Journal of Pediatric Nursing (2010) **25**, 566–579

Use of Complementary and Alternative Medical Interventions for the Management of Procedure-Related Pain, Anxiety, and Distress in Pediatric Oncology: An Integrative Review

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Key words:
Procedure;
Pain;
Anxiety;
Distress;
Childhood cancer;
Pediatric oncology;
CAM;
Complementary therapies

This integrative review aims to identify evidence in four electronic databases (MEDLINE, CINAHL, PsyINFO, and COCHRANE) regarding the effectiveness of complementary and alternative medical interventions, either alone or as an adjunct to pharmacological therapy, in alleviating procedure-related pain, anxiety, and distress in children and adolescents with cancer. A total of 32 articles met inclusion criteria. Results suggest that mind–body interventions, including hypnosis, distraction, and imagery, may be effective, alone or as adjuncts to pharmacological interventions, in managing procedure-related pain, anxiety, and distress in pediatric oncology.

FIVE-YEAR SURVIVAL rates for childhood cancer now exceed 80%, a statistic that reflects one of the remarkable medical success stories of the latter half of the twentieth century (Jemal et al., 2008). Successful treatment of childhood cancer relies in part on invasive procedures, such as bone marrow aspiration or biopsy, lumbar puncture, venipuncture, and percutaneous vascular access, to deliver and monitor the effects of contemporary curative therapies. Procedure-related pain, anxiety, and distress may consequently place a significant burden on children and adolescents with cancer. In fact, pediatric oncology patients and their parents have reported that procedure-related pain is one of the most distressing and difficult aspects of the cancer experience (Zernikow et al., 2005); procedure-related distress may persist for years following completion of treatment (Pai & Kazak, 2006).

Pain is a multifaceted experience that may result in adverse physiological, cognitive, emotional, and behavioral responses (Liossi, 1999). Pharmacological management in the form of local anesthetic agents, sedation, or general anesthesia may provide significant relief of procedural pain, anxiety, and distress (Doellman, 2003). Recent studies indicated that 31% to 84% of children and adolescents with cancer use complementary and alternative medical (CAM) therapies (Sencer & Kelly, 2007) and that some CAM therapies may be effective in relieving procedure-related pain and associated anxiety and distress in this population (Evans, Tsao, & Zeltzer, 2008). Evaluation of current evidence regarding the use and effectiveness of CAM therapies in the management of procedure-related pain, anxiety, and distress in children and adolescents with cancer is therefore imperative and was the focus of this review.

Purpose

The purpose of this integrative review was to identify evidence regarding the effectiveness of CAM interventions, either alone or as an adjunct to pharmacological therapy, in alleviating procedure-related pain, anxiety, and distress in children and adolescents with cancer.

This integrative review will address the following questions: (a) What CAM therapies have been used for

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doi:10.1016/j.pedn.2010.01.009

management of procedure-related pain, anxiety, and distress in pediatric oncology? (b) Is there evidence to support the effectiveness of any of these CAM modalities in the management of procedure-related pain, anxiety, and distress? (c) What are the implications of these findings for evidence-based practice?

Background

Complementary and Alternative Medical Interventions

CAM is a term used to describe a group of diverse approaches to health care that are not currently considered to be part of conventional or "mainstream" medicine (Kemper, Vohra, & Walls, 2008). Although *complementary* approaches are generally used together with conventional medicine, *alternative* approaches are used in place of conventional medicine (National Center for Complementary and Alternative Medicine [NCCAM], 2007a). *Integrative medicine* is a term indicative of a combined complementary and mainstream approach for which there is some high-quality evidence to support the safety and efficacy of the practice, whereas *holistic medicine* refers to patient care that includes consideration of the biological, spiritual, psychological, social, and environmental components of health (Kemper et al., 2008). Four domains of CAM are recognized by NCCAM, including (a) mind–body medicine (e.g., meditation, imagery, prayer, art, and music); (b) biologically based practices (e.g., herbs, foods, and vitamins); (c) manipulative and body-based practices (e.g., massage, chiropractic, or osteopathic manipulation); and (d) energy medicine (e.g., Reiki, therapeutic touch, and magnetic fields). In addition, *whole medical systems* (e.g., homeopathic medicine and traditional Chinese medicine) are also recognized as forms of CAM that are built on comprehensive systems of theory and practice and cut across the four CAM domains (NCCAM, 2007a). Increasingly, parents of children with cancer are requesting the use of CAM therapies in conjunction with conventional oncological therapy, particularly for control of symptoms, including pain. Incorporation of CAM therapies into the child's treatment plan may increase the patient's and family's feelings of control and promote a sense of active participation and partnership with the health care provider throughout the healing process (Sencer & Kelly, 2007). The decision to use CAM in a child or adolescent with cancer requires consideration of the risks and benefits of the proposed therapy balanced with the developmental needs of the patient and the preferences of the family.

