ORIGINAL ARTICLE

Systematic review of the effective factors in pain management in children

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ABSTRACT

Background: Pain is a stressful experience and a common health problem worldwide, with children being the most vulnerable in society.
Aim: To provide a systematic review of published research evidence related to the effectivefactors inpain management in children focusing on pharmacological and non-pharmacological therapies using valid evaluation criteria.
Methods: The present study is a systematic review which was performed by searching the databases of Elsevier PubMed, Springer, Wiley, and Sage and with the keywords, pain, children, baby, review paper, and systematic management. English articles published between 2002-2019 were selected for further review.
Results: From a total of 1216 articles, 20 articles were selected based on the inclusion and exclusion criteria for further review. The results showed that both pharmacological and non-pharmacological treatment methods in relieving and reducing pain and anxiety in a wide range ofpediatric diseases (such as respiratory tract infections, burns, surgery, dental restorations) are effective, although different side effects (such as nausea, vomiting, diarrhea, and gastrointestinal problems) have been observed in children due to the use of some medications.
Conclusion: Due to the side effects of medications, doctors, nurses and parents are more inclined to use non-pharmacological methods in the management of children's pain, however the accurate and effective implementation of these methods is associated with problems and challenges, which indicates the need for further studies on the use of various non-pharmacological methods.
Keyword: Pain management, children, distraction, analgesia

INTRODUCTION

Pain is the most common symptom of disease that accompanies us from an early age. Pain is actually a defense mechanism of the body against a harmful stimulus. Pain is always an unpleasant feeling. The perception of pain could be caused by the stimulation of pain receptors in the skin, joints and many internal organs. The cause of pain may be damage to the nervous system, peripheral nerves, brain and spinal cord. Pain could also occur without tissue damage, which called psychological pain. The process of pain is a complex phenomenon. The experience of pain depends on the stimulus, sensitivity and individual resistance to pain. Pain receptors are sensitive to mechanical, thermal, or chemical stimuli[1,2].

Pain is a stressful experience and a common health problem worldwide, with children being the most vulnerable in society. Despite the increasing scientific evidence of pain management in children over the past few decades, there are many obstacles and difficulties in applying this knowledge at the clinical level. As a result, children still experience unnecessary pain[3,4]. Some of the problems related to children's pain in hospitals include disagreements among pediatric caregivers regarding the severity of pain in children[5], limited and insufficient information of physicians and nurses about pain assessment tools and available methods for treatment[6,7,8], lack of knowledge and misconceptions of health professionals about prescribing painkillers and addictive opioids[9], inadequate pain management medication in children[10], high incidence of medical errors related to prescribing painkillers[11], and management and control of pain in children, including pharmacological and non-pharmacological strategies[12].

Non-pharmacological strategies in pain management

Non-pharmacological therapy could be used as an adjunct therapy in the treatment of pain in both adults and children. This type of treatment is used to help improve lower levels of anxiety, distress, and pain. Non-pharmacological treatment includes physical and mental therapies;Physical therapies include the use of massage, hot or cold compresses, applying pressure or vibration, and reduction and mental therapies include mental imagery, distraction, and relaxation techniques[12].

Pharmacological treatments in pain management

Over the past two decades, pain assessment and management in children has improved due to the development of age-appropriate pain assessment tools and a better understanding of the role of analgesics in children. The most common analgesics used in pain management in both adults and children are divided into two categories: narcotic and non-narcotic analgesics. Non-narcotic drugs such as acetaminophen and nonsteroidal anti-inflammatory drugs (NSAIDs) are the most common drugs in the treatment of mild pain in adults and children. However, non-narcotic drugs are less analgesic and less effective than narcotic drugs. Narcotic drugs include codeine, morphine, hydromorphone, and oxycodone, which are used to treat moderate to severe pain in both adults and children. Most narcotic and non-narcotic analgesics are combined to relieve pain, which reduces the amount of narcotic by up to 30% and the patient experiences fewer side effects[12].

