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آموزش مهارت های کاربردی در تدوین و چاپ مقاله

# Intranasal Sufentanil for Postoperative Pain Control in Lower Abdominal Pediatric Surgery

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## ABSTRACT

The most important role in postoperative pain management is still played by opioid administration through various modes. For the last few years, there has been an intensive search for alternative mode of opioid administration in pain management. The intranasal modes of opioid administration seems to be an attractive alternative. Sixty boys (aged 0.5-6 yr); ASA (American Society of Anesthesiologists) physical status I, who were candidates for lower abdominal surgery, were included in this prospective randomized, controlled study. Five minutes before extubation, patients were randomized to two groups and allocated to receive intranasal sufentanil (0.7 µg/kg) or normal saline, using a double-blinded study design. Satisfactory analgesia was achieved with intranasal sufentanil. It was effective after 10 minutes with the least pain scores (pain score  $2.3 \pm 0.4$  vs.  $4.1 \pm 0.5$ ) ( $p = 0.001$ ). Pain scores in 15, 20 and 25 minutes were similar in sufentanil group. None of patients had bradycardia, hypotension or SpO<sub>2</sub> (arterial O<sub>2</sub> saturation) <95%. High bioavailability of sufentanil after intranasal administration due to direct entrance of the drug into the systemic circulation and avoidance of the hepatic first-pass effect makes sufentanil an opioid with rapid onset and limited duration. As it has minimal side effects, sufentanil is one of the best choices for postoperative pain control in children. We used 0.7 µg/kg of intranasal sufentanil and found satisfactory analgesia accompanied with least side effects.

**Keywords:** Analgesia, Intranasal, Sufentanil, Pediatric, Postoperative pain

It is now accepted that pain should be anticipated, safely and effectively controlled in all children, whatever their age, maturity or severity of illness. Unfortunately the postoperative pain in pediatric patient is not adequately managed [1]. The most important role in postoperative pain management is still played by opioids administered through various modes. In the last few years, there has been an intensive search for alternative mode of opioid administration in pain management. The intranasal mode of opioid administration seems to be an attractive alternative, especially in patients who have not intravenous access.

Supported by extensive research into novel form of drug delivery, nasal administration of medications is emerging as a promising method of delivering drug with several advantages [2]. Pharmacokinetic studies have demonstrated a high bioavailability (71%, 65% and 78%) and a rapid rise in plasma concentrations follow intranasal fentanyl, alfentanil and sufentanil. Sufentanil is the most extensively used for sedation [3]. The elimination half life of intravenous sufentanil is 15-20 min

utes [4]. Intranasal administration induces no clinically significant change in vital signs, whereas after intravenous sufentanil, a clinically significant decrease in PaO<sub>2</sub> (arterial partial pressure of oxygen) is seen at 5 min [5].

## METHODS

After approval by University Research Committee and obtaining parental consent, sixty normal healthy boys, aged 0.5-6 yr, scheduled to lower abdominal surgery (such as, herniorrhaphy, orchiopexy, hydrocolectomy, urethroplasty) undergoing general anesthesia enrolled in this prospective double blinded study. Exclusion criteria included emergency operations and upper respiratory tract infection. All patients received fentanyl 1µg/kg and atropine 10µg/kg before induction of anesthesia. Induction of anesthesia accomplished with thiopental Na 6 mg/kg and atracurium 0.6 mg/kg (for facilitation of tracheal intubation). Anesthesia was maintained by administration of halothane and N<sub>2</sub>O in