Procedures in Pediatric Oncology

It is not unusual for children and adolescents with cancer to perceive invasive medical procedures, particularly bone marrow aspiration or biopsy and lumbar puncture, as worse than the disease for which they are being treated, and children may develop symptoms of anxiety, fear, and distress before, during, and after these procedures (Kuppenheimer & Brown, 2002). As treatment progresses, distress and anticipatory anxiety related to procedures may increase over time (Kellerman, Zeltzer, Ellenberg, & Dash, 1983). In addition, pediatric oncology patients often undergo other potentially painful procedures, such as venipuncture, injections, and percutaneous venous access throughout their treatment and during the follow-up period.

Management of Procedure-Related Pain

Pharmacological interventions for procedure-related pain in pediatric oncology may include local anesthetics, such as topical creams (e.g., lidocaine, prilocaine, and eutectic mixture of local anesthetics) and injectable lidocaine (which can be prepared in a pH-adjusted buffered solution that reduces the injection-associated pain; Luhmann, Hurt, Shootman, & Kennedy, 2004), sedation of varying levels ranging from premedication (Sandler et al., 1992) to conscious or deep sedation (Marx et al., 1997; Reeves, Havidich, & Tobin, 2004), and general anesthesia (Crock et al., 2003; Iannalfi et al., 2005). Pharmacological management of procedure-related pain in children with cancer is included as a major recommendation by the American Pain Society in their *Guideline for the Management of Cancer Pain in Adults and Children*; nonpharmacological alternatives for managing pain are recommended for patients who decline procedural sedation (Miaskowski et al., 2005).

Significance to Nursing

The provision of atraumatic care forms the basis for much of pediatric nursing practice (Wong, 1989) and is a core value in pediatric oncology nursing practice (Hockenberry-Eaton, Barerra, Brown, Bottomley, & O'Neill, 1999). The use of evidence-based resources to identify effective treatments that prevent or reduce procedure-related pain, anxiety, and distress for pediatric oncology patients is a valuable tool for the nurse in providing the highest level of care possible. This integrative review provides the basis for the nurse to evaluate the effectiveness of CAM modalities, with or without pharmacological interventions, to reduce or treat procedure-related pain, anxiety, and distress in children and adolescents with cancer.

Methods

Definitions

The terms *integrative review*, *systematic review*, *research synthesis*, and *literature synthesis* have been used in the nursing literature with varying meaning. For the purposes of

this study, *integrative review* is defined as a type of literature review that is systematic in nature and qualitative in methodology, in which results of primary studies are combined in a narrative description to draw overall conclusions (Bowman, 2007). Furthermore, this study is a "summative" subtype of integrative review, in which the findings from primary studies are merged into general summative statements using narrative description (Cooper, 2003). The integrative review is designed to facilitate "decision making regarding actions and interventions that could result in the most effective, cost-efficient care" (Stetler et al., 1998, p. 195).

Setting and Sample

Inclusion criteria for this study consisted of the following: (a) case reports, clinical series, or clinical trials that included at least one CAM intervention aimed at reducing procedure-related pain, anxiety, and distress; (b) CAM intervention studied in the context of one or more of the following procedures: bone marrow aspiration or biopsy, lumbar puncture, injection, venipuncture for the purposes of blood sampling or initiation of intravenous injection or infusion, or percutaneous access of implanted vascular access device (e.g., portacath), excluding surgical procedures; and (c) sample included at least some children or adolescents with cancer between the ages of 2 and 18 years.

A search of the literature was conducted via the MEDLINE, CINAHL, PsyINFO, and COCHRANE databases from inception of each database through 2009 (Sood, Erwin, & Ebbert, 2004; Vincent, Vincent, & Ferreira, 2006; Wong, Wilczynski, & Haynes, 2006). The search strategy employed various combinations of the following search terms using Boolean operators (with asterisk [*] as an open-ended term): *Proced**, *NOT surgery*, *Lumbar puncture*, *Bone marrow*, *Venous access*, *Pain*, *Pain/*prevention&control*, *Anxiety*, *Distress*, *CAM*, *complementary therapies*, *Child**, *Adolesc**, and *Cancer*. The following limits were employed during the MEDLINE search: *English language*, *humans*, *complementary medicine*, and *preschool child: 2–5 years*, *child 6–12 years*, or *adolescent: 12–18 years*. An additional subset of articles was identified through the reference lists of retrieved articles using ancestral methodology (Conn et al., 2003).

These search strategies resulted in 195 citations. After reviewing abstracts of the retrieved citations for eligibility based on study inclusion criteria, 32 articles were retrieved and included in the final sample. The search strategy and retrieved articles were reviewed on two separate occasions to ensure adequate sampling.