There has been a great deal of research on pain in children over the past decade that has led to the development of multiple standards and guidelines for pain in children. Despite the increasing scientific evidence of pain management in children over the past few decades, there are many obstacles and difficulties in applying this knowledge at the clinical level. Therefore, children still experience unnecessary pain[3,13,14]. Systematic reviews that evaluate pharmacological and non-pharmacological pain relief strategies could be the most effective way to manage pain in children. They could also help develop guidelines and standards, decisions and future research plans. Therefore, the present study aimed to provide a systematic review of published research evidence related to effective factors in pain management in children, focusing on pharmacological and non-pharmacological therapies using valid evaluation criteria.

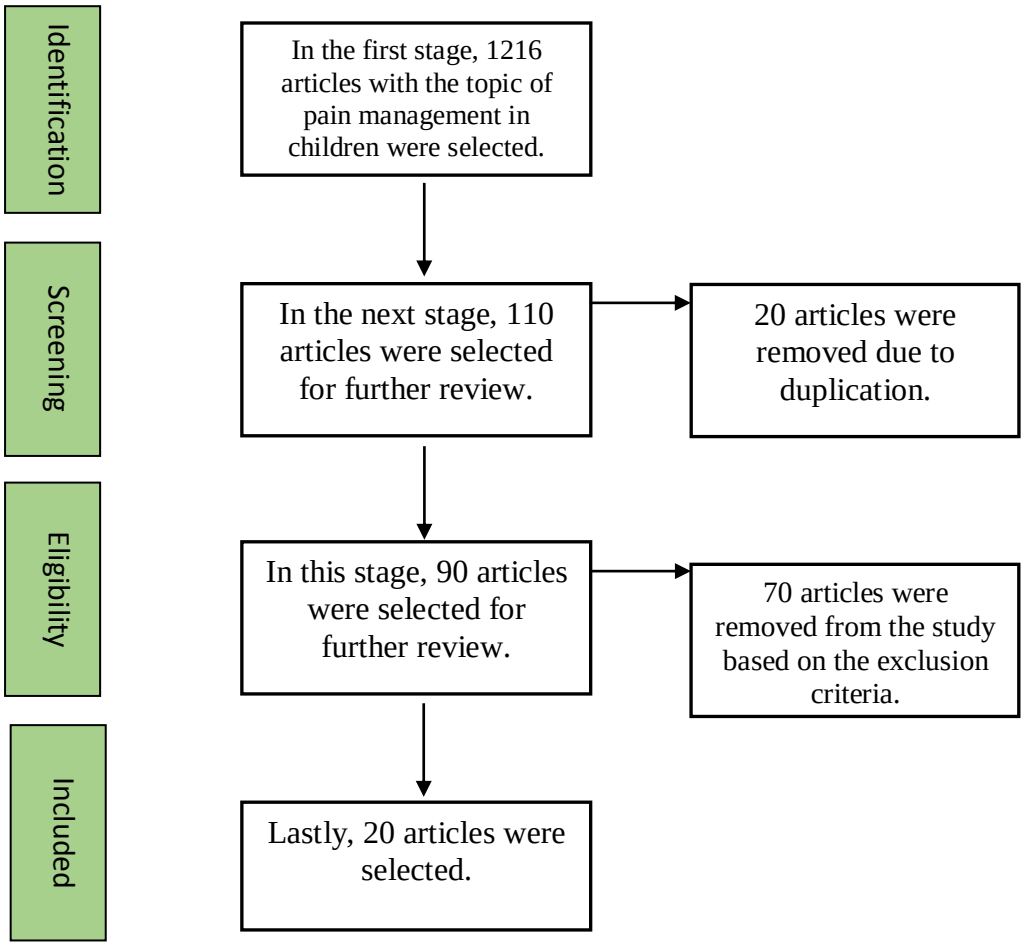
MATERIALS AND METHODS

The present study is a systematic review which was performed by searching the databases of Elsevier PubMed, Springer, Wiley, and Sage and with the keywords, pain, children, baby, review paper, and systematic management. These words were often used separately and in some cases as a combination of two words. Inclusion criteria: Full-text articles in the field of children's pain management considering the limitation of the year of publication (after 2000) and articles published in English focusing on pharmacological and non-pharmacological methods; exclusion criteria: Articles without full text, studies related to out-of-hospital pain management, articles published before 2000 and review articles. In the analysis phase, the information collected from the studies included the author (s), year, purpose, main concepts studied, methods, and research environment. These studies were regularly collected in files and used as raw data for this review study. No interpretation was used during the data collection and the authors' main phrases were used.

