

Utilizing complementary therapy to enhance quality of life and reduce stress and fatigue in pediatric cancer patients

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Abstract

The international scientific literature presents still incipient results regarding the management of cancer symptom clusters by oncology nursing, especially in pediatric oncology. This is a promising field of investigation for clinical nurses and researchers, and when it is subsidized by medium-range theories, they corroborate the diagnoses and interventions of nursing in oncology, enhancing the science of nursing care. This minireview article aims to discuss the utilizing the hospital clowns as a complementary therapy, to enhance quality of life and reduce stress and fatigue in pediatric cancer patients. Overall, the evidence presented so far pointed out that complementary therapy might help improve the quality of life of pediatric cancer patients, and that complementary therapy usage should be part of a health comprehensive care model, delivering therapeutic approaches that might enhance the mind-body during a pediatric cancer patients' life span. The results of scientific investigations by nurses, particularly those linked to the basic sciences, play a critical role in advancing personalized care in pediatric integrative oncology.

Key Words: Cancer symptom clusters; Pediatrics; Pediatric cancer patients; Pediatric integrative oncology; Complementary therapies; Oncology nursing; Hospital clowns; Cancer-related fatigue; Psychological stress; Biomarkers

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Core Tip: The international scientific literature presents still incipient results regarding the management of cancer symptom clusters in pediatric oncology. This is a promising field of investigation for clinical nurses and researcher. The evidence presented so far pointed out that complementary therapies might help improve pediatric cancer patient's quality of life, and that complementary therapies usage should be part of a health comprehensive care model, delivering therapeutic approaches that might enhance the mind-body during a pediatric cancer patients' life span. The results of scientific investigations carried out by nurses linked to the basic sciences, are the hallmarks of personalized care in pediatric integrative oncology.

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INTRODUCTION

More than 15000 new cases of cancer are diagnosed in children and adolescents annually, resulting in 1960 deaths according to the Global Burden of Disease study 2017[1]. For pediatric patients aged 1 to 19 years in the United States, cancer is the leading cause of death by disease. Remarkably, advances in cancer treatment over the past four decades have improved the 5-year survival rate from 10% to approximately 90% in children. However, childhood cancer incidence rates have continuously risen[1,2]. Compared with the adult cancer population, pediatric patients tend to experience higher levels of cancer symptom clusters (CSC)[3,4]. Many of them may live with these symptoms for years after completion of treatment[4]. Parents and caregivers also shoulder a substantial emotional and physical burden due to CSC [5]. Hence, palliating physical and emotional symptoms and providing support to pediatric patients throughout their procedures and treatments, is crucial in cancer care[3,4].

Complementary therapy (CT) can be described as a health care set of techniques aimed at integrating physical, mental, and spiritual dimensions. The National Center for Complementary and Alternative Medicine-National Institutes of Health mainly categorizes them as biologically based therapies, mind-body interventions, manipulative, and body-based methods[5]. The National Center for Complementary and Alternative Medicine classification system was used to discuss the evidence from studies utilizing CT for CSC management in pediatric oncology in this study. The science of CT has significantly grown in the past 60 years with breakthroughs in molecular-level research which help increase the understanding of biological pathways underlying CT use[6].

This minireview aims to discuss the utilizing the hospital clowns (HC) as a CT to enhance quality of life (QoL) and reduce stress and fatigue in pediatric cancer patients. This paper presents the significant contributions made to the field of pediatric integrative oncology (PIO) through the use of CT. In addition, the present study is aligned with objective 3 of the sustainable development goals, which aims to ensure a healthy life and promote well-being for all, at all ages, demonstrating the societal relevance of this work and its potential to address pressing global issues.

TRANSLATIONAL RESEARCH AND CSC IN PEDIATRIC ONCOLOGY

Translational research (TR) refers to the bridge between the new knowledge from the basic sciences and clinical practice. TR has bidirectional phases know as '3 Bs' - bench, bedside, and back again[7]. Biomarkers can be used to characterize both cancer risk and treatment efficacy[8,9]. Immunological biomarkers have been recognized as important in the study of CSC, mainly cytokines[10]. Despite the variety of biomarkers used in early detection, diagnosis, and cancer management the use of biomarkers to assess CSC in pediatric patients remains elusive[3,4]. One of the greatest challenges in oncology nursing is to establish the link between the basic science and application in clinical practice[7].