Data Analysis

Each paper in the sample was read in its entirety, and data elements were then extracted and entered into a matrix according to the method of Garrard (2007). Data elements collected included authors, publication year, study design, medical procedures performed, CAM modalities studied, description of the study sample (diagnosis, number, and age of participants), level of evidence, and a summary of results. Some of the studies included measures of parent anxiety and distress; however, because the focus of this study was on patient-related outcomes, parent-related outcomes were not recorded or analyzed for this study. Level of evidence was assigned according to the method of Stetler et al. (1998) in which strength of evidence is rated on a scale from *I* to *VI*, with *I* being the strongest level of evidence, and quality of evidence is rated on a scale from *A* to *D*, with *A* being the highest quality of evidence (Table 1). Only studies that contained clear descriptions of methodology and analysis procedures, including power calculations or justification of sample size, were given an A rating. Studies with a D rating contained at least one significant methodological flaw that raised concerns about the believability of the results (Stetler et al., 1998); in this analysis, one such study was identified, and its findings were not included in the analysis. Results were then analyzed for themes, which were identified

Table 1 Stetler's Evidence Ranking System *

Level (Quality of Evidence) †	Source of Evidence
I (A–D)	Meta-analysis of multiple controlled studies ‡
II (A–D)	Individual experimental study ‡
III (A–D)	Quasi-experimental study such as nonrandomized controlled single group pretest–posttest, time series, or matched case-controlled studies ‡
IV (A–D)	Nonexperimental study, such as correlational descriptive research and qualitative or case studies ‡
V (A–D)	Case reports or systematically obtained, verifiable quality, or program evaluation data
VI	Opinion of respected authorities (e.g., nationally known) based on their clinical experience or the opinions of an expert committee, including their interpretation of nonresearch-based information. This level also includes regulatory or legal opinions.

* From Stetler et al. (1998), Reprinted from Applied Nursing Research, 11 (4), Stetler, C. B., Morsi, D., Rucki, S., Broughton, S., Corrigan, B., Fitzgerald, J., Giuliano, K., Havener, P., & Sheridan, E. A., Utilization-focused integrative reviews in a nursing service, p. 202, Copyright 1998, with permission from Elsevier.

† Level I = strongest rating per type of research; however, quality for any level can range from A to D and reflects basic scientific credibility of the overall study/project. An *A* reflects a very well-designed study/project. If quality is rated as *D* (i.e., the study or project has a major flaw that raises serious questions about the believability of the findings), it is automatically eliminated from consideration.

‡ This level includes studies both on the targeted population or issue and studies with other relevant populations or issues.

inductively and coded according to the method of Miles and Huberman (1994). Themes were compared across studies prior to combining data for the final analysis.

Results

Types of Designs

Table 2 provides an overview of all studies in the final sample and of all data elements used during the data analysis process. Study designs included 2 meta-analyses, 18 experimental studies, 9 quasi-experimental studies, 1 nonexperimental study, and 2 case reports.

Sample Characteristics

Geographic Location

Twenty-one of the studies were conducted in the United States, 3 in the United Kingdom, 3 in Greece, 2 in Italy, and 2 in Canada, and 1 report did not specify where the study was conducted.

Ages of Children

Seven studies included only young children (aged 10 years or younger), 3 studies included older children or adolescents (aged 10–17 years), and 22 studies included participants from both age groups.

Disease Characteristics

Eleven studies included children with leukemia only, an additional 13 studies included children with various cancer diagnoses other than leukemia, and 8 studies included children with a range of pediatric illnesses including cancer.

Themes Identified

CAM interventions identified in this study that were used alone, or as adjuncts to pharmacological interventions, for management of pain, anxiety, and distress for children and adolescents with cancer undergoing invasive procedures all fell within the domain of mind–body medicine. None of the CAM interventions identified through the literature search in this study were biologically based practices, energy therapies, or manipulative or body-based practices. The three most common CAM interventions identified for management of procedural pain, anxiety, and distress include hypnosis, distraction, and imagery. None of the studies reported prior to 1996 included pharmacological interventions. Overall, 28% (9/32) of the studies reported use of pharmacological interventions in addition to the CAM intervention or used a pharmacological agent in at least one arm of the study; of note, 46% (6/13) of the studies reported during the most recent decade (1999–2009) included pharmacological interventions, reflecting the gradual adoption of more aggressive pharmacological management of procedure-related pain in children (Liossi, 1999).