RESULTS

In the first stage, 1216 articles were selected. At this stage, the title and, if necessary, the abstract of the articles were reviewed and finally 110 articles were selected. In the second stage, the full text of the articles was studied and 20 articles were deleted due to duplication. Out of the remaining 90 articles, 70 articles were removed from the study based on inclusion /exclusion criteria, and finally 20 full-text articles published in English and books on pain management in children were included in the final study. The studies between 2002-2019 were reviewed (Figure 1).

Figure 1: Method of selecting articles



Results of the non-pharmacological therapies in pain management in children: The results related to this section are stated in Table 1. Table 1 shows the characteristics and results of 10 studies on non-pharmacological therapies in children. The first study in this table examined the method performed during dental restorative treatments in children, which showed that the treatment method based on distraction (using audio-visual glasses) is an effective way to reduce pain (measured by combined instruments) and anxiety (measured by heart rate) in children.

Subsequent two studies evaluated the method performed during burn-related therapies in children, indicating that distraction-based therapies (play therapy) were a more effective way to reduce pain (measuredby the Wong-Baker Face Scale) compared to standard care and control groups in children. Studies 4-6 in this table have examined different methods performed during venipuncture in children, which showed that treatment methods based on distraction (using a musical ball, inflating a balloon and watching cartoons) significantly reduce duration of venipuncture and its associated pain (measured by the Visual Analogue Scale (VAS) and the OUCHER Standard scale) compared to control groups. The next two studies evaluated the different methods performed during injection in children, which indicated that therapies based on distraction (using audio-visual glasses and watching animation) were more effective in reducing pain (measured by the revised face pain scale (FPS-R) and visual analog scale (VAS) and anxiety (measured by heart rate) compared to control groups in children. Finally, the last two studies examined different methods performed during surgery in children, which showed that therapies based on distraction (mental imagery and relaxation)significantly reduce postoperative pain (measured by the Visual Analogue Scale (VAS) and the Face, Legs, Activity, Cry, Consolability scale (FLACC)) and preoperative anxiety (measured by the modified Yale Preoperative Anxiety Scale (mYPAS)) compared to control groups.

In total, out of 768 children aged 5 to 12 years who received non-pharmacological treatments in these 10 studies, in 163 children (21.22%) the distraction technique based on watching cartoons or animations, in 91 children (11.85%) distraction technique based on the use of audio-visual glasses (AV), in 88 children (11.54%) distraction technique based on play therapy, and in 60 children (7.81%) distraction technique based onrelaxation and mental imagery, reduced children's pain and anxiety during surgery, dental services, burns, venipuncture and injections. These results suggest that watching cartoons is a more effective method to reduce children's pain and anxiety than other activities.

Results of the pharmacological therapies in pain management in children: The results related to this section are stated in Table 2. Table 2 shows the characteristics and results of 10 studies on pharmacological therapies in children. The first study in this table examined the drugs used (acetaminophen codeine and ibuprofen) in relieving acute injuries (fractures and dislocations) in children, which showed that the analgesic power of both analgesics is the same. The use of these two analgesics is associated with few side effects (vomiting, nausea and pruritus) in children. The next three studies evaluated the medications used (ibuprofen acetaminophen, morphine, and codeine) to relieve surgical pain (abdomen and tonsils) in children, indicating that among the drugs used, the most effective medications were morphine and codeine, respectively, and acetaminophen and ibuprofen had the same analgesic effect. It was also found that the frequency of morphine side effects was 56% and codeine was 29%. The next three studies were related to upper respiratory tract infection and its complications (such as fever). Drugs used included ibuprofen, dexibuprofen, and acetaminophen intravenously. The results of these three studies suggest that intravenous acetaminophen has fewer side effects (such as gastrointestinal problems and increased liver enzymes) and better efficacy in reducing the fever due to pediatric respiratory infections compared with ibuprofen and dexibuprofen. But there was no significant functional difference between ibuprofen and dexibuprofen. Finally, the last three studies examined the drugs used (acetaminophen and ibuprofen) in relieving dental-related pain (pulpectomy and tooth extraction) in children, which showed that the use of ibuprofen and acetaminophen analgesics could reduce pain compared to the placebo group. Also, Ibuprofen is more effective in reducing dental-related pain than Acetaminophen.

