

Comparing the Effect of Acupressure and Oral Midazolam on Controlling Preoperative Anxiety in Children: A Randomized Trial

Alireza Ebrahimsoltani¹, Mehrdad Goudarzi¹, Anahid Maleki¹, Bita Malekianzadeh^{2*}

¹Children's Medical Center, Tehran University of Medical Sciences, Tehran, Iran.

²Department of Anesthesiology, Tehran University of Medical Sciences, Tehran, Iran.

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ABSTRACT

Background: Preoperative anxiety in children is a common problem that can affect the anesthesia and postoperative period. Numerous methods, mainly pharmacological ones, have been used for controlling preoperative stress. Acupressure is a simple, noninvasive, and cost-effective method that has been used as a perioperative medicine for controlling pain or preventing postoperative nausea and vomiting. The present study aimed to comparatively investigate the effect of acupressure and oral midazolam on preoperative anxiety control.

Methods: 76 patients were randomly included in the study before surgery. Whereas in one group, 0.5 mg/kg oral midazolam was prescribed 15 minutes before the induction, in another group, acupressure of EXHN-3 point was applied for 15 minutes. In both groups, the patients' separation anxiety level, Ramsay score, recovery length, and RN satisfaction factor were recorded and compared.

Results: Children aged 1–7 years received either oral midazolam or acupressure. Although the children in the midazolam group had lower rates of preoperative anxiety and showed easier separation from their parents, the difference was not statistically significant ($P=0.076$). Ramsay sedation scale, was compared in the two groups. The overall difference was not statistically significant. The satisfaction of the PACU nurse was recorded using a 4-point scale. The two groups were statistically comparable in this regard ($P=0.155$). The only variable with a significant difference between the two groups was the mean recovery time, which was significantly shorter in acupressure group ($P<0.001$).

Conclusion: Acupressure can reduce preoperative anxiety in children; however, this effect is less than the effect of oral midazolam.

Introduction

Preoperative anxiety in children is a common problem which not only causes the child's and the parent's disturbance, but also increases the perioperative complications such as emergence agitation, postoperative pain, and airway complication. Numerous methods, mainly pharmacological ones, have been used to manage anxiety. A simple, cost-effective, and less

complicated method can be beneficial in this regard [1]. Complementary and non-pharmacological therapies have played a leading role in caring, preventing, and treating the patients [2]. Acupressure is one of the well-known methods that act by the meridians.

Acupressure that has been employed in various treatment and prevention cases is applied by pressure on acupoints or reflex areas. It is performed by activating acupoints using the fingers or hand-held devices. Meridians are connected to various body organs and

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*Corresponding author.

E-mail address: malekian.bit@yahoo.com

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tissues. There are different theories about the acupressure mechanism of action. According to Gate Control Theory, the application of acupressure to specific points leads to the release of pleasant impulses at a rate 4 times faster than the painful stimuli triggering the brain. As a result, slower pain messages are blocked. Acupoints stimulation triggers complex neurohormonal responses and activates hypothalamic-pituitary adrenocortical axis. As a result, cortisol secretion and relaxation increase. This stimulation also improves the transmission of endorphins and serotonin to the brain and specific organs through nerves and meridians [2-3]. Acupressure and massage are noninvasive methods that had been effective in relieving procedural pain in neonates, children, and addressing multimodal analgesia [4]. Acupressure has been effective in decreasing myopia progression and insomnia in children [5-7]. Additionally, acupressure has positively affected nausea and vomiting prophylaxis and treatment in leukemic patients [8-9]. The performance of acupressure and acupuncture is based on acupoint activation across the meridians. Acupressure and acupuncture methods have used in perioperative period for several purposes. The previous studies demonstrated the effect of acupressure on preoperative anxiety in tonsillectomy and dental procedures in children [10-11]. However, few studies have been conducted on children. In this study, acupressure was compared to the most common drug for preoperative sedation, oral midazolam, in children.

