survival of patients.3

Most antineoplastic chemotherapies are non-specific and hurt both malignant and benign cells, especially those capable of rapid cell division such as hematopoietic and germinal tissue, hair follicle, and epithelium that line the gastrointestinal system.2 Hence, the main side effects include neutropenia, thrombocytopenia, anemia, nausea and vomiting, and mucositis in addition to cardiac, liver and renal toxicities.1-2

A common condition that affects hematologic cancer patients during treatment, whether it is caused by the primary disease or chemotherapy, is neutropenia.

Neutropenia increases the risk of developing infection, which is enhanced by exposure of patients to the hospital setting, invasive procedures, and lengthy hospitalizations.4

Orientation and teaching provided by the nursing staff to patients and caregivers is essential to enable them to meet the various needs that arise during treatment, to prevent and/or control signs and symptoms caused by the side effects of high-dose chemotherapy induction and/or consolidation protocol as well as in hematopoietic stem cell transplantations.

Therefore, nurses should be aware of the specificities of hematologic cancer patients and treatment-related side effects as nursing care should be focused on the prevention and management of potential therapeutic complications.

OBJECTIVE

● To assess nursing care provided to adult hematologic cancer patients receiving high-dose chemotherapy by investigating the Brazilian and International literature.

METHOD

This paper originated from the thesis << Nursing care provided to hematologic cancer patients receiving high-dose chemotherapy >>, presented to the University of São Paulo at Ribeirão Preto, College of Nursing, SP, Brazil, 2012.

Integrative literature review based on six stages: establishment of the guiding question, sampling, extraction of data from primary studies, assessment of studies selected, analysis and synthesis of results, and presentation of the integrative review.4 The guiding question was: “What type of nursing care is provided to adult hematologic cancer patients receiving high-dose chemotherapy, regardless of subsequent HSCT?”


Criteria used to include the primary studies were: primary papers, full texts, published from January 1st 2001 to July 31st 2013, written in Portuguese, English, or Spanish, measuring a nursing intervention conducted among adult hematologic cancer patients, and using an quantitative approach.

Hence, after identifying the studies, two independent reviewers read the titles and abstracts and applied inclusion criteria. A
third reviewer, expert on the subject, assessed inconsistencies.

The results of the database search are presented in Figure 1 according to recommendations proposed by PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses).6

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**Figure 1. Selection of primary studies included in the sample, Ribeirão Preto, SP, Brazil 2001-2013.**

Two independent reviewers collected data from the studies included in the integrative review using an instrument addressing the following items: author(s), objective, methodological detail, and main results. Evidence from the intervention studies were hierarchically classified to enable a critical appraisal.7

The methodological quality of the randomized clinical trials was assessed using Jadad Scale8, a reliable instrument that contains three questions: 1) is the clinical trial described as randomized?; 2) is the clinical trial described as double blind?; 3) is there a description of withdrawals and dropouts? The maximum score is five, so that scores 1 and 2 refer to poor quality, 3 refers to moderate, while 4 and 5 denote high quality.

The critical analysis of data and qualitative synthesis of the primary studies were descriptively presented according to the thematic categories, level of evidence7, and Jadad score8.

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**RESULTS AND DISCUSSION**

A synthesis of the 13 primary studies is presented according to thematic categories, namely: physical activity and fatigue9-13.
patient safety\textsuperscript{14-18} and care provided to mucositis\textsuperscript{19-21}, considering an expanded guiding question and diversity of subjects.