In total, out of 1398 children aged 6 months to 15 years who underwent drug treatment in these 10 studies, in 387 children (27.69%) acetaminophen (orally, intravenously and suppository), in 548 children (31.20%) dexibuprofen, in 346 children (24.75%) ibuprofen, in 75 children (5.36%) acetaminophen codeine, in 51 children (3.65%) ibuprofen with acetaminophen, and in43 children (3.08%) Morphine and diclofenac, were used to relieve the pain associated with injuries, surgery, fever, and complications from upper respiratory tract infection and dental-related pain.

Table 1. Results of the non-pharmacological therapies in pain management in children

Autor	Subject	sample number and methods used	Type of pain	Method of measuring pain intensity	Results
Mitrakulet al. 2015 (15)	Effect of Audiovisual Eyeglasses During Dental Treatment in 5-8-Year-Old Children	Sample number: 42 children 5 to 8 years old with tooth decay. Methods: These children were randomly divided into two groups. The first group had injections without using audio-visual glasses (AV) in the first visit and injection using these glasses in the second visit. The second group is the opposite of the first group. All variables were	Pain from dental restorative treatments in children	Pain intensity was measured using the Revised Face pain Scale (FPS-R) and The Face, Legs, Activity, Cry, Consolability scale (FLACC), and Anxiety was measured by heart rate in children.	AV glasses could reduce pain and heart rate before the procedure and at the time of the first use of high-speed hand pieces in both groups, which shows that AV glasses can be used as an adjunct method during dental treatment in children.

