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REVISIONES

Pain management in children and teenagers during the hematopoietic stem cell post-transplant period: an integrative review

Gerenciamento da dor de crianças e adolescentes no período pós-transplante de células-tronco hematopoéticas: revisão integrativa

Gestión del dolor de niños y adolescentes durante el período post-trasplante de células-tronco hematopoyéticas: una revisión integradora

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ABSTRACT:

This study aims at the identification of strategies used for pain management in children and teenagers during the hematopoietic stem cells post-transplant period. An integrative review of literature was employed as methodology for this work, using as sources of information the following databases: MEDLINE, LILACS, SCIELO, BDENF, SCOPUS, Web of Science and CAPES periodic portal. The terms used for searching were: pain, pain management, pain pediatric, hematopoietic stem cell transplantation, bone marrow transplantation; and the acronyms BMT and HSCT. The final sample comprised seven articles, based on inclusion and exclusion criteria. The identified strategies for pain management in the studies were: patient-controlled analgesia, caregiver-controlled analgesia; complementary therapies such as: aromatherapy, extra-oral phototherapy with infrared diodes, heat application, cryotherapy, music, games, massage; and results indicators, in order to monitor the pain management effectiveness. As a conclusion, the most effective strategies were: patient or caregiver-controlled analgesia, and the results indicators that allowed pain management in adequate time. Nevertheless, it is important to highlight that other studies are necessary to evaluate the effectiveness of the complementary strategies employed.

Keywords: Pain; Pain management; Hematopoietic stem cell transplantation; Child; Adolescent.

RESUMO:

Este estudo teve como objetivo identificar, em produções científicas, as estratégias utilizadas para o gerenciamento da dor de crianças e adolescentes no período pós-transplante de células-tronco hematopoéticas. Para tanto, utilizou-se como metodologia a revisão integrativa da literatura a partir das

seguintes fontes de informação: MEDLINE, LILACS, ScIELO, BDENF, SCOPUS, *Web of Science* e Plataforma de periódicos CAPES. Os descritores utilizados para a busca foram: *pain*, *pain management*; *pain pediatric*; *hematopoietic stem cell transplantation*; *bone marrow transplantation*; e as siglas BMT e HSCT. A amostra final foi constituída por sete artigos científicos, com base nos critérios de inclusão e exclusão. As estratégias de gerenciamento da dor identificadas nos estudos foram: analgesia controlada pelo paciente, analgesia controlada pelo cuidador; terapias complementares, tais como: aromaterapia; fototerapia extra oral com diodos infravermelhos; aplicação de calor; crioterapia; música, jogos, massagem; e indicadores de resultados para monitorar a eficácia do gerenciamento da dor. Concluiu-se que as estratégias mais eficazes foram: analgesia controlada pelo paciente ou cuidador e o indicador de resultados que possibilitou o controle da dor em tempo hábil. Não obstante, é importante ressaltar que outros estudos são necessários para avaliar a eficácia das estratégias complementares citadas.

Palavras-chave: Dor; Manejo da dor; Transplante de Células-Tronco Hematopoéticas; Criança; Adolescente.

RESUMEN:
Este estudio tuvo como objetivo identificar, en producciones científicas, las estrategias utilizadas en la gestión del dolor de niños y adolescentes durante el período post trasplante de células-tronco hematopoyéticas. Para ello, utilizó como metodología la revisión integradora de la literatura a partir de las siguientes fuentes de información: MEDLINE, LILACS, ScIELO, BDENF, SCOPUS, *Web of Science* y Plataforma de periódicos CAPES. Se utilizó como descriptores: *pain*, *pain management*; *pain pediatric*; *hematopoietic stem cell transplantation*; *bone marrow transplantation*; y las siglas BMT e HSCT. La muestra final fue constituida por siete artículos científicos, a partir de los criterios de inclusión y exclusión. Las estrategias para la gestión del dolor identificadas en los estudios fueron: analgesia controlada por el paciente, analgesia controlada por el cuidador; terapias complementarias, tales como: aromaterapia; fototerapia extra oral con diodos infrarrojos; aplicación de calor; crioterapia; música, juegos, masaje; e indicadores de resultados para medir la eficacia de la gestión del dolor. La conclusión es que las estrategias más eficaces fueron: analgesia controlada por el paciente o cuidador y el indicador de resultados que posibilitó el control del dolor en tiempo hábil. Sin embargo, es necesario hacer hincapié en la importancia de invertir en otros estudios para evaluación de la eficacia de dichas estrategias complementarias.