Methods

Trial design

This study is a randomized double blind controlled trial. Ethic committee (IR.TUMS.CHMC.REC.1398.132) and Iranian Registry of Clinical Trials (IRCT) approval (IRCT20201126049500N20) were received. ASA (American Society of Anesthesia) I, II patients aged 1-7 years candidates for inguinal hernia surgery, were included. Informed consent was obtained from the patients' parents. 76 patients were randomly assigned to two groups: midazolam and acupressure. The control group, the group which no intervention, was not considered in this study. Because it isn't ethical to don't any intervention for preoperative stress reduction in children.

Participants

76 patients aged 1-7 years candidate for inguinal hernia surgery were included. All of them were ASA (American Society of Anesthesia) I, II, without any history of psychologic or mental disorders, ADHD (attention deficit hyperactivity disorder), seizure and sedative or analgesic consumption. Location of the study was day care ward and operating room of Children Medical Center.

Interventions

The patients were randomly allocated in two groups. In midazolam group, the patients received 0.5 mg/kg midazolam syrup 15 minutes before the induction. The parents of the patients in acupressure group were trained to apply pressure on EXHN-3 point (an acupoint located between the eyebrow) for 15 minutes. This training was done by the researcher. The patients' separation anxiety level and Ramsay sedation score were evaluated upon entering the operating room. Inhalation induction was performed for all patients and fentanyl 1µg/kg was injected. The study was double-blind. Ramsay score, separation anxiety, recovery length and RN satisfaction factor in PACU were evaluated by a nurse who did not know anything about the grouping of the patients. Randomization was performed by blocking method.

Outcomes

Primary outcomes: the patients' separation anxiety level and Ramsay sedation score when the patient entering to operating room.

Secondary outcomes: mean recovery time and RN satisfaction factor in the recovery.

Sample size

The sample size was calculated using the Andrew Fisher formula. Confidence interval:2 and confidence level: 95%. it was estimated 77 cases.

Randomization

The samples were identified by randomization (restricted randomization) block method with 6 blocks and using a random number table of Random Allocation Software. The random tool is the random sequence generation software version 2.0, Allocation concealment was used to execute random sequences on participants. Each random sequence was recorded on a card and the cards were sealed in opaque envelopes. In order to maintain a random sequence, the envelopes were numbered in the same way on the outer surface, and finally the letter envelopes were glued and placed in a box., respectively. Registration of participants based on the order of entry of eligible participants into the study, one of the envelopes of the letter was opened in order and the assigned group of the participant is revealed.

The study was double-blind. Ramsay score, separation anxiety, recovery length and RN satisfaction factor in PACU were evaluated by a nurse who did not know anything about the grouping of the patients.

Statistical analysis was done using simple t-test and significant difference between variables in two groups was determined with P value<0.05.

Results

A total of 76 children aged 1–7 years (60 boys and 16 girls; mean [±SD] age, 4.44±1.17 years) with ASA status I, II that underwent elective inguinal hernia repair were

randomly allocated to receive either oral midazolam (36 children) or acupressure (40 children). The patients' demographic characteristics, i.e., gender, age, and weight were similar across the two groups. The demographic and clinical characteristics of both groups are compared in (Table 1).

The children in the midazolam group had lower rates of preoperative anxiety and showed easier separation from their parents, but the difference did not reach the significance level (22.8% vs. 50%, $P=0.076$). Sedation levels, assessed by the Ramsay sedation scale, were compared in the two groups. The patients in the acupressure group reached the sedation levels of 1 (agitated or restless, or both) and 2 (co-operative,

oriented, and tranquil). However, sedation levels of 3 (only responds to commands) and 4 (exhibits brisk response to light glabellar tap or loud auditory stimulus) were merely observed in the midazolam group. The overall difference was not statistically significant ($P=0.137$). The satisfaction of the PACU nurse was recorded using a 4-point scale. Although PACU nurses were more satisfied with the recovery of children in the midazolam group, the two groups were statistically comparable in this regard ($P=0.155$). The only variable with a significant difference level in the two groups was the mean recovery time, which was noticeably shorter in the acupressure group ($P<0.001$).