		measured before the start of the procedure, The time of closing rubber dam (rubber barrier), the time of the first use of the high-speed handpiece (manual parts), and after 5 minutes			
Daset al. 2005 (16)	The efficacy of playing a virtual reality game in modulating pain for children with acute burn injuries: A randomized controlled trial	Sample number: 7 children (4 boys and 3 girls with a mean age of 11.1 years). The technique used: Game therapy (virtual reality games or VR)	Pain from changing dressings in children with severe burn injuries	Pain intensity was measured with the Wong-Baker Faces Scale.	Mean pain intensity using conventional drug therapies was 4.1, while the simultaneous use of play therapy and medication reduced the pain intensity to 1.3.
Lozano,Pottert on.2018 (17)	The use of Xbox Kinect™ in a Paediatric Burns Unit	Sample number: 66 children with a mean age of 7 years, 55% of whom were boys. Methods: control group (35 children and the use of physiotherapy) and the experimental group (31 children and the simultaneous use of physiotherapy and play therapy (Xbox Kinect ™))	Pain resulting from burns	the level of Satisfaction and pain in children from the game were measured with Wong-Baker faces scale	This study showed that the use of Xbox Kinect™ games could be a useful and helpful treatment in rehabilitation and healing and relief of burn injuries in children.
Wang et al.2008 (18)	The Efficacy of Non-Pharmacological Methods of Pain Management in School-Age Children Receiving Venepuncture in a Paediatric Department:	Sample number: 300 children 8 to 9 years old Methods: Children were randomly divided into 3 groups: control (100 people), intervention group (100 people and using routine psychological methods) and experimental group (100 people and using the technique of distraction by watching cartoons)	Pain from venipuncture in children	Pain intensity was measured by the Visual Analogue Scale (VAS)	The time of venipuncture and the amount of pain from it were significantly higher in the control group than the other two groups, while there was no significant difference between the intervention and case groups (watching cartoons) in terms of pain intensity and venipuncture time.
Guptaet al. 2006 (19)	An Evaluation of Efficacy of Balloon Inflation on Venous Connulation Pain in Children: A prospective, randomized, controlled study	Sample number: 75 children 6 to 12 years old. Methods: Children were randomly divided into three groups of control (25 children), distraction group (25 children and the use of a musical ball during IV cannulation), and balloon group (25 children and inflating a balloon during IV cannulation).	Pain from IV cannulation in children	Pain intensity was measured by the Visual Analogue Scale (VAS)	The results showed that the lowest pain belonged to the balloon group, the deviation group and the control group, respectively
Bellien et al.2006 (20)	Analgesic Effect of Watching TV during Venipuncture	Sample number: 69 children 7 to 12 years old. Methods: Children were randomly divided into three groups of control, active distraction (Mothers distract children), and passive distraction (watching a cartoon by a child).	Pain from venipuncture in children	Pain intensity in children was measured by the OUCHER standard scale	The results showed that the technique of distraction by watching cartoons was more effective in reducing children's pain during venipuncture than the other two groups.
Asvanundet al. 2015 (21)	Effect of Audiovisual Eyeglasses During Local Anesthesia Injections in 5- To 8-year-old Children	Sample number: 49 children 5 to 8 years old. Methods: Children were randomly divided into two groups. The first group was injected anesthesia without using audio-visual glasses (AV) in the first visit and injected using these glasses in the second visit. The second group was the opposite of the first group	Pain due to local anesthesia injection in dental procedures	Pain intensity was measured using the Revised Face pain Scale (FPS-R) and The Face, Legs, Activity, Cry, CONSOL ability scale (FLACC), and heart rate was also measured in children.	The use of AV glasses during anesthesia injection reduces pain, anxiety and heart rate in both groups.
Oliveiraetal. 2017 (22)	Audiovisual Distraction for Pain Relief in Pediatric Inpatients: A Crossover Study	Sample number: 40 children 6 to 11 years old. Methods: The children were randomly divided into two groups that all children received the intervention factor (distraction by watching short animations) and acted as the control group. The first group received the intervention agent before or during the injection, and the next day the injection was performed without watching the animation, and in the second group, the opposite happened.	Pain from injection in children	Pain intensity was measured using the Revised Face pain Scale (FPS-R) and the Visual Analogue Scale (VAS)	In both groups, the amount of pain in the state of distraction and watching animation was less than the state without intervention, which shows that distraction effectively reduces the intensity of pain perception in hospitalized patients.

Polkki et al.2008 (23)	Imagery-Induced Relaxation in Children's Postoperative Pain Relief: A Randomized Pilot Study	Sample number: 60 children 8 to 12 years old. Methods: These children were randomly divided into two groups of control (30 children with standard care) and experimental group (30 children with the use of visual audio CDs)	Postoperative pain in children	Pain intensity was assessed using the Visual Analogue Scale (VAS) in three stages: before the intervention or standard care (stage 1), immediately after them (stage 2) and 1 hour after them (stage 3).	The amount of pain in the children in the experimental group was significantly lower than the children in the control group, which shows that the mental imagery technique can be effective in reducing postoperative pain in children, although its effect is short-lived.
Vagnoli et al. 2019 (24)	Relaxation-guided Imagery Reduces Perioperative Anxiety and Pain in Children:	Sample number: 60 children 6 to 12 years old Methods: Children were randomly divided into two groups of control (30 children receiving standard care) and the experimental group (30 children who underwent Relaxation-guided Imagery before anesthesia).	Perioperative Anxiety and postoperative Pain in children:	pain intensity was measured using the Revised Face pain Scale (FPS-R) and The Face, Legs, Activity, Cry, Consolability scale (FLACC) and anxiety was measured by the modified Yale Preoperative Anxiety Scale (mYPAS)	The results showed that there was a significant difference between control and experimental groups in terms of pain intensity and anxiety, and mental relaxation-guided Imagery reduced perioperative anxiety and postoperative pain.