In clinical practice cancer symptoms rarely occur separately. A cluster is defined as a set of symptoms that are related to each other and that can be predictable[11]. Symptoms group together creating a synergistic effect, which can predict the development of future symptoms. The progression of cancer and treatment can lead to the development of several CSC, *e.g.*, cancer-related fatigue (CRF), pain, sleep disorders, anxiety, depression, *etc.* Nurses in pediatric oncology must be sensitive to CSC, which may be linked to age, socio-cultural-spiritual aspects, diagnosis and treatment[11]. Overall, these CSC reduce the individual's functional state and decrease QoL[10,11].

One study compared the levels of interleukin-12 (IL-12) p70 and IL-10 in 59 children with soft tissue sarcoma age range 2-15 years at different stages of treatment, showed that children in remission had decreased IL-10 and increased IL-12 production ($P < 0.01$)[12]. A recent pilot study which examined the biomarkers associated with stress and CRF in pediatric osteosarcoma patients receiving chemotherapy and under interaction with HC showed reduced cortisol levels over time and also a similar pattern of levels in tumor necrosis factor α for all patients. Also, patients with metastatic osteosarcoma showed a linear trend for reduced levels of matrix metalloproteinase-9 after the HC[13]. Indeed, there is great potential for advancing nursing through research that evaluates the psycho-neuro-immuno-endocrine pathways in the genesis of CSC. Once the association, sensitivity, and specificity of biomarkers has been identified, they can be used in response to accurately determine their effectiveness[12].

Table 1 Summary of evidence about use of complimentary therapies in pediatric oncology

Type of complementary therapy	Patient-reported outcomes	Main findings	Ref.
Manipulative and body-based methods			
Therapeutic massage	Mood and blood cells	Decrease depressed mood as well as to increase white blood cell and neutrophil counts in pediatric cancer patients ($P < 0.05$)	[21,22]
Acupuncture	Nausea and vomiting	Reduce chemotherapy-induced nausea and vomiting in children with cancer ($P < 0.05$)	[23]
Mind-body interventions			
Music, art, and play therapy	Anxiety, pain, psychological stress, and CRF	Dance therapy may help reduce the symptoms pediatric patients experience during hospitalization, such as anxiety, pain, and fatigue. Total levels of psychological stress and CRF improved after the hospital clown intervention compared with baseline ($P = 0.003$) and ($P = 0.04$), respectively. A significant decrease in salivary cortisol after clown intervention was observed ($P < 0.05$)	[13,24-28]
Animal-assisted therapy program (pet-therapy)	Stress, pain, mood, anxiety, irritation, depression, quality of life, heart rate, and blood pressure	Pain, adjustment difficulties, mood changes and symptom management can be improved in inpatient pediatric cancer patients receiving animal-assisted therapy, thus improving overall quality of life. Decrease in pain ($P = 0.046$), irritation ($P = 0.041$), and stress ($P = 0.005$)	[29,30]
Yoga	Pain and anxiety	Adolescents and parents had a significant decrease in anxiety post yoga intervention ($P < 0.05$)	[31]
Meditation, hypnosis, guided imagery	Pain, nausea and vomiting	Decrease pain, nausea, and vomiting ($P < 0.05$)	[32,33]
Biologically based therapies			
Vitamins and dietary supplements	Hepatotoxicity and febrile neutropenia	For hepatotoxicity, small studies found milk thistle, omega-3 fatty acids, and black seed oil to decrease liver enzymes ($P < 0.05$). For febrile neutropenia, wheat germ extract, probiotics, and honey showed promise in small studies	[34-38]

CRF: Cancer-related fatigue.

Although the growing body of evidence indicates the usefulness of CT in pediatric settings, most studies focus primarily on the adult cancer patient[5]. PIO provides a relationship-centered, evidence-informed personalized approach to the whole child and family system utilizing mind and body practices, natural products and/or lifestyle modifications alongside conventional oncology care[14]. PIO is offered throughout the illness trajectory to optimize health and wellness, enhance healing, minimize suffering, improve QoL and empower children and families to become active participants before, during, and beyond cancer treatment[14]. PIO is still an evolving field requiring further study and efforts should be made with patients, families, and caregivers to participate in these investigations[14]. Pediatric cancer patients may benefit from nonpharmacological interventions including CT to decrease use of medications rendering unwanted side effects[15,16].