Palabras clave: Dolor; Manejo del dolor; Trasplante de Células-Tronco Hematopoyéticas; Niño; Adolescente

INTRODUCTION

Pain is one of the oldest symptoms described by man. It is a complex phenomenon which affects individuals since the very beginning of life and during their development[1,2]. It serves as a warning mechanism, helping detect harmful physical or chemical events[3], being described by the *International Association for the Study of Pain* (IASP)[4] as “an unpleasant sensory and emotional experience, associated with actual or potential tissue damage. Each individual learns to use this term through earlier experiences”.

Literature also describes pain as a subjective experience, hard to be quantified due to its affective and sensory components[3-5]. A great number of studies highlight pain management as challenging to professionals, mainly when it entails children and adolescents[6]. However, only in the 1980s, pediatric pain started to be particularly examined by researchers, who reported psychological and emotional outcomes when it was not properly managed[5].

It is common for hospitalized children and adolescents to experience pain on a daily basis, due to procedures or pathology itself[2]. A study held in hospital settings showed that pain was present in 86% of the assessed children[7]. In patients, who underwent Hematopoietic Stem Cell Transplantation (HSCT), pain can be aggravated by

chemotherapy side effects and acute post-transplantation complications, among them, gastrointestinal complications, oral mucositis, venous-occlusive disease, and Graft Versus Host Disease (GVHD)[8].

The number of HSCT has been gradually increasing in Brazil[9], once it is considered a type of therapeutics with high potential of cure for oncological, hematological, immunological and genetic diseases. Treatment aims to regulate hematopoiesis by replacing individuals' faulty cells with donor's healthy hematopoietic cells[10]. Despite its benefits, such a population gets vulnerable to multiple comorbidities, which lead them to a painful, often debilitating state, such as nausea, vomit, GVHD, infections, gastrointestinal complications and mucositis[8].

Studies carried out with pediatric population point out that pain self-reporting post-HSCT may vary between 43% and 69%, having oral mucositis as well as gastrointestinal complications as the main causes[8]. Pain management, in this context, is hard as it fundamentally depends on the resolution of its cause, and professionals' endeavor by using different management strategies, aiming at the child or teenager's well-being as a qualitative study showed, in which children and parents reported the need to improve pain management, once they considered that the nursing team had failed in their assessment and guidance on pharmacological therapy[11].

By considering pain one of the main symptoms of pediatric HSCT, as evidenced by literature, as well as the existence of several pharmacological and non-pharmacological strategies for pain management in children and adolescents, it was verified the need to reflect on the theme[11]. Thus, the current study objectified to identify, in scientific productions, strategies of pain management for children and adolescents undergoing HSCT.

METHODOLOGY

It is an integrative literature review. This method comprises the process of elaboration and organization of a body of literature, which allows the inclusion of experimental and non-experimental studies to interpret a certain theme. Thus, it contributes to the development of a clinical and practical theory, informing new evidences in scientific research.

In the process of elaboration of this study, six steps were used: 1) theme identification and formulation of the guiding question; 2) definition of the sample inclusion and exclusion criteria; 3) profile of the pre-selected studies; 4) analysis of the findings; 5) result interpretations; and 6) synthesis of the results[12].

In the first step, the following guiding question was formulated: "What are the strategies used for pain management in children and adolescents who underwent HSCT?".

For sample selection, inclusion criteria were defined as follows: articles whose addressed theme entails strategies of pain management for children or adolescents undergoing HSCT, indexed in national and international databases, with complete texts in English, Portuguese or Spanish. It should be pointed out that, facing the scarcity of findings; it was opted for not using temporal clipping.

Regarding the exclusion criteria, they consisted of review articles or the ones which did not involve research with human beings, studies exclusively carried out with adult population, theses, dissertations and abstracts.

Search was held between June and July, 2017, in electronic databases: MEDLINE, LILACS, ScIELO, BDENF, SCOPUS, Web of Science, and the platform of Brazilian journals from the Coordination for Higher Education Personnel Improvement (Coordenação de Aperfeiçoamento de Pessoal de Nível Superior - CAPES), using the boolean operators “AND” and “OR” in order to match MeSH descriptors: pain, pain management; pain pediatric; hematopoietic stem cell transplantation; bone marrow transplantation; and the acronyms BMT and HSCT. The amount of articles found per database, and in the platform of CAPES journals are organized in Table 1.