Table 2. Results of the pharmacological therapies in pain management in children

Autor	subject	sample number and methods used	Type of pain	Method of measuring pain intensity	Results
Friday et al. 2009 (25)	Ibuprofen Provides Analgesia Equivalent to Acetaminophen-Codeine in the Treatment of Acute Pain in Children with Extremity Injuries:	Sample number: 66 children Methods: Acetaminophen codeine was prescribed for 32 children at a dose of 1 mg / kg and a maximum of 60 mg, and for 34 children ibuprofen at a dose of 10 mg / kg and a maximum of 400 mg.	Pain from acute injuries	Pain intensity was measured by the color analog scale (CAS) at the start and 20, 40, and 60 minutes after drug administration.	The results of this study indicated similar performance of acetaminophen-codeine and ibuprofen in reducing pain from acute injuries (fractures and dislocations) in children. On the other hand, the side effects of these drugs were shown to be minimal as follows: vomiting (one patient after acetaminophen-codeine), nausea (one patient after ibuprofen) and pruritus (one patient after acetaminophen-codeine)
Kashefi,Mirdamadi 2005 (26)	Preemptive Analgesia with Ibuprofen and Acetaminophen in Pediatric Lower Abdominal Surgery	Sample number: 75 children 3 to 12 years old. Methods: Children were randomly divided into three groups as follows: 25children with a prescribed dose of 20 mg/kg of ibuprofen, 25 children with a prescribed dose of 35 mg/kg of acetaminophen and 25 children with a placebo	Pain from abdominal surgery	Pain intensity and anxiety in children was measured by the OUCHER standard scale, 3 and 24 hours after the surgery	The results showed that the preoperative prescription of ibuprofen and acetaminophen could reduce anxiety and distress during the recovery period, in which there was no difference between the ibuprofen and acetaminophen groups. But in terms of pain intensity 3 and 24 hours after surgery, no significant difference was observed between the three groups
Dashtikhavidaki et al. 2018 (27)	Comparing the Effect of Acetaminophen Suppository before and after Tonsillectomy on Pain Severity in Children	Sample number: 100 children 5 to 15 years old. Methods: Children were randomly divided into two groups as follows. The first group (50 children: 28 boys and 22 girls) receiving acetaminophen suppository at a dose of 40 mg/kg before the surgery and the second group (50 children: 26 boys and 24 girls) receiving acetaminophen suppository at a dose of 40 mg/kg after the surgery	Pain from tonsillectomy	Pain intensity was measured using the Visual Analogue Scale (VAS), 1,2,6,12, and 24 hours after the surgery	The results showed that there was no significant difference between the groups in terms of gender, and on the other hand, the amount of pain in all hours after surgery in the first group compared to the second group showed a lower intensity, which indicates that The use of acetaminophen suppositories before tonsillectomy significantly controls postoperative pain.
Williams et al.2002 (28)	Pharmacogenetics of Codeine Metabolism in an Urban Population of Children and Its Implications for Analgesic Reliability	Sample number: 86 children were randomly divided into two groups. The first group with 43 children received a dose of 1.5 mg/kg of codeine and 1 mg/kg of diclofenac and the second group with 43 children received a dose of 0.15 mg/kg of morphine and 1 mg/ kg of diclofenac	Pain from tonsillectomy	Pain intensity was measured by self-report and pain measuring instruments	The results showed that most children needed analgesics again 2 and 4 hours after receiving codeine. On the other hand, 56% of children after using morphine and 29% of them after using codeine vomited and nauseated; Codeine was also shown to be less analgesic than morphine.
Yoonet al. 2008 (29)	The Effects and Safety of Dexibuprofen Compared with Ibuprofen in Febrile Children Caused by Upper Respiratory Tract Infection	Sample number: 255 children from 6 months to 14 years. Methods: These children were randomly divided into three groups. The first group: 86 children received 5 mg / kg ofdexibuprofen, the second group: 84 children received 7 mg / kg ofdexibuprofen and the third group 85 children received 10 mg / kg of ibuprofen. Lastly, 23 children were excluded from the study during three days due to reasons such as withdrawal, higher dose of these analgesics and their side effects, and the study was	Fever caused by an upper respiratory tract infection	Measuring children's fever	The results showed that there was no significant difference between the three groups in terms of controlling the severity and duration of fever and the side effects of the analgesics used. As a result, dexibuprofen was as effective as ibuprofen, and two 5 or 7 mg/kg doses of dexibuprofen instead of 10 mg/kg ibuprofen would be sufficient to control the fever associated with respiratory infection in children.

