http:// ijp.mums.ac.ir
Review Article (Pages: 10635-10642)

The Effectiveness of Sedative and Non-pharmacological Premedication in Pediatric Anesthesia: A Review Article

Farzaneh Barkhordari Ahmadi[1], *Ghasem Sobhani[1], Alireza Abdulahzade Baghaee[2], Ahmad Ali Jalalinezhad[3], Bita Mirzaie Feiz Abadi[4]

[1]Department of Anesthesia, Faculty of Para-medicine, Hormozgan University of Medical Sciences, Bandar Abbas, Iran. [2]Anesthesiology Critical Care and Pain Management Research Center Hormozgan University of Medical Sciences Bandar Abbas, Iran. [3]Department of Physiology, Faculty of Medicine, Zabol University of Medical Sciences, Zabol, Iran. [4]MD, Fellowship of Psychosomatic Medicine, Mashhad University of Medical Science, Mashhad, Iran.

Abstract

Many children who undergo surgery experience significant perioperative anxiety. Preoperative anxiety can prolong induction of anesthesia and postoperative recovery, increase the risk of postoperative delirium, increase pain, and increase analgesic use. Researchers are looking for ways to treat or prevent preoperative anxiety in children and possibly reduce its negative effects after surgery, such interventions include non-pharmacological and premedication interventions with sedation drug prior to surgery. Pretreatment, however, is often performed for children but it is not clear what the best medicine is and how it is prescribed. Among the ways to reduce children's anxiety, the anesthesiologist can use a combination of methods to achieve the best results.

Key Words: Anesthesia, Effect, Non-pharmacological, Pediatric, Premedication.

*Please cite this article as: Barkhordari Ahmadi F, Sobhani Gh, Abdulahzade Baghaee A, Jalalinezhad AA, Mirzaie Feiz Abadi B. The Effectiveness of Sedative and Non-Pharmacological Premedication in Pediatric Anesthesia: A Review Article. Int J Pediatr 2019; 7(12): 10635-642. DOI: **10.22038/ijp.2019.44668.3692**

Corresponding Author:

Ghasem Sobhani, Department of Anesthesia, Faculty of Para-medicine, Hormozgan University of Medical Sciences, Bandar Abbas, Iran.

Email: ghasemsobhani@yahoo.com

Received date: Aug.22, 2019; Accepted date: Nov. 22, 2019

1- INTRODUCTION

Every year, many children undergo surgery that requires anesthesia, which will be stressful for them and their parents in the pre-operative room before surgery. These stresses for pediatric patients can be due to anticipation of separation from parents, helplessness, facing the strange environment and fear of pain and anesthesia, according to the observations of studies, anesthesia is the most stressful procedure for children during the entire period prior to surgery (1). Preoperative stress and anxiety, which is a feeling of tension, worry and nervousness, can be associated with crying, agitation, anger, behavioral and verbal unrest, uncontrollable urination (2, 3). Preoperative anxiety can prolong induction of anesthesia and postoperative recovery, increase the risk of postoperative delirium, increase pain, and increase analgesic use (4). Preoperative anxiety is associated with some maladaptive behaviors (e.g., sleep disturbances, eating disorders, separation anxiety, nightmares and behavioral conflict with parents) that impair the child's daily functioning and it can have a negative impact on children's response to future medical care (2, 4). Since about 60% of children experience anxiety before surgery (5), and because of the problems that cause anxiety, researchers are looking for ways to treat or prevent preoperative anxiety in children and possibly reduce its negative effects after surgery, such interventions include non-pharmacological and premedication interventions with sedation drug prior to surgery (6). The purpose of this review was to identify the existing research on the various modes of intervention for reducing anxiety in pediatric anesthesia.

2- MATERIALS AND METHODS

We conducted an extensive search on online databases (Medline (via PubMed), EMBASE, Web of Science, Scopus, Cochrane Library, and CINAHL) from inception until Mar 2019. No language limitations were undertaken. Two authors independently searched titles and abstracts of articles and then each relevant article was reviewed in detail. Afterwards, the research team designed a form to include extracted information.