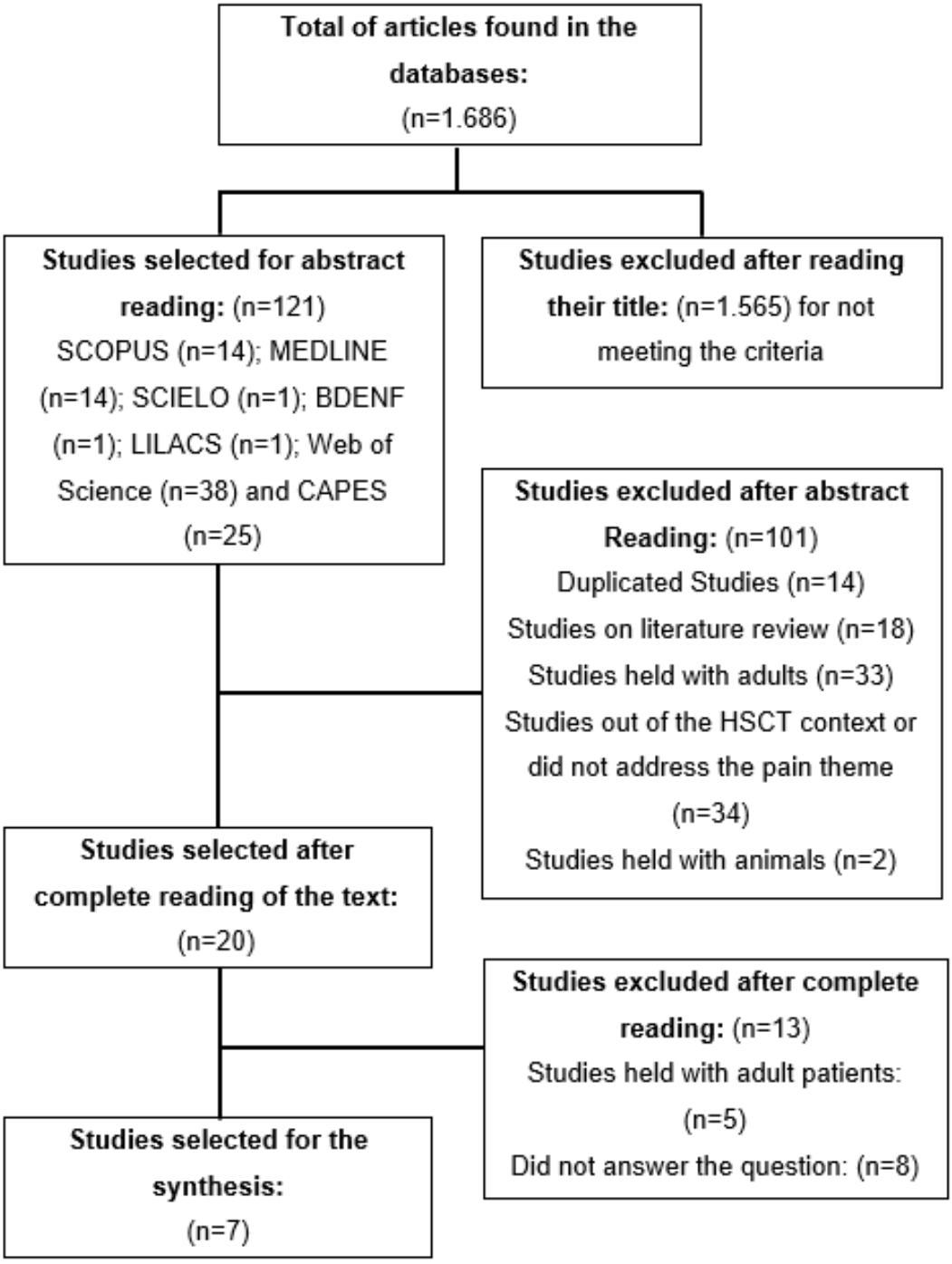
Table 1: Distribution of the total studies found in the electronic search, organized by databases and platform of CAPES journals. Curitiba-Paraná State, Brazil, 2017

Descriptors	Data Sources	Total of the found studies
Pain management AND Stem Cell Transplantation OR Bone Marrow Transplantation.	SCOPUS	49
	MEDLINE	323
	SCIELO	80
	BDENF	3
	LILACS	307
	Web Of Science	285
Pain AND pedriatric AND BMT OR HSCT.*	Platform of CAPES journals*	639
Total		1,686

*In the platform of CAPES journals, search was carried out by means of filters to make results more accurate.