		conducted with 232 children.			
Choi et al. 2018 (30)	The antipyretic efficacy and safety of propacetamol compared with dexibuprofen in febrile children: a multicenter, randomized, double-blind, comparative, phase 3 clinical trial	Sample number: 263 children from 6 months to 14 years. Methods: Children were randomly divided into two groups of experimental (125 children with intravenous acetaminophen and oral placebo) and the control group (138 children with 100 ml of 0.9% sodium chloride solution intravenously without prostamol and oral dexibuprofen).	upper respiratory tract infection	Patients' fever was measured 30 minutes, 1, 1.5, 2, 3, 4, and 6 hours after using dexibuprofen and oral placebo.	The results showed that the fever in the experimental group was significantly lower up to 2 hours after prescription of prostamol and placebo. On the other hand, there was no significant difference between the two groups in terms of lowering body temperature during the 6-hour period of the experiment and also no side effects of drugs such as digestive problems, increased liver enzymes and decreased blood platelets was observed. As a result, intravenous acetaminophen may act as a safe and effective choice in children with respiratory infections and febrile fever, who are unable to take oral medications or need to control fever more quickly.
Kim et al. 2013 (31)	Dexibuprofen for Fever in Children with Upper Respiratory Tract Infection	Sample number: 260 children from 6 months to 14 years. Methods: These children were randomly divided into three groups; 1 or control (receiving 5 or 10 mg / kg ibuprofen), the second group (receiving 2.5 or 5 mg / kg dexibuprofen), and the third group (receiving 3.5 or 7 mg / kg dexibuprofen). Children with a body temperature below 38.5 ° C received lower doses of the drug	upper respiratory tract infection	fever in children was measured 4 hours after drug administration.	The results showed that there was a significant difference only between the control group and the second group in terms of changes in mean body temperature after 4 hours, and there was no significant difference between the groups in terms of side effects. As a result, a dose of 3.5 or 7 mg/kg of dexibuprofen is as effective as ibuprofen in treating fever due to upper respiratory tract infection in children.
Bahrololomi, Amrollahi2019 (32)	Effects of Acetaminophen and Ibuprofen on Pulpal Anaesthesia Immediately after Pulpectomy of Primary Maxillary Molars	Sample number: 60 children (22 boys and 38 girls) 5 to 9 years old. Methods: These children were randomly divided into three groups: group 1 or control (21 children and receiving placebo), group two (20 children receiving ibuprofen) and group three (19 children receiving acetaminophen).	pain from pulpectomy of primary maxillary molars	Pain intensity was measured using the Visual Analogue Scale (VAS)	The results showed that the use of ibuprofen and acetaminophen analgesics before Pulpectomy of Primary Maxillary Molars in children could reduce pain compared to the control group (placebo). Ibuprofen also showed less pain intensity than acetaminophen, but this difference was not statistically significant.
Baygin et al. 2011 (33)	Comparison of pre-emptive ibuprofen, paracetamol, and placebo administration in reducing post-operative pain in primary tooth extraction	Sample number: 45 children 6 to 12 years old. Methods: These children were randomly divided into three groups: group 1 or control (receiving placebo), group two (receiving ibuprofen) and group three (receiving acetaminophen).	Pain from dental extraction	Pain intensity was measured using the Visual Analogue Scale (VAS) and self-report during local anesthesia before and after dental extraction.	The results showed that the use of ibuprofen and acetaminophen analgesics could reduce the pain from dental extraction compared to the control group (placebo). In addition, the use of ibuprofen reduces pain for 15 minutes and 4 hours compared to acetaminophen.
Gazal et al. 2007 (34)	A Comparison of Paracetamol, Ibuprofen or Their Combination for Pain Relief Following Extractions in Children Under General Anaesthesia	201 children were randomly divided into 4 groups as follows: Group 1 or control (55 children and a dose of 15 mg/kg acetaminophen - the usual dose of acetaminophen), group 2 (48 children and a dose of 20 mg/kg acetaminophen - a high dose of acetaminophen), group 3 (47 children and a dose of 5 mg/kg ibuprofen), and group 4 (51 children receiving acetaminophen/profen combination at a dose of 15.5 mg /kg)	Pain from dental extraction	Pain intensity and anxiety were measured by the visual analog scale (VAS) before dental extraction, after anesthesia, and after 15 minutes.	The results showed that there was a significant decrease in the severity of pain and anxiety in both of the ibuprofen group and in the ibuprofen/acetaminophen combination group compared to the control group (usual dose of acetaminophen) in 15 minutes after tooth extraction. It has been shown that oral administration of ibuprofen only or in combination with acetaminophen is effective in reducing the pain of dental extraction in children.