3- RESULTS

3-1. Non-pharmacological interventions

Being in the operating room and induction of the child's anesthesia can be stressful, using non-pharmacological methods to reduce anxiety and co-operate with the treatment team may prevent the side effects of preoperative sedation (7). Various non-pharmacological strategies to reduce pre-anesthetic stress in children can be broadly categorized as: Psychological (cognitive or behavioral); Environmental; Equipment modification; Social interventions, including communication (8). Interventions that are more important and more researched are entered in the article, however other non-pharmacological interventions such as acupuncture, hypnosis, behavioral interventions and animal-assisted therapy have also been performed to reduce children's anxiety before inducing anesthesia (9). The following is an overview of more commonly used interventions that are less costly and require less time.

3-1-1. Parental presence at the time of induction of anesthesia in children

Parental presence during induction of anesthesia has also been used to minimize anxiety. For many, parental presence intentionally reduces anxiety and improves quality of anesthesia induction (10). However, some studies have shown parental presence has an undesirable effect (11) and, in some cases, can actually increase anxiety (12). In some studies, the level of anxiety in children was not

significantly correlated with the presence or absence of parents (13, 14), this may be because parental stress affects children, which means that in studies of parental presence during anesthesia induction, their level of anxiety should be examined in the intervention. The effect of parental presence at the time of anesthesia may be influenced by different cultures (15). Parental authorization may be restricted by operating room regulations and by the collaboration of anesthesia team.

3-1-2. Interventions that involve children, such as video games, video clip

The use of video games and video clips are potential non-pharmacological interventions that have been shown to be effective in children, many studies have used digital interventions for pure distraction to reduce anxiety (16, 17). However, the approach being investigated by new research focuses on achieving behavior change and reducing anxiety by educating children in a fun and engaging way through experiential learning and game which can not only be cheap and accessible, but also can transfer knowledge about the anesthesia and surgery process. Interactive and engaging, can lead to behavioral changes in children (18).

Studies have also shown the positive impact of watching animated cartoons and using familiar children's toys on preoperative anxiety in preschool children (19). Generally, involvement in an interesting game can reduce pre-operative anxiety in preschool children and improve their anesthesia compliance (20, 21). This method is sometimes accompanied by other interventions and can be more effective in reducing anxiety. As new studies have shown preoperative anxiety was low in cases where electronic devices were used for distraction with parental presence at time of anesthesia (22).

3-1-3. Music Therapy

Listening to music (a safe and low-cost intervention) can make it easier for children to be separated from their parents and enter the operating room. Some studies show that music interventions in children undergoing surgery have a statistically significant effect on reducing anxiety and distress and children in the operating room listening to music needed less pain relief and reported less pain after surgery (23). One study found that audiovisual presentations may be more effective in reducing children's anxiety than auditory presentations, but both methods have the same effect on postoperative behavioral changes (24). Given the safety, feasibility and low cost of music therapy, it can be used as a complementary treatment in the control of pain and anxiety, especially in local anesthesia (25-27).

3-1-4. Lown doctors

Clowns or clown doctors significantly lessened children’s anxiety in the operating/induction room. However, this reduction with clowns/clown doctors present was not seen in measuring anxiety, also at mask introduction (28, 29). In clown doctors' interventions, children have significantly less anxiety during induction of anesthesia and for hospitalization, medical procedures and illness and its consequences. Lastly, in relation to co-operation, studies reported children in the clown group to have significantly increased affective valence, but lower arousal (30); and in another study, clowns are effective in reducing the duration of crying as a pain-related issue[1]. Clown health care providers today are an integral part of the health system, and their numbers are increasing every day (**Error! Bookmark not defined.**).