Subsequently, a triage of the articles was held for the sample selection, with a more critical, deeper look at the texts. The selection was carried out according to the recommendations of the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA). (Figura 1).

Figure 1 – Flowchart for the study selection



An instrument of data collection was elaborated by the researchers in order to characterize the selected articles by means of the Microsoft Office Excel® 2016, contemplating: authors, year of publication, journal and venue, in addition to major information about the studies, such as objectives, method, strength of evidence and results.

The authors elaborated another instrument for the analysis of the quantitative studies in order to facilitate the interpretation of the findings, comprising the following data: strategies used for pain management, instruments of pain assessment, pain location, assessment frequency and involved professionals.

The analysis of the studies, as well as their classification according to their strength of evidence, was held according to the recommendations of the Agency for Health care Research and Quality (AHRQ), which rates the strength of evidence in: level I, meta-analysis and systematic review; level II, single experimental studies, level III, quasi-experimental study; level IV, descriptive qualitative studies; level V, case studies; level VI, descriptive studies; and level VII, expert opinion[9].

RESULTS

The selected studies for the synthesis are available on the SCOPUS, MEDLINE and Web of Science databases. From the seven studies, two are available in these three databases, three were located by means of CAPES platform of journals, and are available in the SCOPUS and Web of Science databases concomitantly.

Regarding the characteristics of the analyzed studies, all of them were carried out in the United States, and published exclusively in English for the past twenty years, between 1995 and 2015.

As for the type of study, six were identified as quantitative ones, being two descriptive, two randomized clinical trials, one crossover study, and one qualitative study. Their strength of evidence ranged between II and VI. It follows the table with the detailed features of the studies used for knowledge synthesis (Table 2).

Table 2: Distribution of the analyzed studies featuring: title, reference, country of origin, objectives, method, results and strength of evidence rating (ER). Curitiba-Paraná State, Brazil, 2017.

Reference and country	Objective, method and results	ER*
Vasquenza K, Ruble K, Billet C, Atwater S. Pain management for children during bone marrow and stem cell transplantation. Pain Manag Nurs. 2015; 16(3):156-62[8]. **Country:** USA.**	**Objective:** to report practices of pain management for children and adolescents undergoing HSCT*** focusing on the use of analgesia strategies controlled by the patient (PCA) and by the caregiver (CCA). **Method:** descriptive retrospective study carried out by means of 51 children and teenagers' medical records, mean age of 11.1 years in the group with controlled analgesia and 12.5 years in the group with non-controlled analgesia. **Results:** 69% (35/51) of the participating children and teenagers (54% males and 46% females) had controlled analgesia, being oral mucositis the main etiological pain factor in 97% (34/35**)**. In that group, eight children were under 6 years of age and had CCA. Before controlled analgesia, pain level in the PCA group was 3/10 (Likert Scale from 0 to 10), being reduced to 0.7 between 48 and 72 hours. In the CCA group, former pain intensity was 4.9/10, and between 48 and 72 hours, it was reduced to 1.9/10.	VI
Collins JJ, Geake J, Grier HE, Houck CS, Thaler HT, Weinstein HJ, Twum-Danso NY,	**Objectives:** to test safety and efficiency of a clinical protocol for opioid administration by using PCA for the treatment of oral mucositis-related pain in children after HSCT, to compare efficiency, effect profile and	IV

