

ORIGINAL RESEARCH

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Comparison of the effects of ketamine-midazolam and ketamin-propofol anesthesia on recovery of circumcision operations

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Abstract

To compare the effects of ketamine+midazolam or ketamine+propofol on analgesia, sedation and recovery time in children premedicated with midazolam for circumcision operations. Eighty American Society of Anesthesiologists physical status I-II, 5-12 years old children who undergone circumcision operations were included in the study. Both groups were administered of midazolam 0.04 mg/kg intravenously in the presence of besides their parents in the pre-operative holding area. Patients were induced with midazolam-ketamine in Group I or ketamine+propofol in Group II. There were no differences observed between the groups according to sedation and analgesia. None of patients needed additional hypnotic agent doses. Recovery was faster in ketamine-midazolam group. Midazolam+ketamine provided faster recovery than ketamine-propofol in pediatric circumcision operations. No complication was observed during sedation. It is observed that ketamine+midazolam has provided a faster recovery in circumcision operation.

Keywords: Circumcision, children, sedation, ketamine, propofol

Introduction

Circumcision is a stressful and painful process for children [1-5]. Pain in children is treated far less vigorously than in adults. Anesthesia techniques for circumcision include penile block[6,7] and caudal block[8-10].The patients are sedated during these procedures [1,7,9,10]. General anesthesia can also be performed with a laryngeal mask[10-13].The ideal anesthetic to be used for the procedure should provide sufficient analgesia, amnesia, sedation, short-acting effects, and also should not cause cardiovascular and respiratory depression, nausea-vomiting, and agitation [1]. Preferred agents include opioids, ketamine, propofol, and dexmedetomidine [1,9,10]. In addition, penile block [7,10] with bupivacaine was used for postoperative analgesia in addition to sedative agents[4].

The aim of our study was to compare the effects of ketamine-midazolam and ketamine-propofol combinations on recovery from anesthesia.

Material and Methods

After ethical committee approval, 80 children, ASA I-II physical status, aged 5 to 12 years, and who will be circumcised in elective

conditions, were included in the study. Exclusion criteria: ASA III or IV clinical status, patients (parents) who do not want to be included, additional hypnotic need, emergency conditions.

Institutional Protocol For Circumcision Operations:

All cases are premedicated with midazolam (0.04 mg/kg intravenous) before the operation. Premedications are administered in the presence of parents in the pre-operative holding area (5 minutes before surgical sedation).

Group 1: ketamine (2 mg/kg) + midazolam (0,05 mg/kg)

Group 2: ketamine (1 mg/kg) + propofol (3 mg/kg)

Additional penile block is administered by the surgeon using 0.5 % bupivacaine 1 mg/kg and 2 % lidocaine 2 mg/kg.

There is no involvement of the work team for the preference, desire or combination of these agents. Anesthesia protocol was not restricted, institutional protocols were selected by anesthetists not included in the study. The study team has observed the clinical outcomes. Postoperative early recovery profile and pain of patients were observed. Additional penile block was administered by the surgeon using 0,5 % bupivacaine 1 mg/kg and 2 % lidocaine 2 mg/kg.

Parameters that assessed as early recovery profile:

Spontaneous breathing time (time from the end of surgery to the time when spontaneous breathing returns), eye-opening time (time

from the end of surgery to eye-opening with verbal stimuli).

Face, Legs, Activity, Cry, Consolability (FLACC) Pain Scale and visual pain scale (0 - 10, 0 - no pain, 10 - maximum pain) were used for pain evaluation.

SPSS software version 21.0 (IBM® SPSS® Statistics V21.0) was used for statistical analysis. Chi-square test was used for categorical data and other personal variables. The level of significance was accepted as $\alpha = 0.05$.

Results

The age, weight, height, eye-opening with spoken stimuli, spontaneous respiratory return time, and FLACC pain scores were compared between the groups. There was no difference in demographical data of the groups. There was no difference in FLACC pain assessment. No additional hypnotic drug doses were needed in any patient. The time for eye-opening with verbal stimuli and spontaneous respiratory return was shorter in Group 1. The duration of spontaneous breathing with the combination of ketamine and midazolam and the duration of eye-opening with verbal stimulation were found to be significantly shorter than the group sedated with the propofol-ketamine combination. The penile block was applied to all patients and there was no significant difference between postoperative FLACC scores. Demographic data has been presented in table 1.

Table 1. Demographic and anesthetic data of two groups

	Group 1 (ketamine+midazolam)	Group 2 (propofol+midazolam)
Patients (n)	40	40
Age (year)	7±1,6	7,6±1,8
Weight (kilograms)	23±6,8	26,7±7,1
Height (centimeter)	124,7±9,5	129,9±10
Spontaneous breathing start time (minute)	4,4±3,4	6,6±4
Eye opening time with verbal stimulus (minute)	10,8±4	15,2±5,5
FLACC pain score	1,1±1,8	1±1,7