3-2. Sedative premedication

Since untreated children's anxiety can lead to problems such as lack of co-operation, hard induction, increased postoperative

pain, need for more pain relief and behavioral problems, despite many advances in non-pharmacological interventions, practitioners still depend on sedative premedication (32, 33). Premedication is often used for children today, but the best medicine and the best way to prescribe it are debated (34). Oral prescription is the most commonly used route, although it reduces access to bioavailability. Other methods of prescribing sedative medications include the musculoskeletal method, which is an aggressive and painful method for children and should be avoided if possible. Another method is transmucosal which can be used by sublingual, intranasal and buccal and since the mucosa has good blood supply, better drug absorption is achieved. There is also an intra-rectal procedure that is often painful and difficult to use in older children, and in young children the medications given in this way can be easily excreted (5, 35). The most widely used sedative drugs are reviewed in this article.

3-2-1. Midazolam

Midazolam is a short-acting benzodiazepine and gamma-Aminobutyric acid receptor inhibitor (36). Midazolam, a very common drug in the premedication, has anti-anxiety, sedative, anticonvulsant and skeletal muscle relaxant activity, rapid onset and a short duration of action and it reduces postoperative vomiting (5, 37). Due to its rapid onset and recovery, it is one of the top premedications to obtain conscious sedation. Although the elimination half-life of midazolam in toddlers and pre-school children is 1 to 2 hours, this time in infancy is not significantly longer (38). Midazolam administration is generally intravenous, as with other oral, rectal, subcutaneous and buccal routes of administration, delaying the onset of efficacy and high interpersonal variability in onset of efficacy (39). Since the intravenous method is invasive, in children, the drug can be used transmucosal, which is well absorbed due to extensive blood supply to the mucosal tissue. Nasolam is a new nasal midazolam formulation that does not damage the nasal tissue and provides insufficient volume for full absorption of the nasal mucosa, yet it contains sufficient concentrations of midazolam to produce systemic midazolam concentrations (40). Despite the benefits of midazolam there are other medications used today, this is because of its adverse effects, from an ideal premedication drug, which include restlessness, adverse cognitive reactions, post-operative behavioral changes, amnesia, confusion and sudden respiratory distress (41).

3-2-2. Ketamine

Ketamine, an *N*-methyl-D-aspartate (NMDA) antagonist, is another popular drug that has a sedative and analgesic effect (42). However, its side effects, such as excessive saliva, and nausea, vomiting, hallucinations, nystagmus, dizziness, blurred vision and postoperative mental disorders limit its use (43). A combination of dexmedetomidine and ketamine can reduce the cardiovascular adverse effects and postoperative delirium incidence produced by ketamine (44). The pharmacokinetics of ketamine have been studied in analgesic doses after intravenous, intramuscular and oral administration, with only 17% of the drug being absorbed in the oral administration, and this method is not suitable for ketamine use, when administered orally, as a single pretreatment, it produces side effects such as saliva and anxiety (45). Studies have also investigated the use of the drug combination, results showed that ketamine plus midazolam has a better analgesic quality, easier separation from parents and better acceptance of the face mask (46).

3-2-3. Dexmedetomidine

Dexmedetomidine α-2 adrenergic receptor agonist, is increasingly used in the pediatric population that provides sedation, analgesia, and anxiolytic effects without causing significant respiratory depression at the clinically approved dosage (47). As a result, dexmedetomidine is used to reduce postoperative negative behaviors including emergency agitation and aggression. The use of dexmedetomidine in children undergoing anesthesia results in a favorable recovery with reduced postoperative pain and agitation, with no adverse postoperative hemodynamic effects (48), it reduces blood pressure and heart rate in a dose-dependent manner (49).Studies have shown that dexmedetomidine is superior to midazolam because it results in enhanced preoperative sedation relief and reduced postoperative pain (5), and have also shown that nebulized dexmedetomidine premedication had more satisfactory sedation scores at the time of admission to the OR, higher acceptance of the medication, and shorter recovery times after sevoflurane anaesthesia and lower incidence of postoperative agitation than those who received another drug like nebulized ketamine or midazolam (50). However, dexmedetomidine has not been approved for use in children in some countries (54).