Berde CB. Patient-controlled analgesia for mucositis pain in children: a three-period crossover study comparing morphine and hydromorphone. J Pediatr. 1996; 129(5): 722-8[13]. **Country:** USA.	effect-power relation between morphine and hydromorphone. **Method:** double-blinded crossover study with 10 children and adolescents, being five randomly assigned for group 1 (morphine – hydromorphone – morphine), mean age of 13.7 years, and five for group 2 (hydromorphone – morphine – hycromorphone), mean age of 15.3 years. **Results:** the beginning of the clinical protocol varied from day zero to the 9th after HSCT. Only one patient began morphine continuous infusion dosage in the first 24 hours. Eight patients demanded rapid increase of the opioid dosage during the first days, followed by a variable plateau phase, being the opioid dosage reduced when the oral mucositis was healed. Mean scores for pain level in groups 1 and 2 were 4.0 (0 to 8.5) and 4.0 (0 to 10), respectively. There was no statistical difference in the daily mean scores of pain between the different phases of the study. However, patients used 27% more hydromorphone than expected. It was evidenced that morphine is more efficient than hydromorphone for this type of pediatric protocol.	
Dunbar PJ, Bucldey P, Gavrin JR, Sanders JE, Chapman R. Use of patient-controlled analgesia for pain control for children receiving bone marrow transplant. J Pain Symptom Manage. 1995; 10(8): 604-11[14]. **Country:** USA.	**Objetivo:** to report the experience of HSCT-related pain management for children by using PCA. **Method:** descriptive experience report with 39 children between four and twelve years of age. **Results:** morphine (20 µg/kg, initial bolus) or hydromorphone (2 µg/kg) with or without continuous infusion were prescribed. On the11th day, after the beginning of the PCA, there was the peak use of morphine. 95% (n=39) of the children could control pain in an efficient way by using PCA, which was observed by the reduction in the use of opioids.	VI
Mantell P, Hartwell LP, Branowicki PA. Development of an outcome measure to monitor the effectiveness of pain management. Clin J Oncol Nurs. 2014; 18(1): 30-2[15]. **Country:** USA.	**Objective:** to describe the development of an outcome indicator to monitor the efficiency of pain management by nursing. **Method:** randomized pilot study with 960 medical records of children and adolescents admitted to oncology, hematology and HSCT units of a child hospital, with 320 records of each unit for randomization. **Results:** a universal target was created to all the units included in the study: 80% of pain level 4 or higher would be reduced to 30% in 120 minutes. Initially, 70% of the scores for pain level 4 or higher were reduced in 30% of the requested time. In 7 months, the units experienced 10% improvement, comparing to the initial phase, with averaged 80% reduction in pain level 4 or higher within 120 minutes. Due to the positive outcomes of the project, the measure was successfully implemented in the oncology, hematology	VI

	and HSCT units.	
Hodgson BD, Margolis DM, Salzman DE, Eastwood D, Tarima S, Williams LD, Sande JE, Vaughan WP, Whelan HT. Amelioration of oral mucositis pain by NASA near-infrared light-emitting diodes in bone marrow transplant patients. Support Care Cancer. 2012; 20(7): 1405-15[16]. **Country:** USA.	**Objective:** to investigate the use of extraoral near-infrared light-emitting diode phototherapy for oral pain in pediatric and adult patients undergoing HSCT. **Method:** clinical double-blinded randomized case-controlled trial with 30 children and adolescents, ages between 3 and 18 years, and 50 adults, ages between 20 and 74 years (n=80). **Results:** there was significant reduction in the self-reported pain by patients. Pain assessment scale showed significant global difference (p=0.280). The allocated low-risk control group for low level laser application reported less pain than the regular group. In the regular-risk group, there was 44% reduction in average pain level at the end of the study period.	II
Ndao DH, Ladas EJ, Cheng B, Sands SA, Snyder KT, Garvin JHJ, Kelly KM. Inhalation aromatherapy in children and adolescents undergoing stem cell infusion: results of a placebo-controlled double-blind trial. Psychooncology. 2012; 21(3): 247-54[17]. **Country:** USA.	**Objectives:** to determine the effects on anxiety after the administration of inhaled essential bergamot oil during HSCT, to assess its effects on nausea and pain reduction, to assess whether parents' anxiety influences child's temperament and coping strategies or discomfort increase. **Method:** randomized, double-blinded, placebo-controlled study carried out with children and adolescents undergoing transplantation (n=40). Control group (n=20), mean age of 14.5 years, 30% females and 70% males, and the treated group (n=17), mean age of 13.1 years, 24% females and 76% males. There were three exclusions in the treated group for treatment quit or discontinuity. **Results:** participants from the aromatherapy treatment group with essential bergamot oil evidenced higher rate of anxiety (*p* 5 0,05) and nausea (*p* 5 0,03), and a significantly higher pain baseline (81%) in relation to the control group (45%) (*p* 5 0,04) in the first assessments before transplantation (T1 and T2). However, along the pain treatment with essential bergamot oil aromatherapy, there was significant reduction to 53% after the end of the hematopoietic stem-cell infusion (T3), and 45% an hour after the end (T4), not evidencing significant difference from the control group (40%). No correlation was found between the scoring of parental anxiety and children's complaints.	II
Pederson C, Parran L, Harbaugh B. Children's Perceptions of Pain During 3 Weeks of Bone Marrow	**Objective:** to understand children's perceptions on: (a)HSCT-related pain, (b) effective interventions to relieve pain, and (c) caregivers' role in pain management. **Method:** exploratory -descriptivequalitative study with	IV