DISCUSSION AND CONCLUSION

The aim of this study was to systematically Review the effective factors in pain management in children, focusing on pharmacological and non-pharmacological therapies. From a total of 1216 studies with similar topics to therapeutic and non-pharmacological methods of pain management in children, finally, 20 articles were selected for further review. By studying the articles related to the subject, it was found that the use of pharmacological and non-pharmacological strategies could reduce and relieve various types of pain in children. 10 studies examined non-pharmacological therapies through play-based distraction techniques, watching cartoons, using audio-visual glasses, and mental imagery, in order to relieve and reduce the pain from injections, venipuncture, surgery, burns and dental restorations in children[15-24] and 10 studies evaluated the effect of pharmacological therapies using non-narcotic analgesics such as acetaminophen, ibuprofen, and dexibuprofen and narcotic analgesics such as codeine and morphine in relieving pain caused by surgery, acute injuries, Upper respiratory infections and dental restorations in children[25].

One of the most important non-pharmacological methods in reducing pain in children is the distraction technique. distraction techniques such as making bubbles, counting, talking, music, watching TV, toys, and video games may be used by nurses or parents of children[35]. Studies show that non-pharmacological therapies may be used singly or as adjuncts to pharmacological therapies in the management of pain, anxiety, and pain-related anxiety with minimum risk of side effects[36,37]. Also, in studies

conducted by other researchers, the positive effects of various distraction techniques on reducing pain and anxiety in children have been observed[38-41]..

Studies related to pharmacological therapies could be reviewed in two parts of narcotic analgesics and non-narcotic analgesics.

Non-narcotic analgesics include Non-steroidal Anti-inflammatory drugs (NSAIDs), which have anti-inflammatory, analgesic, antipyretic, and antiplatelet properties[42]; They inhibit prostaglandin synthesis by acting on the enzyme cyclo-oxygenation[43,38]. The most important drugs in this class are salicylic acids (aspirin), acetic acids (ketorolac), and propionic acids (ibuprofen, naproxen and specific inhibitors of cyclooxygenase-2 (celecoxib)),among these, oral or intravenous ibuprofen is a common analgesic and antipyretic in children[42]. Acetaminophen is an analgesic for mild to moderate pain as well as an antipyretic. Acetaminophen has a central function and has no effect on the gastric mucosa or platelets[44]. In the present study, it was found that acetaminophen could be used due to limited side effects and high efficacy in relieving various pains in children.

Narcotic analgesics have been used for many years to relieve severe pain in all age groups. Major concerns about the use of narcotic analgesics in children include efficacy, safety, misuse, overdose, and accidental deaths[45,46,47]. Depending on the severity of the pain, narcotic and non-narcotic analgesics are the most common analgesics used in pain management in both children and adults[48]. Studies by other researchers have also shown the positive effects of analgesics in reducing pain and anxiety caused by diseases such as cancer, sore throat, headache, earache, and musculoskeletal pain in children, although their use is associated with side effects[49-52].

Although during this systematic review it was found that both pharmacological and non-pharmacological treatment methods are effective in relieving and reducing a wide range of pediatric diseases, due to the side effects of medications, doctors, nurses and parents are more inclined to use non-pharmacological methods in the management of children's pain, however the accurate and effective implementation of these methods is associated with problems and challenges, which indicates the need for further studies on the use of various non-pharmacological methods.

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