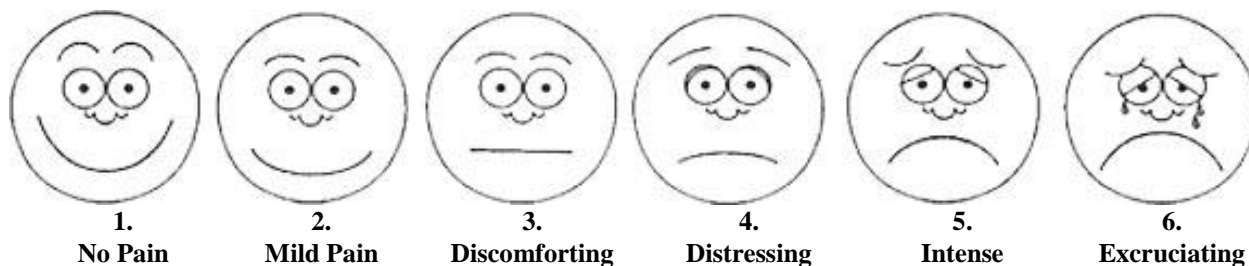


Fig 1. FACES pain rating scale. We considered FACES pain rating scale < 4 as satisfactory postoperative analgesia.

50% O<sub>2</sub>. Patients randomized (according to table of randomized numbers) in two groups, group 1 (n=30) received intranasal normal saline (N/S) and group 2 (n=30) received intranasal sufentanil (0.7 µg/kg), 5 min before extubation. Heart rate, blood pressure, respiratory rate, arterial O<sub>2</sub> saturation (PaO<sub>2</sub>), vomiting, pain and sedation scores were recorded by a nurse who was not informed of the content of administered solutions. Pain was measured according to FACES pain rating scale (Fig 1) and sedation was measured according to Ramsay Sedation Scale at arrival and every 5 min until 30 min in recovery room. We considered FACES pain rating scale < 4 as satisfactory postoperative analgesia and Ramsay Sedation Scale ≥ 4 as over sedation.

#### DATA ANALYSIS

To analyze differences between two groups Log linear models was used. Fisher-Exact test was considered for nominal data using SPSS software. Statistically differences between two groups of patients was considered at  $p < 0.05$ .

#### RESULTS

There was no difference between the groups, with respect to age, weight, duration of surgery and anesthesia. Pain scores were significantly reduced in sufentanil group vs. normal saline group (pain score  $2.3 \pm 0.4$  vs.  $4.1 \pm 0.5$ ) ( $p = 0.001$ ). Sufentanil was effective after 10 minutes with the least pain scores (Fig 2, Fig 3). Pain scores in 15, 20 and 25 minutes were similar in sufentanil group. Patients did not have bradycardia, hypotension or SpO<sub>2</sub> < 95%. Two patients in sufentanil group had nausea, which in one of them occurred immediately

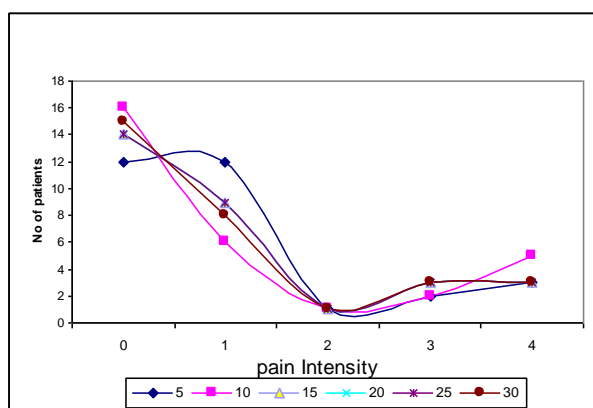


Fig 2. The effect of intranasal sufentanil on postoperative pain scores.

after instillation of drug. This problem might be not related to sufentanil. It seems the cause of nausea in this patient was related to awake extubation. Four patients in sufentanil group and two patients in normal saline group had over sedation. But none of them SpO<sub>2</sub> < 95% or loss of protective reflexes.

#### DISCUSSION

Our results show that intranasal sufentanil is quite effective in relieving pain in pediatric patients. Most patients experienced significant pain relief after 10 min.