<table>
<thead>
<tr>
<th>Author(s)</th>
<th>Objective</th>
<th>Methodological detailing</th>
<th>Main Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kim, Kim, 2005a</td>
<td>To assess the effect of breathing relaxing exercises on anxiety, depression, and leukocyte count among patients receiving allogeneic HSCT.</td>
<td>Randomized clinical trial (RCT).</td>
<td>Breathing exercises to relax may be an effective nursing intervention to relieve depression and anxiety during hospitalization but it did not show positive impact on leukocyte count. Further research, however, is needed to assess the efficacy of this intervention over the long run.</td>
</tr>
<tr>
<td>Kim, Kim, 2005b\textsuperscript{10}</td>
<td>To investigate the effect of breathing exercises to relax and to relieve fatigue among patients receiving allogeneic HSCT.</td>
<td>RCT</td>
<td>The intervention group presented statistically significant changes on fatigue scores when compared to the control group’s scores. Therefore, breathing exercises can relieve the fatigue of patients receiving allogeneic HSCT.</td>
</tr>
<tr>
<td>Kim, Kim, 2006\textsuperscript{11}</td>
<td>To investigate the effect of exercises performed at the bedside during hospitalization on the lymphocyte count of patients receiving HSCT.</td>
<td>RCT</td>
<td>Even though this intervention has favored increased lymphocyte total count at the short run (6 weeks), its efficacy at the long run requires that new randomized controlled clinical trials are conducted.</td>
</tr>
<tr>
<td>Hacker, Ferrans, 2007\textsuperscript{12}</td>
<td>To describe the experience of applying the Ecological Momentary Assessment (EMA) and discuss it’s applicability to real-time fatigue monitoring among patients receiving HSCT.</td>
<td>Descriptive study</td>
<td>EMA is a feasible scale to monitor real-time fatigue among cancer patients. 87% of the patients who received HSCT were able to report real-time fatigue even when experiencing the side effects of the conditioning regime.</td>
</tr>
<tr>
<td>Jarden et al., 2009\textsuperscript{13}</td>
<td>To explore the benefits of a multimodal intervention composed of physical exercises, progressive relaxation, and psycho-education to control symptoms related to HSCT.</td>
<td>RCT.</td>
<td>The intervention was efficacious to decrease allogeneic HSCT-related symptoms (gastrointestinal, cognitive, affective, functional and mucositis).</td>
</tr>
</tbody>
</table>

Figure 1 presents the studies addressing physical activity and fatigue.

Figure 1. Synthesis of primary studies addressing nursing care associated with physical exercises and fatigue according to author, objective, methodological detail, and primary results. Ribeirão Preto – SP, Brazil 2001-2013.
Physical activity and fatigue

Employing deep breathing and stretching relaxation techniques at the bedside relaxes the body and provides physiological and mental rest so that neuromuscular activity is reduced, decreasing proprioceptive input in the hypothalamus, which in turn results in decreased activation of the simpatico nervous system and excitability of the cerebral cortex. Relaxing techniques involve teaching patients to adjust to external stimuli, which favors the acquisition of a sharper internal awareness enabling them to recognize their physiological and psychological states. Fatigue should be seen as a multi-causal and multidimensional condition, the complexity of which is similar to pain.9–11

The level of fatigue in patients receiving HSCT is greater after routine activities such as taking a shower, medical assessment, eating, and after healthcare providers have applied dressings and it may be worsened when the functional state of patients is altered due to mucositis, infection, pain or medication.12

Exercises practiced by patients during hospitalization and after discharge improve their functional state in addition to psychological aspects and quality of life. Gastrointestinal, cognitive, affective, functional symptoms and those related to mucositis showed statistically significant improvement in the intervention group, especially from three to six months after HSCT. The functional status of patients was also assessed in this study using the Karnofsky Performance Status Scale to predict clinical conditions among patients before physical exercise.13

Figure 2 synthesizes studies addressing patient safety.