COMPLEMENTARY THERAPIES IN PEDIATRIC CANCER PATIENTS

The CT usage for CSC management in pediatric patients range from 31%-84% [17-19]. In PIO, CT are used to help relieve several CSC and side effects, *e.g.*, pain, nausea/vomiting, CRF, sleep disturbance, stress, anxiety, depression, constipation, and diarrhea[20]. Some CT have been well-studied and have significant research to support their use, *e.g.*, relaxation, guided imagery, biofeedback, yoga, and other mind-body therapies (Table 1)[13,21-38].

A recent systematic review aimed to assess evidence on the effectiveness of HC for a range of symptom clusters in pediatric patients. Patients with both acute and chronic disorders demonstrated that the presence of HC during medical procedures, induction of anesthesia in the preoperative room, and for chronic conditions might be a beneficial strategy to manage symptom clusters compared to those who received only standard care[39]. A clown is a comic performer who employs theatrical production often in a mime style and wears outlandish and brightly colored costume to entertain a given public. In a hospital setting, clowns are called "hospital clowns" and are usually part of "therapeutic clowning" programs. There are currently many hospital clowning programs operating in several countries, such as Australia, New Zealand, United States, United Kingdom, Canada, Israel, Hong Kong and Brazil. Overall, HC provide a CT for health care by using several techniques such as music, juggling, improvisation, magic, storytelling, and puppets. They help create a positive emotional state that promotes interaction between parents and the child and fosters a hopeful attitude[39].

Table 2 Protocol intervention hospital clowns as a complementary therapy for management psychological stress and cancer-related fatigue and enhancing the quality of life

Item	Description
Ref.	Lopes-Júnior <i>et al</i> [26]
Objective	To assess the effect of a hospital clown intervention on the levels of stress and CRF in pediatric cancer patients receiving chemotherapy by measuring the levels of salivary cortisol and salivary alpha amylase
Sample	16 children and adolescents (6-14 years old, mean \pm SD: 11.40 \pm 3.44) with cancer receiving a hospital clown intervention
Protocol of intervention	The participants served as their own controls before and post-intervention over a 3-day period. Each patient received 1 session of the HC and provided eight saliva samples (4 samples at pre-intervention and 4 samples at post-intervention). All saliva samples were collected each day at the same time for all patients to maintain comparability among participants and to avoid that differences would be a result of normal daily oscillations in biomarkers. Data were collected at + 1, + 4, + 9, and + 13 hours after awakening (8:30 am), <i>i.e.</i> , at 9:30 am, 12:30 pm, 5:30 pm, and 9:30 pm, respectively. The 8 points chosen for saliva collection were based on international recommendations for children and adolescents, to allow a better characterization of the biomarker circadian rhythms. In order to minimize external influences of measurements, at all sample collection time points, pediatric cancer inpatients had no invasive procedures or any other acute stresses in the last hour before sample collection and underwent preparation for saliva collection - which consisted of not ingesting any food or drinks 1 hour before the procedure and not brushing the teeth or using mouthwash before collection. After preparation had been completed, participants were requested to refrain from swallowing briefly (for 30 seconds) and then "drooling" the saliva from the mouth directly into the collection device
Outcome measure	CRF and psychological stress. Children: PedsQL MFS (CRF scale-cancer module) and ESI (stress scale). Parents: PedsQL MFS
Main results	Participants mean age was 11.4 \pm 3.4 years old. 50% were white, and 68.7% had completed primary school. Regarding the neoplasms, 6 was osteosarcoma, 4 ALL and 4 lymphoma. Most (81.3%) were primary neoplasm, and among the 16 patients, 68.7% had metastases. Also, 56.3% were using corticosteroids during the chemotherapy protocol. In comparison with baseline measurements, the total stress and CRF levels improved at the post-hospital clown intervention ($P = 0.003$ and $P = 0.04$, respectively). Salivary cortisol showed a significant decrease after clown intervention at the collection time points + 1, + 9, and + 13 hours ($P < 0.05$), but not α -amylase. The total ESI stress scores from the pediatric patients correlated positively with AUC for cortisol at pre-intervention ($r = 0.35$, $P = 0.03$). Decreased stress scoring after the clown intervention correlated positively with decreased levels of cortisol ($r = 0.02$, $P = 0.04$). Contrary, the total ESI stress scores from the patients correlated negatively with AUC for α -amylase at pre-intervention ($r = -0.57$, $P = 0.02$), but not at the post-intervention. These findings suggest that the hospital clowns as a complementary therapy may improve stress and CRF

CRF: Cancer-related fatigue; HC: Hospital clowns; PedsQL: Pediatric quality of life; MFS: Multidimensional fatigue scale; ESI: Escala de stress infantil (child stress scale); ALL: Acute lymphocytic leukemia; AUC: Area under curve.