Distraction

The aim of distraction in managing procedural anxiety, distress, and pain is to focus the child's attention away from the painful procedure. Distraction is particularly effective for young children or when minimal preparation time is available and may take the form of counting, singing, watching a video, playing a game, or otherwise engaging the attention of the child away from the medical procedure (Doellman, 2003). Distraction was used as an interventional strategy in 18 of the 32 studies reviewed and was employed in various forms, ranging from controlled breathing with a party blower (Blount et al., 1994) to high-tech virtual reality games (Gershon et al., 2004; Gold et al., 2006).

Hypnosis

Hypnosis is a procedure during which a person is guided by a therapist to respond to suggestions that allow for changes related to a subjective experience (such as alterations in perception, emotion, thought, behavior, and sensation). In some cases, participants can be taught self-hypnosis, with the goal of self-management of symptoms such as pain and distress and promotion of feelings of self-efficacy and mastery (Richardson, Smith, McCall, & Pilkington, 2006). Hypnotic susceptibility, or the tendency to respond to hypnotic suggestions, varies between individuals. The capacity for hypnotic susceptibility begins to increase starting at the age of 3 years, peaks between the ages of 8 and 12 years, and then declines through the age of 16 years, after which it tends to remain stable for life (Accardi & Milling, 2009). Hypnosis in various forms was used as an interventional strategy in 11 of the 32 studies reviewed, including direct and indirect hypnosis (Hawkins et al., 1998; Liossi & Hatira, 2003), self-hypnosis (Liossi et al., 2009), and a hypnosis variant (imaginative involvement; Kuttner et al., 1988).

Imagery

Imagery focuses the child's attention away from the procedure by harnessing the imagination. For example, a child may be asked to imagine themselves in a pleasant place (such as at the beach) and to focus on the physical sensations that they may experience in their imagined place (such as the sounds of the ocean and the warmth of the sun). This technique requires the active cooperation of the patient and is most effective when used for children over the age of 8 years (Doellman, 2003). Imagery was employed as an interventional strategy for management of procedural pain, anxiety, and distress in 6 of the 32 studies in this review and was commonly employed in combination with distraction, relaxation, and play (Broome et al., 1992; Kazak et al., 1998).

Other Mind–Body Interventions

Additional mind–body interventions used in the studies in this review include relaxation (four studies); play (three

Table 2 CAM and Procedural Pain, Anxiety, and Distress in Pediatric Oncology: Studies and Findings

Authors	Journal	Year	Procedures	CAM modality	Outcomes measured	Study design	Sample	Level of evidence	Results
Data from Blount, Powers, Cotter, Swan, and Free (1994)	*Behavior Modification*	1994	BMA, LP	Distraction (party blower)	Distress, Coping	Multiple baseline across participants	3 children (aged 4–7 years) with ALL	III-C	Increased coping and decreased distress noted after initial training compared with baseline; 1 of 3 children returned to baseline at remainder of procedures; other 2 children maintained improved coping and decreased distress
Data from Broome, Lillis, McGahee, and Bates (1992)	*Oncology Nursing Forum*	1992	LP	Relaxation, distraction, imagery	Pain, Fear	Multiple case studies	14 children (aged 3–15 years) with ALL	V-B	Children's pain ratings decreased over time; behavioral responses during procedure varied considerably; fear scores stable over time
Data from Broome, Rehwaldt, and Fogg (1998)	*Journal of Pediatric Nursing*	1998	LP	Relaxation, distraction, imagery	Pain, Distress	Repeated measures, one group design	28 children (4–18 years) with cancer	III-B	Significant improvement in pain scores ($p < .01$) over 5-month study, but behavioral distress did not change significantly ($p < .10$)
Data from Caprilli, Anastasi, Grotto, Abeti, and Messeri (2007)	*Journal of Developmental and Behavioral Pediatrics*	2007	Venipuncture	Music	Pain, Distress	Randomized controlled trial (parent support ± musician)	108 children (aged 4–13 years) undergoing blood tests	II-B	Distress and pain intensity significantly lower ($p < .001$; $p < .05$) before, during, and after blood tests in music group compared with control group.
Data from Chen, Zeltzer, Craske, and Katz (1999)	*Journal of Consulting and Clinical Psychology*	1999	LP	Memory reframing	Distress	Randomized controlled trial (memory reframing vs. standard care)	50 children (aged 3–18 years) with leukemia	II-B	Children in the intervention group showed reductions in distress compared with control
Data from Dahlquist et al. (2002)	*Journal of Pediatric Oncology Nursing*	2002	iv starts, port access, im injections	Distraction (electronic toys)	Pain, Distress	Multiple baseline across participants	6 children (aged 2–8 years) with cancer or immunologic disorder	III-C	Reductions in distress were observed in 5 of 6 cases
Data from Dahlquist, Gil, Armstrong, Ginsberg, and Jones (1985)	*Journal of Behavior Therapy and Experimental Psychiatry*	1985	iv starts	Relaxation, controlled breathing, imagery, positive self-talk	Distress	Multiple baseline across participants	3 children (aged 11–14 years) with cancer	III-C	46%–68% reductions in observed distress from baseline levels