<table>
<thead>
<tr>
<th>Author(s)</th>
<th>Objective</th>
<th>Methodological detail</th>
<th>Primary Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sharda et al., 200114</td>
<td>To assess the need for late-night vital signs checks.</td>
<td>Descriptive study. 20 inpatients receiving autologous or allogeneic HSCT both related and unrelated donors.</td>
<td>Monitoring vital signs is indicated only in risk situations, the predictive factors of which can be identified during the day, such as: fever and alterations in the central venous system.</td>
</tr>
<tr>
<td>Fonseca, Secoli, 200815</td>
<td>To characterize the profile of medications in regard to times they are administered and potential interaction and identify combinations among potentially interactive antimicrobial drugs and other drugs co-administered to patients receiving HSCT.</td>
<td>Descriptive study. 70 medications prescribed to HSCT inpatients one day before the bone marrow transplantation (D-1).</td>
<td>Most medications have potential to interact, especially precipitators that may affect the hepatic metabolism. The co-administration of antimicrobial drugs with potential to interact occurred in half the sample; fluconazole was the agent most frequently found. Polypharmacy and simultaneous administration of medications predisposes patients to adverse events and compromises the therapy safety.</td>
</tr>
<tr>
<td>Apostolopolou et al., 201016</td>
<td>To assess the predictive power of three scoring systems: IPS (Infection Probability Score), APACHE II and KARNOFSKY to assess infections associated to health care provided to hematologic cancer patients.</td>
<td>Descriptive study. 102 patients hospitalized in hematologic unit for more than 48 hours were included in the analysis.</td>
<td>Among the three instruments statistically assessed, the systematic use of IPS better predicts and early detects HAIs (healthcare-associated infections) among hematologic cancer patients.</td>
</tr>
<tr>
<td>Mank et al., 201017</td>
<td>To identify groups of patients who can be safely discharged immediately after receiving high-dose chemotherapy.</td>
<td>Cohort. 55 patients treating hematologic cancer diseases assigned to four groups according to the therapeutic regime: induction, consolidation, and autologous and allogeneic HSCT.</td>
<td>Hematologic cancer patients treated with high-dose consolidation chemotherapy and those with a good clinical status receiving autologous HSCT are suitable candidates to early discharge, immediately after stem cells infusion.</td>
</tr>
</tbody>
</table>
| Boonstra et al., 201018 | To identify the level of | Descriptive study. | Difficulty to sleep is a...
sleep disorders among HSCT patients, the factors that contribute to decreased ability to sleep during hospitalization, and compare age, sex, type of transplantation, and between hospitalization to receive transplantation versus hospitalization due to complications arising from the HSCT among those with sleep disorders.

69 autologous or allogeneic HSCT patients hospitalized for at least 14 days.

Level of evidence: VI

significant concern among transplantation patients. The frequent need to use the bathroom and the need of care were the factors most frequently reported. Interventions that could be tested in the future include grouping late-night nursing care to minimize interruptions, schedule nurses’ visits before night time, encourage the use of bathroom, and if possible, decrease the volume of fluids infused during night.

Figure 2. Synthesis of primary studies addressing nursing care regarding patient safety according to author, objective, methodological details, and primary results. Ribeirão Preto - SP, Brazil 2001-2013.

Noise, lights, pain, anxiety, depression, late-night nursing and medical procedures performed among HSCT patients can affect their quality of sleep. The real need to assess vital signs in the middle of night was verified and results indicate that nurses can predict those patients who may be at risk and require such procedures. Another aspect is the possibility of early discharging low-risk patients and implementing outpatient monitoring as patients would experience better quality sleep at home. The need to use the bathroom, interruptions during the night because of procedures provided by the nursing staff, physical symptoms, anxiety, and noise were reported in this order as the reasons that contribute to sleep disorders. Nurses could propose care that minimize sleep disorders such as encouraging the use of the bathroom before sleeping, helping patients to manage signs and symptoms that arise from lack of sleep, providing medication when necessary, and decreasing the level of noise in the environment.

Another aspect related to patient safety refers to the use of medications and potential interaction. Nurses should carefully assess the prescriptions of HSCT patients to decrease the risk of drug interaction. Preventive measures include seeking information regarding medications and intervening when there is simultaneous administration of medication, and when intervention is not possible, monitoring potential adverse effects.