Transplant Experience. J Pediatr Oncol Nurs. 2000; 17(1): 22-32[11]. **Country:** USA.	20 children and adolescents from 5 to 17 years of age, undergoing HSCT. The structured interviews were held in four moments: the first, on the day of the transplant, and successively, three interviews focusing on children's perceptions regarding their experiences of transplant-related pain. **Results:** in the interview, children reported that they communicated their parents or nurses whenever they felt pain. Several children used non-pharmacological strategies for pain relief, such as: warm compresses, massages, games and music. However, in the follow-up interviews, they reported that pain killers were more efficient for pain reduction. They mainly reported oral cavity and throat pain, and children, as well as their parents claimed that pain management should be improved in the following aspects: pain assessment, guidance on painkillers and nursing therapeutics.	

* Strength of evidence rating. ** United States of America. ***Hematopoietic stem-cell transplantation.

The reviewed studies were rated according to the tested strategies, in three types: "pharmacological strategies"[8-13-14], "non-pharmacological strategies"[16-17], "management strategy"[15] , and a qualitative study which verified children's perception on the effectiveness of pharmacological and non-pharmacological pain strategies[11].

The subsequent table describes the quantitative studies, considering the data for critical review, such as: description of the tools used for pain assessment, frequency of such evaluations, whether the pain site was mentioned, which strategy was used to manage the symptoms, and the professionals participating in this process (Table 3).

Table 3: Description of the quantitative studies regarding reference, pain assessment, strategy specification and implementation. Curitiba-Paraná State, Brazil, 2017.

	Reference	Pain assessment	Strategy specification and implementation
Pharmacological Strategy	VASQUENZA et al[8].	**Frequency:** every 4 hours or every hour in the first 24 hours of controlled analgesia. **Tools:** FLACC Scale (Faces, legs, activity, cry and consolability); FPS-R (Faces Pain Scala - Revised); and verbal numeric ´pain scale. **Pain site:** oral cavity, throat and head. **Professionals:** nursing team.	1. Patient-controlled analgesia for children and adolescents from 6 years on, using morphine. 2. Caregiver-controlled analgesia for children under 6 years old, using morphine, hydromorphone and fentanyl. **Frequency and duration:** continous, average duration between 25 and 40 days. **Professionals:** doctors and nurses. **Target public:** children and adolescents.
	COLLINS, et al[13].	**Frequency:** every 4 hours.	1. Clinical protocol for opioid administration, by means of patient-

		Tools: Visual analogue scale. **Pain site:** oral cavity and throat. **Professionals:** nurses.	controlled analgesia. Group 1 began with morphine on the 1st, 2nd, and 3rd days, hydromorphone on the 4th, 5th and 6th days, and morphine on the 7th, 8th and 9th days. Group 2 began with hydromorphone on the first three days, followed by morphine and hydromorphone interchangeably every three days. **Frequency:** averaging 19 days, depending on the oral mucositis severity. **Professionals:** nurses and doctors. **Target public:** children and adolescents.
	DUNBAR, et al[14].	**Frequency:** non-specified. **Tools:** non-specified. **Pain site:** oral cavity, throat and abdomen. **Professionals:** nurses.	1. Patient-controlled analgesia, using morphine and hydromorphone, when preferred by the child in case of allergies. 2. Use of continuous opioid infusion for children younger than 6 years of age. **Frequency and duration:** continuous with duration ranging from 10 to 33 days. **Professionals:** doctors and nurses. **Target public:** children.
Non-pharmacological strategy	Hodgson et al[16].	**Frequency:** three times a week. **Tools:** visual analogue scale and Wong-Baker faces. **Pain site:** oral cavity. **Professionals:** nurses.	1. Extra-oral infra-red laser diode phototherapy. **Frequency and duration:** three times a week for 14 days. **Professionals:** nurses. **Target public:** children, adolescents and adults.
	Ndao et al[17].	**Frequency:** a week before HSCT (T1), on the day of the transplantation, before the hematopoietic stem-cell infusion (T2); soon after the end of the cell infusion (T3); and one hour after the end of the infusion (T4). **Tools:** visual analogue scale. **Pain site:** non-specified. **Professionals:** research assistant and nurses.	1. Essential bergamot oil aromatherapy. **Frequency and duration:** 1 application on the day of the transplant for 4 hours. **Professionals:** research assistant. **Target public:** children, adolescents and parents.