Data from Favara-Scacco, Smirne, Schiliro, and Di Cataldo (2001)	*Medical and Pediatric Oncology*	2001	LP, BMA	Art therapy	Anxiety, fear, distress	Experimental group (art therapy) vs. Historical control group (no art therapy)	32 children (aged 2–14 years) with leukemia	III-D	Researchers reported that children hospitalized prior to inception of the art therapy program "exhibited resistance and anxiety during and after painful procedures," and children provided with art therapy from their first hospitalization "exhibited collaborative behavior." Researchers concluded that art therapy was a "useful intervention" that "can prevent permanent trauma and support children and parents during intrusive procedures."
Data from Frankenfield (1996)	*Journal of Pediatric Oncology Nursing*	1996	Port access	Humor	Anxiety	Case report	1 child (aged 5 years) with retinoblastoma	V-C	Use of humor and play by nurse decreased anxiety and decreased time required for port access from 25 minutes to less than 5 minutes
Data from Gershon, Zimand, Pickering, Rothbaum, and Hodges (2004)	*Journal of the American Academy of Child and Adolescent Psychiatry*	2004	Port access	Distraction (virtual reality)	Pain, anxiety, distress	Randomized controlled trial (standard of care = EMLA; computer game without VR; VR)	59 children (aged 7–19 years) with cancer	II-B	Potential benefit from virtual reality distraction as evidenced by reduced distress, lower pain ratings by nurse, and significantly lower pulse rates during procedure
Data from Gold, Kim, Kant, Joseph, and Rizzo (2006)	*CyberPsychology & Behavior*	2006	iv starts	Distraction (virtual reality)	Pain, anxiety	Randomized controlled trial (standard of care = topical anesthetic spray ± virtual reality)	20 children (aged 8–12 years) undergoing MRI	II-B	Children in the virtual reality group had significantly greater satisfaction with their pain management ($p < .001$) than did those in the control group

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Table 2 (*continued*)

Authors	Journal	Year	Procedures	CAM modality	Outcomes measured	Study design	Sample	Level of evidence	Results
Data from Hawkins, Liossi, Ewart, Hatira, and Kosmidis (1998)	*Contemporary Hypnosis*	1998	LP	Hypnosis	Pain, anxiety	Randomized trial (hypnosis with direct vs. Indirect suggestion of pain relief)	30 children (aged 6–16 years) with cancer	II-C	Significant reduction in pain and anxiety in both groups compared with baseline; direct and indirect suggestion methods equally effective; level of hypnotizability significantly associated with magnitude of treatment outcome
Data from Jay, Elliott, Fitzgibbons, Woody, and Siegel (1995)	*Pain*	1995	BMA	Imagery, distraction, positive incentive, behavioral rehearsal	Distress, pain, fear, anxiety	Repeated measures crossover design (general anesthesia; behavioral intervention)	18 children (3–12 years) with leukemia	II-B	No significant difference in self-reported pain, fear, or anticipatory anxiety between groups. More behavioral distress in behavioral intervention group during the first minute but more adjustment symptoms in the anesthesia group
Data from Katz, Kellerman, and Ellenberg (1987)	*Journal of Pediatric Psychology*	1987	BMA	Hypnosis, play	Pain, distress	Randomized controlled trial (hypnosis vs. Play)	36 children (aged 6–12 years) with ALL	II-B	Improvement in self-reported distress over baseline with both interventions but no differences between interventions
Data from Kazak et al. (1996)	*Journal of Pediatric Psychology*	1996	LP, BMA	Distraction, play, guided imagery (customized intervention for each child)	Distress	Randomized, controlled trial (pharmacological only vs. Pharmacological + psychologic); with retrospective comparison group (usual care)	162 children (aged 0–17 years) with leukemia	II-B	Lower levels of distress reported for the combined pharmacological + psychological intervention group than those for the pharmacological only group ($p < .03$ for mothers' ratings; $p < .05$ for nurses' ratings)