3-2-4. Clonidine

In 1993, the first report on the use of oral clonidine administration in children reported that oral clonidine administration in a dose-dependent manner prior to induction of anesthesia improved sedation, better parental separation quality, and higher mask acceptance and side effects such as bradycardia, hypertension or respiratory depression have not been observed (51).
In pediatric surgical patients, the sedative and anxiolytic effect of oral clonidine has been found to produce similar degrees of sedative and anxiolytic effect and also better drug acceptance score than oral midazolam (52, 53), although some studies have shown the opposite (54). Clonidine reduces the incidence of postoperative confusion in children younger than 5 years compared to midazolam (43). Pre-oral administration of clonidine in children produces similar or even better relaxation compared to diazepam. In addition, administration of clonidine reduces the need for an inducible factor and reduces stress response induced by tracheal intubation, postoperative pain relief and shivering, clonidine, unlike midazolam, has no effect on respiration (55).

4- DISCUSSION

Anesthesia and hospitalization can be stressful for children and their parents, and are associated with pain, helplessness, fear, and boredom. Given the negative psychological and clinical consequences of preoperative anxiety, identifying patients at high risk is a clinically significant opportunity to improve their surgical experience and outcomes. To reduce the incidence of preoperative anxiety in children, anesthesiologists have used a number of prevention strategies including sedation, non-pharmacological interventions to induce anesthesia. Pretreatment, however, is often performed for children but it is not clear what the best medicine is and how it is prescribed. Some interventions are more common and some less common. The use of sedatives is criticized for its side effects, such as the effect on the airway, the impact on patient recovery, or the effect of patient behavior after anesthesia (5, 32-55). On the other hand, some studies use non-pharmacological methods such as parenting presence, music therapy, and clown doctors, etc. that may be cost effective but time consuming (7-30). There are several ways that are now available to allow patients to control pain and anxiety, all healthcare professionals must be aware of all the anxiolytic options available. The goal of anesthesiologists is to reduce the

incidence of anxiety and improve the quality of postoperative status of children with the help of various interventions. Sometimes using a combination of both pharmacological and non-pharmacological methods can be a more appropriate choice. The positive effect of some of these combined approaches have been considered like the presence of parents at the time of induction of anesthesia and the use of sedatives such as midazolam.

5- CONCLUSION

Among the ways to reduce children's anxiety, the anesthesiologist can use a combination of methods (such as sedation and non-pharmacological interventions) to achieve the best results, depending on the type of anesthesia, the extent of surgery, the history of previous anesthesia and hospital facilities and costs.

6- CONFLICT OF INTEREST: None.

7- REFERENCES

1. Hasanpour M TM, Aein F, Yadegarfar G. The effects of two non-pharmacologic pain management methods for intramuscular injection pain in children. Acute pain 2006; 8(1):7-12.

2. Kaheni S, Rezai MS, Bagheri-Nesami M, Goudarzian AH. The Effect of Distraction Technique on the Pain of Dressing Change in 3-6 Year-old Children. International Journal of Pediatrics 2016; 4(4):1603-10.

3. Groß M, Warschburger P. Evaluation of a cognitive-behavioral pain management program for children with chronic abdominal pain: a randomized controlled study. Int J Behav Med 2013; 20(3):434-43.

4. Turk D MR. Hand book of pain assessment. 2 ed: New York: Gulford Press; 2001.

5. American academy of pediatrics. Committee on psychosocial aspects of Child and family Health. Task force on pain in infants Children and adolescents a. The assessment and management of acute pain in infants, children and adolescents. Pediatric 2001;108(3):793-7.

6. Wong DL HM, Wilson D, Winkelstein ML, Kline NE. Wong's nursing care of infants and children. 7th ed: Louis: Mosby; 2003.