Management strategy	MANTELL et al [15].	**Frequency:** every 2 hours. **Tools:** use of pain measurement tools (0 to 10 rating, according to the Likert scale), depending on patients' age, but not specified which ones. **Pain site:** non-specified. **Professionals:** nurses.	1. Determination of outcome indicators to monitor the effectiveness of the pain management. **Frequency and duration:** continuous. **Professionals:** nursing manager, nursing coordinator and medication quality analyst. **Target public:** children and adolescents.

As for the qualitative study, it was observed that the authors did not use pain measurement tools, only considering children's report of mild, moderate or severe pain. In relation to the therapeutic strategies for pain management, children reported that they requested painkillers when they felt pain, and asked their parents for other comfort devices: back or foot massage, warm compresses or recreational games to distract them. Regarding nurses' strategies, all children reported that they administered medication to relieve their pain, and some mentioned the use of other strategies, such as warm compresses and cryotherapy[18].

DISCUSSION

The reviewed studies pointed out that the effective control of pediatric post-HSCT pain is challenging for professionals in the area, demanding commitment, attention and will of those professional in order to assess, implement strategies for pain relief, to reassess the effectiveness of these strategies and adapt them to children and adolescents, according to their needs[8].

The obtained outcomes indicated several strategies of pain management, although pharmacological therapies stood out in at least four studies[8,11,13,14]. The use of opioid painkillers by means of PCA and CCA pointed to the possibility of using this strategy for children and adolescents[8,13,14].

PCA is a therapeutic type for acute pain control[8,18]. The American Society for Pain Management Nursing (ASPMN)[18:177] supports and regulates such a therapeutic type, defined as: "approach that enables patients to self-administer small dosages of painkillers within a prescribed time, by pressing a dosage key of a previously programmed infusion pump". That pain management strategy has become common due to its effectiveness by allowing individualized treatment, where patients themselves can control their pain[8,18].

Although it is an effective strategy, its recommendation for pediatric patients has been argued since its development, as some professionals believe that children and adolescents are not mature enough to distinguish medication risks and benefits[8,13,14]. However, studies have contradicted such arguments. For example, a study held in the USA showed that 95% of the children between 4 and 12 years of age successfully mastered PCA, achieving effective pain control. Moreover, improper use of opioids was not reported, or parental adulteration, or even accidental overdose. Nevertheless, by carrying out a critical review of this study, it should be taken into account the

reduced number of participants and lack of methodological accuracy, once it does not provide enough information on pain assessment[14].

Therefore, we found other studies held in the HSCT context, which corroborate those data. A study tested the safety and effectiveness of a clinical PCA protocol in children and adolescents using morphine and hydromorphone, and achieved successful outcomes. However, the number of participants was also a limitation in this study[13]. Apart from those, another recent study identified that such therapeutics was used for 69% (n=51) of children and adolescents undergoing HSCT, being PCA for children older than 6 years of age and CCA for children younger than 6 years of age, evidencing that in both cases, the strategy was effective for reduction of pain complaints[8].

It is important to point out that CCA or authorized agent controlled analgesia (AACA) is also allowed by the ASPMN for patients who are unable to independently use PCA, as long as the agent, that is, parents or caregivers, have a prescription and are oriented by the healthcare team on the probable risks of this practice[18].

Regarding the use of pain management medication in the HSCT context, a qualitative study pointed that even using different strategies for pain management, children considered medication as the most effective therapeutics. In this study, they reported the use of several complementary strategies for pain management, carried out with their parents' help, such as: listening to music, massages, playful activities and recreational games. In addition, they mentioned the use of heat application and cryotherapy held by nurses. However, we noticed that the authors did not properly explore such strategies, and did not report how they were performed, simply mentioning which ones[11].

Concerning musical intervention as a complementary therapy, literature points out its contribution in an effective way for pain reduction in children with cancer [19,20]. In addition, another study held with adults undergoing HSCT evidenced positive outcomes for this strategy to improve mood and pain (p=0,061)[21]. Thus, it can be inferred that it is possible to use that intervention in order to relieve pain in children and adolescents undergoing HSCT, once that method is non-invasive and inexpensive.

