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Oral clonidine premedication reduces postoperative pain in children

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ABSTRACT

Preoperative anxiety and postoperative pain are great concern to parents. The objectives of this experiment were to evaluate and compare postoperative effect of oral clonidine on surgical pain with Mepridine analgesia in children. We also compared the influence of these two different medication regimens on hemodynamic status and oxygen saturation (SPO2) of patients during and after surgery. This double-blind, prospective, randomized study, was performed on 44 children, ASA status I or II, aged between 1 and 3 years, that underwent elective herniotomy. The patient was elected randomly into two groups: group C (Clonidine) (n = 22) received clonidine 4 µg/kg given orally 60 min prior to anesthesia induction and, group M (Mepridine) (n = 22) received mepridine 0.5 mg/kg after surgery. Degree of Postoperative analgesiawas assessedby using FLACC scalesystem .Preoperative oral clonidine at 4µg/kg reduced postoperative pain score and requirement for supplementary analgesic in children compared with postoperative Mepridine as analgesia. The results showed no significant difference on hemodynamic status and oxygen saturation (SPO2) between the two groups .According to the hypotensive effects of clonidine, not significant difference in blood pressure and heart rate were observed in the two groups.

Key words: Clonidine, Meperidine, postoperative analgesia

INTRODUCTION

Preoperative anxiety and postoperative pain aregreat concern to parents and anesthesiologists, If they are not controlled by appropriate medication, these can cause maladaptive behavior in the postoperative period [1]. A multimodal approach consisting of sedative drugs, parental presence, play therapy, familiar environment and effective pain therapy is necessary to reduce preoperative anxiety and postoperative pain [2,3]. Recently, drugs such as the alpha 2-agonists have emerged as alternatives for premedication in pediatric anesthesia. Clonidine, a selective centrally acting partial alpha 2-agonist, has been reported to improve preoperative hemodynamic stability, provide analgesic properties, and decrease anesthetic requirements [4-6]. However, the reports about administrating dosage of clonidine have remained inconsistent [7,8]. Clonidine improves the analgesic effects of anti-inflammatory agents and has peripheral (intra-articular, intravenous, regional) antinociceptive effects in combination with local anesthetics, opioids and ketamine [9]. It is an effective analgesic and sedative in combination with NSAIDS for ophthalmic surgery [10], tonsillectomy and adenoidectomy [11]. The analgesic effect of clonidine 2 µg/kg as an adjuvant to 0.25% bupivacaine is similar when administered intravenously or caudally [12].Clonidine has given preoperatively to children, provides preoperative sedation and a decrease in the thiamylal dose required for induction of anesthesia [13,14]. Many investigators have focused on the analgesic properties of the drug. Intravenous (IV) administration of clonidine after spinal surgery provides postoperative analgesia [15]. Intrathecal

clonidine successfully prolongs spinal anesthesia [16]. Oral clonidine premedication produces a significant prolongation of spinal anesthesia with bupivacaine[17] or tetracaine[18] and provides better pain relief in the early postoperative period after minor orthopedic surgery [19]. Clonidine produces analgesia without significant respiratory depression after systemic, epidural, or intrathecal administration [20-22]. Clonidine's analgesic effect is more pronounced after neuraxial injection, which suggests a spinal site of action and makes this route of administration preferable [20,23]] However, no studies about the effect of premedication with oral clonidine on postoperative pain in children are available. The current study has been done to investigate whether oral clonidine premedication provides postoperative pain relief in children or not. The main aim of this research was to evaluate and compare the influence of different premedication regimens on preoperative sedation, separation apart from parents, and mask acceptance in children. We also compared postoperative analgesia, hemodynamic status, and adverse effects.

MATERIALS AND METHODS

After approval of the Golestan University of Medical Science and Obtaining informed consent from parents, 44 children, ASA (I, II) aged between 1 and 3 years who underwent elective Herniotomy were included in this double-blind, prospective, randomized study. Children with abnormal liver function and renal and mental disease were excluded. Children were randomly divided into two groups: group C (n = 22), received clonidine 4 µg/kg given orally 60 min prior to anesthesia induction and group M (n = 22) patients received mepridine 0.5 mg/kg after the end of surgery. All children who refused to take the premedication or spat it out were excluded from the study protocol.Anesthesia was induced with thiopental sodium (5 mg.kg), fentanyl (1µg/kg) and Atracurium (0.6 mg/kg). LMA inserted in all patients and then maintenance of anesthesia was carried out with inspired isoflurane1. 4 %.Heart rate (HR), blood pressure (BP), oxygen saturation (SPO2), was monitored routinely during operation. Ringer's lactate solution was infused according to the child's weight. Patients in Group M were received mepridine 0.5 mg/kg after the end of surgery.At the end of the surgery, patients were transferred to the recovery room and postoperative level of analgesic was assessed by using FLACC scale system.Post operative analgesia and sedation were determined by an anesthetist who had no knowledge of the type of premedication. A strict anesthetic protocol was applied. All data were recorded on separate forms**.**

Statistical analysis

Data were analyzed by SPSS 16 and using Man-Whitney to detect the differences such as the age, operation time, duration of anesthesia, and various scores between two groups. P - Value less than 0.05 were considered as significant.