7. C VHV. Nurses' perceptions of children's pain: a pilot study of cognitive representations. J Pain Symptom Manage 2007; 33(3):290-301.

8. Alavi A ZA, Abdi Yazdan Z, Nam Nabati M. The comparison of distraction and EMLA cream effects on pain intensity due to intravenous catheters in 5-12 years old Thalassemic children. Shahrekord University of Medical Sciences Journal 2005; 7(3):15-9.

9. Genik LM, McMurtry CM, Breau LM. Observer perceptions of pain in children with cognitive impairments: vignette development and validation. Pain Manag 2015; 5(6):425-34.

10. Spacek A. Modern concepts of acute and chronic pain management. Biomed Pharmacother 2006; 60(4):329-35.

11. M P. Effect of oral glucose solution on some physiological and behavioral indices of pain due to blood sampling in hospitalized neonates in Rasht hospital: Nursing Faculty of Guilan University of Medical Sciences; 2006.

12. Lee EK, Yeo Y. Relaxation practice for health in the United States: findings from the National Health Interview Survey. J Holist Nurs 2013; 31(2):139-48.

13. A G. Primary health care of infants. Children and adolescents: New York: Mosby; 2002.

14. Alavi A ZA, Abde Yazdan Z, Namnabat M. Study of distraction and Emla cream on the pain intensity catheter insertion in children with thalassemic age 5- 8 years old. Shahrekord Uni Med Sci J 2005; 7(3):9-15.

15. Uman LS CC, McGrath PJ, Kisely S. Psychological interventions for needlerelated procedural pain and distress in children and adolescents. Cochrane Database Syst Rev 2006; 18(4):CD005179.

16. Migdal M C-PE, Vause E, Henry E, Lazar J. Rapid, needle-free delivery of lidocaine for reducing the pain of venipuncture

among pediatric subjects. Pediatric 2005; 115(4):393-8.

17. Wang ZX SL, Chen AP. The efficacy of non-pharmacological methods of pain management in school-age children receiving venepuncture in a paediatric department: a randomized controlled trial of audiovisual distraction and routine psychological intervention. Swiss Med Wkly 2008; 138(39-40):579-84.

18. Bagheri-Nesami M, Mohseni-Bandpei MA, Shayesteh-Azar M. The effect of Benson relaxation technique on rheumatoid arthritis patients. Int J Nurs Pract 2006; 12: 214-19.

19. Masoumeh Bagheri-Nesam, Fatemeh Espahbodi, Attieh Nikkhah, Seyed Afshin Shorofi, Jamshid Yazdani Charati. The effects of lavender aromatherapy on pain following needle insertion into a fistula in hemodialysis patients. Complement Ther Clin Pract 2014; 20(1):1-4.

20. Heidari Gorji MA, Bagheri Nesami M, Ayyasi M, Ghafari R, Yazdani J.Comparison of Ice Packs Application and RelaxationTherapy in Pain Reduction during Chest Tube Removal Following Cardiac Surgery. N Am J Med Sci 2014; 6(1):19-24.

21. Masoumeh Bagheri Nesami, Nahid ZargaR, Afshin Gholipour Baradari The Effect of Foot Reflexology Massage on Pain and Fatigue of Patients undergoing Coronary Artery Bypass Graft. Journal of Mazandaran University of Medical Sciences 2012; 22(92):51-62.

22. Alavi A, Namnabat M, Abde Yazdan Z, Parvin N, Akbari N, Samipour V, et al. Pediatric pain management by nurses in educational hospitals of Shahrekord in 2006. Shahrekord University of Medical Sciences Journal 2008; 10(2):66-71. [Persian]

23. Yoo H KS, Hur HK, Kim HS. The effects of an animation distraction intervention on pain response of preschool children during venipuncture. Appl Nurs Res.2011; 24(2): 94-100.