The following variables were assessed to check the safety of early discharging patients receiving high-dose chemotherapy, followed by HSCT or not: the occurrence of neutropenia, functional status, fever, infection, the use of antibiotics, and mucositis in different groups of patients (induction, consolidation, and autologous and allogeneic HSCT). The results show that the group receiving consolidation treatment can better adapt to early hospital discharge but autologous HSCT patients can also be considered according to their functional status, mucositis and neutropenia.

The power of the scoring instruments, Infection Probability Score (IPS), APACHE II and Karnofsky to predict infection among patients was also assessed. The results show that IPS was more accurate in predicting hospital infections. The IPS favors early detection of infections among high-risk hematologic patients, especially in the first three days of hospitalization, which can improve measures to prevent and control infection. The conclusion is that adherence to these measures is required from professionals involved in care delivery as they need to integrate these measures in their practice despite emphasis and improved care intended to avoid the transmission of infections.

Figure 3 presents a synthesis of mucositis-related studies.
Carlucci VDS, Braga FTMM, Rei PED dos et al.

Nursing care provided to hematologic cancer...
to the effects of therapy and stress experienced during and after treatment.23

There are studies presenting the implication for nursing care indicating that exercises improve one’s physical and psychological health along with quality of life and are easily implemented among cancer patients.24-27 Elastic bands can be used during exercises because they are portable and easy to handle and also relatively cheap in comparison to dumbbells or other equipment. An exercise program to be implemented at the outpatient clinic or at home is feasible during the initial phase or recovery after high-dose chemotherapy and transplantation.25

Therefore, exercises contribute to the functional state of patients, alleviate fatigue and control the side effects presented by patients during and after hospitalization. Nurses can implement low-impact activities to improve the performance of patients during hospitalization.

In regard to fatigue, this is acknowledged as one of the most frequent side effects, with prevalence between 25% and 99%.1 Hence, it is essential to constantly measure and assess fatigue during and after the infusion of high-dose chemotherapy.

Patient safety

Quality of sleep can be compromised by various factors: insomnia, clinical conditions, and environmental and psychological factors. Lack of sleep is associated with changed immune function and metabolism, psychological disorders, and quality of life.28 Additionally, lack of sleep is directly related to safety patient, as it is a risk factor for falls.

A study addressing the prevalence, nature, and causes of sleep disorders during the HSCT acute phase reports that the prevalence of sleep disorders was 32% before hospitalization, 77.3% during hospitalization, and 28% 100 days after HSCT. The results show higher prevalence rates during hospitalization, while women and elderly individuals experience worse quality of sleep when compared to adult and young men. Patients receiving allogeneic transplantation experience worse quality of sleep compared to those receiving autologous HSCT. Decreased functional activity increases fatigue, stress, anxiety and depression. Sleep disorders experienced by patients during hospitalizations present a multifactorial etiology, while noise of equipment, need to use the bathroom, and late-night nursing care, stand out.29

Routine care provided to hematologic cancer patients receiving high-dose chemotherapy interrupts the rest of hospitalized patients, changing their sleep patterns, characterized by short periods of sleep during the day and night. Nurses need to carefully assess and discuss with the medical team the real need of late-night interventions, such as the time medications are administered to improve the patients’ quality of sleep.

In regard to the safety of medication therapy, incidents with the administration of drugs suggest that programs to monitor and report adverse events should be implemented in hospitals. These programs facilitate documentation and reporting, providing mechanisms that enable the safe use of medications by high-risk patients and also encourage professionals to identify potential events.29 Critical and elderly patients are more susceptible to adverse events due to the number of medications they require coupled with physiological changes caused by the disease, comorbidities, and decreased vital functions. Medications that may cause interaction include low therapeutic index drugs, which in combination with other drugs can enhance toxicity, worsening the clinical conditions of patients. Therefore, the knowledge of nurses regarding the medications prescribed to patients is key to prevent and observe potential side effects accruing from drug interactions. Another preventive measure is paying attention to the times when medications are administered to avoid enhancing or decreasing the effect of any of the medications.29