Table 1- The patients demographic and clinical characteristics

	Midazolam (n = 36)	Acupressure (n = 40)	P value
Gender, n (%)			
Boys	28(78.8%)	32(80%)	0.999
Girls	8(21.2%)	8(20%)	
Age (year), mean±SD	4.44±1.19	4.45±1.19	0.989
Weight (kg), mean±SD	18.8±4.7	18.25±3.97	0.652
Preoperative anxiety state, n(%)			
Calm	28(77.8%)	20(50%)	0.076
Anxious	8(22.2%)	20(50%)	
Levels of sedation, n(%)			
Level 1	8(22.2%)	20(50%)	0.137
Level 2	22(61.1%)	20(50%)	
Level 3	4(11.1%)	0(0%)	
Level 4	2(5.6%)	0(0%)	
Nurse's satisfaction level, n(%)			
Very dissatisfied	4(11.1%)	14(35%)	0.155
Somewhat dissatisfied	4(11.1%)	6(15%)	
Somewhat satisfied	12(33.3%)	14(35%)	
Very satisfied	16(44.4%)	6(15%)	
Recovery time (min), mean±SD	14.88±2.32	11.9±2.46	<0.001

Discussion

Midazolam, a benzodiazepine, is a well-known effective anxiolysis that could be effectively used as a preoperative medicine in both children and adults. The preoperative anxiolysis effect of midazolam has been approved in the literature. Midazolam enjoys the faster onset of sedation, higher sedation score, and easier separation compared to other sedative drugs such as clonidine and dexmedetomidine. However, in some cases, prolonged recovery time, excessive sedation in young children, and paradoxical reaction could be observed [12-13]. Acupressure, the noninvasive form of acupuncture, has been extensively used due to its noninvasiveness and absence of side effects. The present study is the first clinical trial that compared the sedative effect of acupressure with midazolam in children. Most of the patients in midazolam group were calm without any separation anxiety. Half of the patients in the acupressure group were relaxed and did not experience

separation anxiety. However, the difference between the two group was insignificant. This indicated that the effect of midazolam was more significant than acupressure. In most of the previous studies, the effect of anxiolysis acupressure was compared to the control group (not another drug). In evaluation of the preoperative sedation score, the acupressure group was more anxious and had a lower Ramsay score compared to the midazolam group, but this difference was not statistically significant. In adults, the effectiveness of acupressure in preoperative anxiety has been shown in cesarean patients and reduction of preoperative parental anxiety [14-16]. Acupressure on Yintang point (Ex-HN) has been demonstrated as effective in the preoperative anxiety in tonsillectomy, endoscopy, and dental operation [10-11, 17]. For reducing venipuncture pain in children, acupressure is as effective as topical anesthesia [18-19]. Furthermore, the effect of acupressure on post tonsillectomy pain in adolescents has been addressed in the literature [20]. In neonates, it is effective on lancing blood sample pain [21]. Acupuncture and acupressure

had anxiolysis effects on preoperative anxiety in a preliminary review, but more comprehensive studies are required. The present study has represented the preoperative acupressure-based anxiolysis effect on children, but this effect is less than the effect of oral midazolam. The molecular mechanism of acupressure anxiolysis effect is not clearly pinpointed. Yintang point(Ex-HN3), an acupoint located between the eyebrows, is used for the reduction of anxiety [22]. A number of transmitters and modulators including β endorphin, serotonin, substance P, interleukins, and calcitonin gene-related peptide are released via acupuncture and relevant techniques. In perioperative instances, using acupuncture can not only reduce postoperative nausea, vomiting, anxiety, and analgesic consumption, but also enhance the post-surgery recovery (ERAS) [23-24]. Several studies have been done in emotional freedom techniques (EFT) that combine different methods in this area such as cognitive therapy with acupressure. Recently, the role of noncoding ribonucleic acid(RNA) molecules as the modulator of gene expression has been acknowledged in EFT [25]. Recovery length was longer in the midazolam group. The limitations of the present study are lack of control group, no comparison of vital signs and the duration effect in the two groups. The other is small sample size. Future studies with larger sample size for examining the effect of acupressure anxiolysis and its molecular mechanisms are needed. Acupressure is a simple and noninvasive method that could effectively control stress in children.

Conclusion

Acupressure on Yintang point has anxiolysis effect that could relieve stress in children in the preoperative period. However, this effect was less significant than oral midazolam. Acupressure is a simple, noninvasive and cost-effective method that can be useful for controlling preoperative anxiety in children.

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