24. Gupta D ea. An evaluation of efficacy of balloon inflation on venous cannulation pain in children: a prospective, randomized, controlled study. Anesth Analg 2006; 102(5):1372-5.

25. Press J GY, Maimon M, Gonen A, Goldman V, Buskila D. Effects of active distraction on pain of children undergoing venipuncture: Who benefits from it? The Pain Clinic 2003; 15(3):261-9.

26. LL C. Comparative study of distraction versus topical anesthesia for pediatric pain management during immunizations. Health Psychol 1999; 18(6):591.

27. Fowler-Kerry S, Lander JR. Management of injection pain in children. Pain 1987; 30(2):169-75.

28. Thrane SE, Wanless S, Cohen SM, Danford CA. The Assessment and Non-Pharmacologic Treatment of Procedural Pain from Infancy to School Age through a Developmental Lens: A Synthesis of Evidence with Recommendations. J Pediatr Nurs 2016; 31(1):23-32.

29. Kleiber C, McCarthy AM. Evaluating instruments for a study on children's responses to a painful procedure when parents are distraction coaches. J Pediatr Nurs 2006; 21(2):99-107.

30. Pellino TA, Gordon DB, Engelke ZK, Busse KL, Collins MA, Silver CE, Norcross NJ. Use of nonpharmacologic interventions for pain and anxiety after total hip and total knee arthroplasty. Orthop Nurs 2005; 24(3):182-90.

31. Association GAotWM. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. J Am Coll Dent 2014; 81(3):14.

32. Diette GB, Lechtzin N, Haponik E, Devrotes A, Rubin HR.Distraction therapy with nature sights and sounds reduces pain during flexible bronchoscopy: a complementary approach to routine analgesia. Chest 2003; 123(3):941-8.

33. Rice BA, Nelson C. Safety in the pediatric ICU: the key to quality outcomes. Crit Care Nurs Clin North Am 2005; 17(4):431-40.

34. Kuttner L, Bowman M, Teasdale M.Psychological treatment of distress, pain, and anxiety for young children with cancer. J Dev Behav Pediatr 1988; 9(6):374-81.

35. Vosoghi N, Chehrzad M, Abotalebi G, Atrkar Roshan Z. Effects of Distraction on Physiologic Indices and Pain Intensity in children aged 3-6 Undergoing IV Injection. HAYAT 2011; 16 (3 and 4):39-47. [Persian]

36. Chiang LC, Ma WF, Huang JL, Tseng LF, Hsueh KC. Effect of relaxation-breathing training on anxiety and asthma signs/symptoms of children with moderate-to-severe asthma: a randomized controlled trial. Int J Nurs Stud 2009; 46(8):1061-70.

37. Kleiber C, Harper DC. Effects of distraction on children's pain and distress during medical procedures: a meta-analysis.Nurs Res 1999; 48(1):44-9.

38. Landolt MA, Marti D, Widmer J, Meuli M.Does cartoon movie distraction decrease burned children's pain behavior? J Burn Care Rehabil 2002; 23(1):61-5.

39. Windich-Biermeier A, Sjoberg I, Dale JC, Eshelman D, Guzzetta CE. Effects of distraction on pain, fear, and distress during venous port access and venipuncture in children and adolescents with cancer. J Pediatr Oncol Nurs 2007; 24(1):8-19.

40. Wang ZX, Sun LH, Chen AP. The efficacy of non-pharmacological methods of pain management in school age children receiving venipuncture in a pediatric department: A randomized controlled trial of audiovisual distraction and routine psychological intervention. Swiss Med Wkly 2008; 138(39–40):579–84.

41. Blount RL, Zempsky WT, Jaaniste T, Evans S, Cohen LL, Devine KA, et al. Management of pediatric pain and distress due to medical procedures. In M.C. Roberts & R.G.Steele (Eds.), Handbook of Pediatric Psychology. New York: Guilford Press; 2009.