Aromatherapy is also considered a complementary strategy to relieve the symptoms. It is defined as the therapeutic use of essential oils from plants by using steam or pressure. The triggering mechanism in this method entails the respiratory system, which absorbs the volatile scent molecules through the nose. Subsequently, the molecules are changed into chemical signs which migrate to the olfatory bulb, amygdalas and lymbic system, interacting with the neuropsychological framework and, finally, generating some effect on the targeted tissues[17].

Essential bergamot oil, used in aromatherapy, was described in the literature as natural anxyolitic and antiemetic for children, and it was applied to assess its effects on anxiety, nausea and pain as a secondary objective. However, it seemed to produce better effects on pain management than on the anxiety and nausea, raising the discussion about the need of further research to check the effect of aromatherapy with the essential bergamot oil for HSCT related-pain management for children and adolescents[17]. One of the study biases consisted of not offering participants a scent

choice, considering that its smell might not have pleased the children, hindering final study outcomes.

As for extra-oral infra-red diode phototherapy, the results evidenced significant effects on oral pain relief in adults as well as in children and adolescents. Studies point to probable mechanisms responsible for such effects, such as the release of endogenous opioids, circulatory and angiogenic micro-effects, anti-inflammatory local action, and action on biochemical markers. However, such mechanisms have not been completely elucidated yet[17].

It should be pointed out that the advantages of the extra-oral phototherapy are related to the reduction of patients' manipulation and the time of the application, once it covers a wider affected area, besides being less invasive. However, there are disadvantages, such as the reduction in reaching over deeper targeted tissues[17]. In spite of evidencing the effectiveness of the extra-oral phototherapy, the study bias consisted of including adults, children and adolescents in the same trial, disregarding many differring factors between children's and adults' pain perception[17-21]. Children have an individual response to pain which modifies along the time, according to their painful experiences throughout their lives. Therefore, children and adolescents' response to treatment may also be different from adults'. It can be observed, for example, that pain response in children is more acute at the beginning, however, it ceases more easily than in adults[21].

Regarding management strategies, a randomized study stood out, as it is a report entailing the elaboration of indicators to monitor the effectiveness of pain management using the goals imposed to hospital units so that pain is controlled within proper time to assure children and adolescents' well-being[15]. However, the study setback lies in its lack of methodological accuracy, making its interpretation difficult. In addition, the study does not show how the results were obtained, even whether PCA or other therapies were used, contributing to achieve its objectives.

Brazilian researchers[1:528] pointed out the main advantages, while taking into consideration the importance of using quality indicators to monitor pain management, such as: "to improve caring process and nursing notes, to provide information in order to help treatment choice, and contribute to enhance internal and public healthcare policies". Thus, the quality indicators contribute to foster care for children and adolescents in pain[1]. Results also pointed out that nurses are in the forefront regarding strategies for pain management, once all studies had their participation, either in the data assessment and collection, or carrying out the strategies for pain management, reassuring their importance for coping with pain in children and adolescents undergoing HSCT[8,11,13-17]. Nevertheless, studies on the theme are scarce and need further exploration by professionals and researchers in the area.

CONCLUSION

Pain is the most frequent and debilitating symptom in children and adolescents undergoing HSCT. Therefore, it has been the target of studies for over 20 years. However, the management of this symptom has still been challenging for professionals in the area and demand successful innovative strategies. The strategies used for pain management were PCA and CCA with opioid painkillers (morphine and hydromorphone); aromatherapy with essential bergamot oil; extra-oral infra-red diode

phototherapy; heat application; cryotherapy, and the elaboration of outcome indicators to monitor the effectiveness of pain management. In addition, complementary therapies were independently used by patients and their parents, such as: music, playful activities by means of games and massages. Among the mentioned strategies, the most effective were PCA, CCA and the outcome indicator, which enabled pain control at due time.

This study is relevant because it invests in the identification of strategies for pain management objectifying to contribute for the knowledge of professionals who work in HSCT services, pointing new ways for nursing decision making, reducing pain rates and favoring children and adolescents' well-being.

Despite pharmacological, technological and complementary advances for the pain management in pediatric patients in the past two decades, the scarcity of scientific production on the theme has been evidenced in the same period. Thus, we highlight the need of further research, searching for innovative alternatives on the theme. Keeping in mind the identified knowledge gaps, we recommend the development of comparative studies between continuous opioid infusion and PCA or CCA, as well as deeper studies on complementary low-cost strategies, such as: massotherapy, music therapy, child psychotherapy, relaxation techniques, guided imagery therapy and aromatherapy.

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