As the lipid solubility of sufentanil is two times more than that of fentanyl [6]. Helmers et al. also suggested a higher bioavailability of sufentanil after intranasal administration. This higher bioavailability is due to direct entrance of the drug into the systemic circulation and avoidance of the hepatic first-pass effect. They compared intranasal and intravenous absorption and sedation preoperatively. Preoperative sedation of rapid onset and limited duration was seen in both groups. At 10 min, all patients in the intravenous group were sedated versus only two in the intranasal group ( $p < 0.01$ ). From 30 min, plasma concentrations were virtually identical for the two routes of administration. Intranasal administration induced no clinically significant changes in vital signs, whereas after intravenous sufentanil, caused a clinically significant decrease in PaO<sub>2</sub> at 5 min [5]. Intranasal fentanyl as an opioid is associated with diminished postoperative agitation without increasing vomiting, hypoxemia, or discharge time, when used during anesthesia for myringotomy [7]. Safety and efficacy of intranasal fentanyl in reducing acute pain of children in the emergency department was reported. Significant reduction in pain intensity (10 min after administration) with duration of analgesia for 30 min was seen [0]. Intranasal midazolam and sufentanil as premedication were compared in 60 pediatric outpatients. Approximately 15-20 min after drug administration, most patients in both groups could be comfortably separated from their parents. The sufentanil group appeared to be more sedated and more cooperative during induction of anesthesia. Vital signs and SpO<sub>2</sub> did not change significantly with either medication before or after surgery. Sufentanil was associated with more nausea and vomiting than midazolam (34% vs. 6%,  $p < 0.02$ ). In conclusion, both intranasal midazolam and sufentanil provide rapid, safe, and effective sedation in small children. Sufentanil provided somewhat better conditions for in-

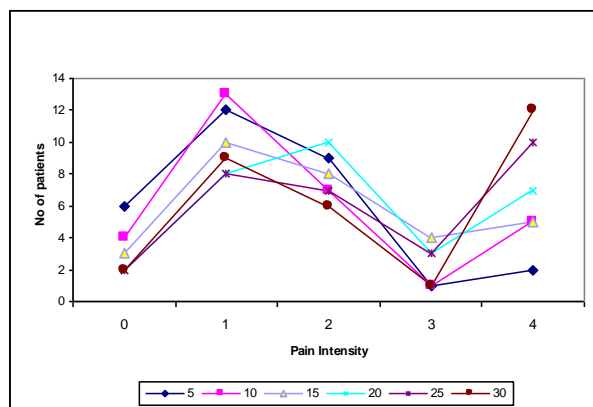


Fig 3. The postoperative pain scores in Saline group .

duction and emergence. Patients in the midazolam group were discharged approximately 40 minutes earlier [9]. Response to sufentanil was more variable in patients groups [10, 11].

Sufentanil 1.5 µg/kg IV ten minutes before the end of surgery had very satisfactory results for postoperative pain relief [12]. Using intranasal sufentanil for break through and incident cancer – associated pain, has been reported with no adverse effects such as vomiting or respiratory depression [13].

In a study intranasal sufentanil (1.5, 3.0, or 4.5 µg/kg) was compared by placebo (normal saline, 0.03 ml/kg). Induction of anesthesia was completed with 5% halothane and O<sub>2</sub> via facemask. After tracheal intubation, anesthesia was maintained with N<sub>2</sub>O (60-70%) and halothane, as clinically indicated. A blinded observer remained with the child from prior to drug administration until discharge from the recovery room. Patients given sufentanil were more likely to separate willingly from their parents and be judged as calm at or before 10 min compared to those given saline. Sufentanil, 4.5 µg/kg, had a higher incidence of vomiting in the recovery room and during the first postoperative day [14]. Intranasal sufentanil (10 or 20 µg) has been successfully used for preoperative sedation in adult patients [15].

We chose sufentanil because of its high bioavailability, rapid onset, short duration and minimal side effects. According to these studies, we used 0.7 µg/kg sufentanil and found it very effective and safe. Side effects such as nausea and over sedation were in acceptable range. We recommend using it as postoperative analgesic in operating room and post anesthesia care unit (PACU), as premedication or even as triage nurse- initiated administration in the emergency department.

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