Data from Kazak, Penati, Brophy, and Himelstein (1998)	*Pediatrics*	1998	LP, BMA	Distraction, play, guided imagery (customized intervention for each child)	Distress	Randomized, controlled trial (pharmacological only vs. Pharmacological + psychologic); with retrospective comparison group (usual care)	162 children (aged 0–17 years) with leukemia	III-B	Lower levels of distress reported for the combined pharmacological + psychological intervention group than did the pharmacological only group ($p < .01$ for mothers' ratings; $p < .02$ for nurses' ratings); predictors of distress included age, intervention group, and procedural variables (medications, doses, technically difficulty of procedure, number of needles required)
Data from Kellerman et al. (1983)	*Journal of Adolescent Health Care*	1983	BMA, LP, iv access	Hypnosis	Pain, anxiety	Single arm pretest and posttest	18 adolescents with cancer	III-B	2 patients rejected hypnosis; the remainder achieved significant reductions in distress after hypnosis training; group reductions in pain and anxiety significant at levels ranging from $p < .02$ to $p < .002$
Data from Kleiber and Harper (1999)	*Nursing Research*	1999	Medical procedures including iv starts, BMA, LP, im injections	Distraction	Pain, distress	Meta-analysis	26 trials with 1026 children (aged 3–15 years)	I-A	Mean effect size for distress was .33 (±0.17); mean effect size for pain was .62 (±.42)
Data from Kuttner, Bowman, and Teasdale (1988)	*Developmental and Behavioral Pediatrics*	1988	BMA	Distraction, hypnosis variant (imaginative involvement)	Pain, distress, anxiety	Randomized controlled trial (3 groups: distraction, hypnosis variant, control)	59 children (aged 3–10 years) with leukemia	II-B	Distress of younger children (3–6 years) best alleviated by hypnotic technique; pain and anxiety of older children (7–10 years) reduced by both distraction and hypnosis techniques; distraction technique required learning over 1–2 sessions, whereas the hypnotic technique was immediately effective

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Table 2 (*continued*)

Authors	Journal	Year	Procedures	CAM modality	Outcomes measured	Study design	Sample	Level of evidence	Results
Data from Lal, McClelland, Phillips, Taub, and Beattie (2001)	*Acta Paediatrica*	2001	Venipuncture	Distraction ± pharmacological therapy: EMLA vs. placebo cream	Pain	Randomized placebo-controlled trial (2 groups: distraction + EMLA; distraction + placebo)	28 children (aged 4–8 years) undergoing venipuncture	II-B	No significant difference in pain scores between treatment and control groups (p = .07); low pain scores in both groups suggest effectiveness of distraction therapy
Data from Lander and Fowler-Kerry (1993)	*Pain*	1993	Venipuncture	TENS	Pain (intensity, affect)	3 x 6 factorial design, double blind, placebo controlled	514 children (aged 5–17 years) undergoing outpatient venipuncture	II-A	3 treatment groups (TENS, placebo-TENS, control); blocked into six 2-year age groups; pain measured with visual analogue scale; pain affect measured with McGrath's faces scale. Pain intensity and affect lowest in the TENS group and highest for control group; pain scores highest in younger groups, lowest in older groups
Data from Liossi and Hatira (1999)	*The International Journal of Clinical and Experimental Hypnosis*	1999	BMA	Hypnosis, cognitive behavioral skills training	Pain, anxiety, distress	Randomized controlled trial (3 groups: hypnosis, cognitive–behavioral, no intervention)	30 children (aged 5–15 years) with cancer	II-B	Hypnosis and cognitive behavioral skills training were equally effective in pain relief; children reported more anxiety and exhibited more distress in the cognitive–behavioral group than in the hypnosis group
Data from Liossi and Hatira (2003)	*The International Journal of Clinical and Experimental Hypnosis*	2003	LP	Hypnosis (direct, indirect)	Pain, anxiety, distress	Randomized controlled trial (4 groups—all received standard medical treatment; +attention control; +direct hypnosis; +indirect hypnosis)	80 children (aged 6–16 years) with cancer	II-B	Patients in the hypnosis groups reported less pain and anxiety and demonstrated less behavioral distress compared with control; direct and indirect suggestions were equally effective