Discussion

Physicians frequently deal with procedures which require sedation of pediatric patients [14]. Circumcision is a stressful and painful process in children [1-5], and sedation is often needed. Preferred hypnotic agents include opioids, ketamine, propofol, and dexmedetomidine. For this purpose, the combination of propofol+ketamine or ketamine+midazolam are used in our institution and the penile block is applied for analgesia, additionally. The choice of these agents is shaped by the experience and preferences of physicians working in our clinic. In circumcision procedures early recovery was aimed because the cases are predominantly pediatric patients and the procedure is short. Early discharge is also preferred. For these reasons, the recovery times of the agents that were used in our clinic have been compared. The duration of spontaneous breathing with the combination of ketamine+midazolam and the duration of eye-opening with verbal stimulation were found to be significantly shorter than those with the propofol+ketamine combination. The penile block was applied

to all patients and there was no significant difference between postoperative FLACC scores. In a study, it was compared that the administration of propofol+ketamine and ketamine only in the study, applied penile block, and reported that a combination of propofol and ketamine provided more effective and safe sedation [1]. However, in our study, a combination of ketamine+midazolam was observed to make recovery earlier. Similarly, there were no significant complications in both groups. However, in the Gulec et al. trial, intramuscular midazolam + ketamine + atropine mixture was used for premedication purposes.

In a study, it was compared the need for ketamine addition and/or general anesthesia in patients who underwent midazolam sedation followed by circumcision. In Bicer et al. study, patients were classified according to their age groups. 1-year-old patients were classified as group 1, 1-7 years as group 2, and 7+ years as group 3. In the study, our patient population is 5-12 years old. In their study in which they applied 0,1 mg/kg midazolam IV and 0,02 mg/kg atropine IV for premedication, group 2 and group 3 required additional ketamine doses 80% and 38% for imperfect sedation and 12,8% and 3% need for general anesthesia was observed. In Group 1, these ratios are 2.7% ketamine supplementation requirement and 0% general anesthesia requirement, but these results are not used for comparison by considering the age range of our study group and our age groups [10]. As can be seen, adequate sedation was achieved in the majority of patients (87.2% - 97%) with ketamine-midazolam combination. The anesthetic awakening durations of the patients were reported as 3 and 1.5 minutes respectively in group 2 and group 3. In our study, when we used ketamine-midazolam, the mean duration of eye-opening by verbal stimulation was verified as 10.8 min. (Table 1)

Observers have applied ketamine intramuscular and thiopental 25 mg/kg rectal to 2-4 mg/kg of patients up to 14 years of age and compared sedation adequacy and duration of action. As a result, sufficient sedation was obtained with ketamine application but it was stated that the recovery times were longer [14]. However, it has been reported to be more useful as it has been necessary to make additional doses. Gauntlett has reported that caudal anesthesia with bupivacaine/ketamine does not confer any advantage over a dorsal nerve block with the doses used in the study [15]. The author has used a dose of 0,5 mg/kg ketamine and it has been thought to be less for the sedation [15]. In our study, similarly, the recovery time in the ketamine+propofol group was delayed, but both groups completed procedure without the need for additional hypnotic doses. It must also be pointed that we used the dose of 2 mg/kg ketamine IV. Additionally, it has been reported that preincisional subcutaneous ketamine infiltration can suppress postoperative pain after the circumcision surgery [16]. We did not observe difference about in the postoperative pain. However, it has been reported that the combination of propofol and ketamine for invasive procedures in pediatric oncology resulted with agitation in recovery [17], agitation was not observed in our study (Table 1).

In a study, comparing IM and IV ketamine administrations, reported that IV administration resulted in more efficacious results in terms of onset of action, duration of action and adequate sedation [18]. In our study, only IV ketamine was used. IM ketamine administration can be easily applied to children without intravenous access and IV treatment can be criticized for this reason. However, in our

pediatric surgery department provides IV access in their clinic with in parental custody (parents are with their children to keep them calm), so we used the existing IV route.

It has been reported that propofol sedation was as effective as midazolam sedation and recovery times were shorter than midazolam in studies performed on pediatric emergency room patients aged 2-18 years [19]. Conversely, when we applied ketamine+propofol in our study, time to eye open with verbal stimuli was longer than in the ketamin+midazolam group. This may be due to differences in the doses used, as propofol 3 mg/kg was used in our study and in the Havel et al study the dose was 1 mg/kg [19]. In a study, it was compared different combinations of propofol+ketamine with respect to sedation quality and side effects in pediatric patients who underwent bone marrow aspiration or lumbar puncture, reported that the 1:3 ketamine-propofol combination was more successful in terms of sedation quality [20]. In our study, the ratio was 1:3, similarly there was no problem with sedation quality and adequacy, but according to the results of our study, the disadvantage of this combination is that the duration of eye-opening with verbal stimulation is longer than that of the ketamine+midazolam group (Table 1).

Conclusion

Midazolam+ketamine combination has provided faster recovery than ketamine-propofol combination in pediatric circumcision operations. No complication has been observed during sedation. Although we have found out that midazolam+ketamine combination may be a preferable choice for circumcision operations, these results must be evaluated furtherly in larger groups for the evidence.

Competing interests

The authors declare that they have no competing interest

Financial Disclosure

The financial support for this study was provided by the investigators themselves.

Ethical approval

The study was approved by the Ethics Committee

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