RESULTS AND DISCUSSION

Children in the two groups were comparable with respect to age, weight, duration of anesthesia. The pain score was assessed the same in all the children (as measured by the Flacc Scale) on arrival in the ward. Clonidine 4 µg/kg in compare with Mepridine provided better postoperative analgesia. The degree of postoperative analgesia was well correlated in children who had received clonidine (P=0. 001), although no correlation was observed in the mepridine group (Table 1). The highest FS (Flacc scale) score was lower in the clonidine 4 µg/kg treated group than in the other group. More children receiving 4 µg/kg clonidine were painfree over the entire 12-h study period than those receiving the other regimens. There were no significant in Heart rate (P=0.19), systolic (P=0.245) and diastolic (P=0.3) Blood pressure and Oxygen saturation (P=0. 45).

Table 1: clinical Effects of Clonidine and Mepridine

	Clonidine	Mepridine	P value
Age	4.01 ± 0.54	4.7 ± 0.53	0.29
Operation time	85 ± 14.2	82.3 ± 16.9	0.38
Duration of anesthesia	113 ± 21	104 ± 17.9	0.41
Weight	15.6 ± 1.06	16.01 ± 1.34	0.12
Heart rate (HR)	13.9 ± 2.9	11.4 ± 2.65	0.19
Blood pressure (BP systolic)	106.2 ± 9.32	104.75 ± 6.03	0.24
Blood pressure (BP diastolic)	56.02 ± 3.04	53.98 ± 3.43	0.3
Oxygen saturation (SPO2)	98.04 ± 0.31	98.6 ± 0.57	0.45
Pain (after surgery)	**2.09 ± 0.34**	**5.27 ± 0.57**	**0.001**

In this present study, we used oral clonidine as premedication for postoperative analgesia. There are a lot of ways of killing pain and administration of clonidine has been investigated in adults and children (24). Use of oral clonidine as an adjunct to commonly used analgesics in the operating room , enhances the quality of pain relief and substantially prolongs the duration of analgesia after operation in children. Our results suggest that use of oral clonidine 4 µg/kg as premeditation one hour before induction of anesthesia can be reduce postoperative pain and opioid needs after surgery and defer it's side effects. A major advantage of clonidine over opioid analgesics is its lower potential for respiratory depression. Oral administration is the simplest and most readily acceptable way of giving the drug to children. In addition, IV access may not always be established for minor surgery [25]. The prophylactic use of analgesics may decrease their postoperative requirements by reducing the noxious input to the central nervous system. Oral premedication may be advantageous according to the concept of "preemptive analgesia." Clonidine has a slow onset (0.5-l h) and a long duration (12 h) of action. However, the absence of severe pre- and postoperative side effects of clonidine in the current study encourages us to conduct a trial of clonidine in children undergoing day surgery in the future. In contrast to other studies, Andre and colleagues [26] concluded that clonidine was injected before surgery cause of reduces postoperative pain in children. However the dosage was used had been less than our study. In the study, Cao and his colleagues [27] achieved the results which quite similar to our even in dosage.

FLACC SCALE (FACE, LEGS, ACTIVITY, CRY, CONSOLABILITY)			
	0	**1**	**2**
FACE	No particular expression or smile	Occasional grimace or frown, withdrawn, disinterested	Frequent to constant frown, clenched jaw, quivering chin
LEGS	**0** Normal position Or relaxed	**1** Uneasy, Restless, Tense	**2** Kicking, Or Legs drawn up
ACTIVITY	**0** Lying quietly Normal position Moves easily	**1** Squirming Shifting back/forth Tense	**2** Arched Rigid Or Jerking
CRY	**0** No Cry (Awake or Asleep)	**1** Moans or Whimpers Occasional Complaint	**2** Crying Steadily Screams or Sobs Frequent Complaints
CONSOLABILITY	**0** Content Relaxed	**1** Reassured by occasional touching, hugging, or 'talking to.' Distractible	**2** Difficult to console or comfort.
The **FLACC** is a behavior pain assessment scale for use in non-verbal patients unable to provide reports of pain. Instructions: 1. Rate patient in each of the five measurement categories 2. Add Together 3. Document total pain score			

CONCLUSION

We observed that preoperative oral clonidine reduced postoperative pain score and requirement for supplementary analgesic in children compared with other opioids and did not have severe side effects. These data suggest that oral clonidine premedication can be a possible approach to pediatric postoperative pain relief pediatric in minor surgery such as herniotomy.

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