Data from Liossi, White, and Hatira (2006)	*Health Psychology*	2006	LP	Self-hypnosis (+pharmacological therapy: EMLA)	Pain, anxiety	Randomized controlled trial (3 arms: EMLA vs. EMLA +self-hypnosis vs. EMLA + attention control)	45 children (aged 6–16 years) with cancer	II-A	Patients in the EMLA + self-hypnosis group reported less anticipatory anxiety and less procedure-related anxiety and pain compared with EMLA or EMLA + attention control
Data from Liossi, White, and Hatira (2009)	*Pain*	2009	Venipuncture	Self-hypnosis or attention control (+pharmacological therapy: EMLA)	Pain, anxiety	Randomized trial (3 arms: self-hypnosis + EMLA; attention control + EMLA; EMLA alone	45 children (aged 6–16 years) with cancer	II-A	Self-hypnosis + EMLA group reported less anticipatory anxiety and less procedure related pain and anxiety compared with other two groups
Data from Manne et al. (1990)	*Journal of Consulting and Clinical Psychology*	1990	Venipuncture	Distraction, reinforcement, parental coaching	Distress, pain, fear	Two groups (behavioral intervention; attention control) repeated measures	23 children (aged 3–9 years) with cancer	II-C	Reductions in distress and parent-reported pain; no reduction in self-reported pain
Data from Pederson (1996)	*Journal of Pediatric Oncology Nursing*	1996	LP	Distraction, focused breathing, relaxation, imagery	Anxiety, distress, pain	Pretest, posttest with control group	8 children with ALL (aged 6–14 years)	III-B	Following intervention, children had lower levels of self-reported pain ($p = .06$), fewer requests for emotional support ($p = .07$) fewer expression of verbal fear ($p = .10$) and fewer information-seeking questions ($p = .10$)
Data from Powers, Blount, Bachanas, Cotter, and Swan (1993)	*Journal of Pediatric Psychology*	1993	iv starts, im injections	Distraction	Distress, pain, fear	Multiple baseline across participants	4 children (aged 3–5 years) with ALL	III-C	Children displayed less behavioral distress following intervention; maintenance-promoting portion of intervention needs further evaluation
Data from Tyc, Leigh, Mulhern, Srivastava, and Bruce (1997)	*International Journal of Rehabilitation and Health*	1997	iv starts	Cognitive–Behavioral interventions (e.g., distraction, hypnosis)	Distress	Randomized controlled trial (intervention vs. Control)	55 children (aged 6–18 years) with central nervous system cancers undergoing MRI	II-A	Cognitive–Behavioral intervention effective at reducing distress according to staff ratings when compared with control

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Table 2 (*continued*)

Authors	Journal	Year	Procedures	CAM modality	Outcomes measured	Study design	Sample	Level of evidence	Results
Data from Uman, Chambers, McGrath, and Kisely (2006)	*Cochrane Database of Systematic Reviews*	2006	Needle-related procedures	Cognitive–Behavioral interventions (e.g., distraction, hypnosis)	Pain, distress	Meta-analysis	28 trials with 1,951 children (aged 2–19 years); 1,039 in treatment conditions; 951 controls	I-A	The largest effect sizes for treatment improvement over control conditions exist for distraction (self-reported pain SMD = −0.24, 95% CI = −0.45 to −0.04), hypnosis (self-reported pain SMD = −1.47, 95% CI = −2.67 to −0.27), and combined cognitive–behavioral interventions (distress SMD = −0.67, 95% CI = −0.95 to −0.38).
Data from Weekes, Kagan, James, and Seboni (1993)	*Journal of Pediatric Oncology Nursing*	1993	Venipuncture, LP, BMA, shunt placement, iv access	Hand holding	Pain	Qualitative semistructured interviews	20 adolescents (aged 11–19 years); 10 with cancer, comparison group of 10 with renal disease	IV-B	Adolescents perceived hand holding to be an effective coping strategy in ameliorating treatment-related pain; strongly preferred mother's hand, if not available, preferred specific nurse's hand
Data from Zeltzer and LeBaron (1982)	*The Journal of Pediatrics*	1982	BMA, LP	Hypnosis, distraction	Pain, anxiety	Randomized controlled trial (hypnosis vs. distraction)	45 children (aged 6–17 years) with cancer	II-B	For BMA, pain was reduced to a larger extent by hypnosis ($p < .001$) than distraction ($p < .01$); anxiety was reduced only by hypnosis ($p < .001$). For LP, only hypnosis significantly reduced pain ($p < .001$); anxiety was reduced to a larger extent by hypnosis ($p < .001$) than distraction ($p < .05$)

Note: BMA = bone marrow aspiration; LP = lumbar puncture; ALL = acute lymphoblastic leukemia; iv = intravenous; im = intramuscular; EMLA = eutectic mixture of local anesthetics; VR = virtual reality; MRI = magnetic resonance imaging; TENS = transcutaneous electrical nerve stimulation; SMD = standardized mean differences; CI = confidence intervals.

studies); combined cognitive–behavioral therapy approaches (three studies); controlled breathing (two studies); positive incentive or reinforcement (two studies); and parental coaching, positive self-talk, behavioral rehearsal, transcutaneous electrical nerve stimulation, hand holding, humor, music, and memory reframing (one study each).

Use of Pharmacological Interventions

Nine studies incorporated pharmacological interventions, either as standard of care or as part of the randomized design. All studies with pharmacological interventions were reported between 1995 and 2009. Pharmacological interventions ranged from local anesthetic creams (Gershon et al., 2004) to general anesthesia (Jay et al., 1995).