A study of HCs recently evaluated its effect on the levels of CRF and stress in pediatric cancer patients receiving chemotherapy[26]. The results demonstrated that the total psychological stress and CRF levels improved after the HC compared to baseline ($P = 0.003$ and $P = 0.04$, respectively)[26]. A significant decrease in salivary cortisol after the HC visit was observed. In this study, the HC intervention was performed by volunteer clowns from the University of São Paulo, Brazil, and were members of the Laugh Company, which is an outreach project aimed to lift pediatric patient mood levels during hospitalization[26]. Their families and the staff were present during the clown visits and were delighted. Children accompanied by their parents interacted simultaneously with two volunteer clowns in the pediatric oncology ward for 30 minutes at a time. In this period, the clowns performed several activities while adapting their techniques to the best of their ability to each patient's age and psychological condition. The 2 clowns arranged common play sessions with patients in their ward and used different methods for entertaining the children such as singing, dancing, magic tricks, gags, puppets, games, mostly using improvisation and their distinctive humor and charisma. All these HC attended specific training sessions focused on practical work situations to develop theatrical and artistic clown competences in addition to psychosocial and pedagogical skills (Table 2)[26].

IMPLICATIONS FOR CLINICAL PRACTICE AND RESEARCH

Perhaps the addition of an HC to the play therapy portion of patient care could be a key addition to the oncology team and could be a valuable supplement to current play therapy practices. This could also be considered for outpatient treatment areas as well. HC have been a mainstay in a child's life for decades[40-43] and may actually be an underused resource[13,26] for improving the oncology child's daily regime while undergoing treatment in the any setting[39]. Nurses play a pivotal role in the identification, monitoring, and risk evaluation of CSCs, including the assessment of biomarkers[44,45]. The understanding of how neuro-immunoendocrine pathways regulate cancer development and the underlying aspects of treatment using biomarkers is urgent to incorporate into clinical practice.

One of the major challenges is to improve the preparation and training of nurses in omics sciences and disruptive technologies for the provision of personalized care, especially adapting curricula at different levels of academic training for these professionals, from undergraduate to postgraduate studies[46,47]. It is worth noting that for this century, one of the main challenges in nursing training is the integration of omics sciences into professional practice, which includes the analysis of biomarkers[47,48]. Therefore, there is an urgent need for extensive continuing education for nursing professionals, undergraduate/postgraduate course teachers and, mainly, the reformulation of more integrated nursing curricula, to adequately prepare the workforce for precision nursing in global health systems[46-48]. One of the main areas

of application and development in precision nursing is oncology, where oncology nurses are already faced with the universe of omics sciences directly in the care of cancer patients, from prevention, diagnosis and oncological treatment through biomarkers, genetic tests, and pharmacogenomics, proteomics, metabolomics, genomics, and bioinformatics[49]. This understanding can contribute to elucidating the diagnosis and prognosis of several cancer types and assist in the selection of personalized CT for each patient and tumor type.

Another challenge is to ensure the transfer of these research results, so that they facilitate clinical decision-making towards personalized care[48]. In the last decade, the substantial growth of TR has opened up perspectives of knowledge in several directions, since they greatly assist in the elucidation of many pathophysiological processes associated with clinical practice and the singularities of patients[49]. Therefore, it is important that nursing is also involved in this type of research, since the application of the discoveries and results of TR carried out by these professionals supports evidence-based nursing[46,49].

CONCLUSION

It is crucial that nurses participate in identifying strategies to accelerate TR for assisting the understanding of the underlying pathophysiological mechanisms associated with CSC to intervene effectively. Overall, the literature suggests that CT may help improve pediatric cancer patient's QoL as part of a comprehensive cancer care model. HCs may be a unique, useful intervention that could be integrated into patient's care to decrease stress, CRF and improve QoL. Finally, oncology nurses using trained qualified CT therapists for various CT interventions can support the patient's recovery from life-threatening illness.

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FOOTNOTES

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