In regard to early discharge, a study assessing the feasibility of an outpatient follow-up program directed to autologous HSCT patients who received high-dose melphalan reports that early hospital discharge is feasible but aspects such as expectation of healing mucositis, fever management, and the need of antibiotics should be taken into account. Another aspect is the need of services to adapt their infrastructure to meet the needs of patients in case of intercurrences and to keep quality care.30

Another study assessing the early discharge of hematologic cancer patients receiving consolidation chemotherapy reports that orientation was provided during hospitalization regarding care provided to neutropenia including: catheter care, body and oral general self-care, paying attention to fever such as elevated body temperature for more than a hour, checking for the presence of petechiae, bleeding, and returning to the health service in case of signs and symptoms.
that require urgent care. The authors concluded that early hospital discharge is safe for feverless neutropenia patients with the exception of elderly patients or those with severe clinical conditions.31

Therefore, early discharging patients with adequate functional capacity, monitored by a healthcare service with outpatient structure, can bring benefits related to diet, contact with family members and friends, and decreased environmental stressors.

The epidemiology and management of infections among HSCT patients should be assessed and based on current knowledge and on the individual characteristics of patients. There are recommendations regarding appropriateness of room ventilation such as the use of heap filters, environmental cleaning, hand washing on the part of healthcare providers, caregivers, visitants and patients, vaccination, and mouth and skin care.32

Knowledge of nurses regarding the patients' treatment regime ensures careful assessment followed by interventions with potential to minimize risks of complications in addition to other stressors during the course of the treatment in the hospital setting.

**Mucositis**

The use of cryotherapy in the oral cavity decreases blood flow through vasoconstriction, which in turn decreases the chance of cytotoxic drugs to reach the oral mucosa, preventing mucositis. It has been used to decrease the severity and incidence of oral mucositis. The Multinational Association of Supportive Care in Cancer and International Society of Oral Oncology (MASCC/ISOO) suggests the use of oral cryotherapy to prevent oral mucositis among patients receiving high-dose melphalan in the HSCT conditioning regime.33

In addition to cryotherapy, some measures are emphasized regarding oral hygiene such as brushing teeth often and using nonabrasive toothpastes and mouthwashes33, in addition to assessing pain and using topical anesthetics or other agents to relieve discomfort and manage mucositis.

Nurses should classify the oral conditions of patients daily and report the characteristics, signs and symptoms of mucositis using instruments and recording these signs and symptoms in order to establish criteria to manage the condition, and define protocols and assessment routines with the staff.

Finally, in regard to the methodological quality of studies, the Jadad scale was applied to all the randomized clinical trials included in the sample, while four studies scored 3 and two studies scored 2.

**CONCLUSION**

This review included 13 primary studies grouped into three thematic categories: physical exercises and fatigue, patient safety, and mucositis care. Most were published between 2007 and 2011, among which six were randomized clinical trials and the level of evidence most frequently observed was II. The most frequent Jadad score was 3, indicating moderate methodological quality.

The interventions proposed in the studies were intended to minimize or improve treatment-related side effects among adult hematologic cancer inpatients receiving high-dose chemotherapy whether it was followed by HSCT or not.

All the side effects presented occur during or after hospitalization and may compromise the patients’ nutritional and functional status, posing risks to the safety of patients.

Fatigue was the outcome most frequently reported by the studies addressing exercise. Primary studies that did not measure fatigue discussed its occurrence in situations such as changed sleep patterns, infections, lengthy hospitalizations, and mucositis. Low-impact exercises are recommended to decrease fatigue, increase the count of leukocytes and decrease treatment-related stress.

In regard to patient safety, we highlight the maintenance of regular sleep and rest patterns, whenever possible, minimization of drug interaction by managing the time when medications are administered, and careful assessment before early discharge.

Suggestions regarding mucositis include daily assessment of the oral cavity and establishment of a care routine, among which cryotherapy.

**REFERENCES**


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Nursing care provided to hematologic cancer…

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