Discussion

Although this integrative review attempted to identify all CAM interventions used to manage procedure-related pain, anxiety, and distress in children and adolescents undergoing cancer treatment (and thus incorporated search terms that should have identified interventions of all types), the only category of CAM therapies that emerged as having been studied in regard to procedure-related symptoms in the pediatric oncology population was that of mind–body therapies. Of note, other types of CAM therapies, including biologically based therapies (such as herbs, foods, and vitamins), energy therapies (such as acupuncture), and manipulative and body-based practices (such as massage) have been used for management of nonprocedural cancer pain and related symptoms (e.g., nausea) in children and adolescents with cancer (Kemper et al., 2008; Ladas, Post-White, Hawks, & Taromina, 2006); however, none of these CAM therapies were identified as having been studied in the context of relief of procedure-related symptoms in children or adolescents with cancer. Mind–Body medicine focuses on the interactions that occur between the mind and body and on the powerful ways that emotional, behavioral, spiritual, and social factors can affect bodily function and symptoms (NCCAM, 2007a). In mind–body medicine, illness is seen as an opportunity for personal growth, each person is seen as having the capacity for self-knowledge and self-care, and health care providers are viewed as catalysts and guides in the healing process (NCCAM, 2007b).

Certain mind–body interventional strategies, including hypnosis and cognitive–behavioral therapies, have been extensively tested over the past several decades and, although still considered mind–body interventions, are now well integrated into conventional care and no longer considered CAM therapies (NCCAM, 2007b). The advantages of these approaches include the fact that once standardized, they can be easily taught and widely disseminated. In addition, the physical and emotional risks related to use of mind–body interventions are minimal (Kemper et al., 2008).

In this review, distraction, hypnosis, and imagery emerged as the three most commonly studied mind–body modalities for management of procedural pain, anxiety, and distress in pediatric oncology. A number of studies in this review suggest that hypnosis may be more effective than distraction in relieving procedure-related symptoms, particularly for procedures highly associated with pain (e.g., bone marrows and lumbar punctures), for children with higher levels of hypnotic susceptibility and when used in combination with pharmacological therapies (Hawkins et al., 1998; Liossi & Hatira, 2003). Self-hypnosis appears to be effective in reducing anticipatory anxiety in certain children, depending on the child's level of hypnotizability (Liossi et al., 2006, Liossi et al., 2009). In addition, cognitive–behavioral techniques, such as distraction and imagery, show promise in reducing fear and distress and decreasing procedure-related pain in some children with cancer (Gershon et al., 2004; Kazak et al., 1998). The self-regulatory skills gained by these children may provide assistance with overall symptom management throughout cancer treatment (Sencer & Kelly, 2007).

Limitations

Limitations of the integrative review method as used in this analysis include the possibility of overlooking relevant literature for review through inadvertent omission of an important search term, which may have resulted in overlooked articles containing important information regarding the topic under study. Because only the MEDLINE, CINAHL, PsyINFO, and COCHRANE databases were searched, unpublished manuscripts, such as dissertations and abstracts, were not included, potentially resulting in publication bias. In addition, the large volume of literature reviewed in a limited time period may have resulted in missed themes, and the study could have been strengthened by corroboration of thematic elements by additional investigators.

Implications for Research

Although multiple studies have demonstrated the value of mind–body CAM interventions in reducing procedure-related pain in children with cancer, many studies reported using small samples; therefore, these findings require confirmation in larger samples. In addition, because many studies incorporated groups of CAM therapies into a single intervention (e.g., distraction plus imagery plus relaxation), additional research is needed to determine the efficacy of specific mind–body interventions in relieving procedural pain, anxiety, and distress in children and adolescents with cancer. Future studies focused on mind–body CAM interventions that are readily applicable by nurses in routine patient care situations (e.g., use of distraction and

imagery during needle-related procedures) could prove particularly valuable in expanding the evidence base for providing atraumatic nursing care to children and adolescents with cancer.

Implications for Practice

Although mind–body interventions for management of procedure-related symptoms in pediatric oncology may be effective, particularly when used in combination with pharmacological agents, individual differences in age, temperament, and prior procedure-related experiences make it imperative for nurses to conduct thorough patient assessments to determine the most efficacious interventions for individual patients. Because there are significant costs and potential complications associated with pharmacological interventions (e.g., deep sedation, general anesthesia), the use of mind–body therapies, such as distraction, imagery, and hypnosis, offers the potential benefits of both symptom relief and increased self-efficacy with minimal risk of adverse effects and should be carefully considered as potentially valuable interventions for symptom management in pediatric oncology patients undergoing invasive procedures.

Acknowledgments

The authors would like to acknowledge the thoughtful review of Karla Wilson, RN, MSN, FNP-C, CPON, nurse practitioner, Childhood Cancer Survivorship Program, City of Hope, Duarte, CA, and M. Teresa Rojas-Cooley, RN, BSN, clinical nurse, Inland Valley Medical Center, Wildomar, CA.

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