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Comparison of premedication with nebulized dexmedetomidine and ketamine in children undergoing elective surgery

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Abstract

Background: Premedication allows smoother induction and stable perioperative hemodynamics. The most favorable and acceptable means of premedication in pediatric population has been a matter of debate in the past. This study was planned to compare nebulized dexmedetomidine with ketamine in terms of level of sedation on arrival in operating room.

Methods: Sixty children (3-10 years of age) ASA physical status I and II undergoing elective surgery were divided randomly into group K (nebulized ketamine) and group D (nebulized dexmedetomidine) of 30 patients each. Sedation score, parental separation anxiety score (PSAS), mask acceptance score (MAS), emergence agitation scale (EAS) and postoperative pain score (Wong Baker scale) were recorded. Statistical analysis was done using SPSS version 21.0.

Results: The mean sedation score on arrival in operating room of Group K was significantly lower than that of Group D (p= 0.011). Parent Separation Anxiety Scale (PSAS) was comparable in the two groups (p=0.384). The recovery time was significantly shorter when nebulized with dexmedetomidine (p = 0.001). The EAS was significantly higher with ketamine as compared to dexmedetomidine at baseline and at 15min postoperatively (p = 0.038, 0.001). Pain was significantly lower in Group D as compared to Group K in the postoperative period, p< 0.05.

Conclusion: Premedication with nebulized dexmedetomidine is better than that with ketamine in terms of level of sedation, recovery time, emergence agitation, postoperative pain whereas they are comparable in terms of parental separation and mask acceptance.

Keywords: Premedication, pediatric, nebulization, dexmedetomidine, ketamine

Introduction

Preoperative period is the most distressing time for children undergoing surgery. Parental separation, fear of strangers, environmental change and needle injections

contribute to preoperative stress.[1] The purpose of premedication is primarily to allay preoperative fear to ensure smooth parental separation. Preoperative anxiety stimulates sympathetic, parasympathetic and endocrine systems leading to undesirable hemodynamic consequences perioperatively.[2] It is also a predisposing factor for emergence delirium, sleep disturbances and chronic psychological disorders.[3]

Several routes for administering premedication have been tried in children in the past like oral, nasal, rectal, transmucosal, intramuscular, intravenous etc. Recently, delivering nebulized drug through inhalational route has been introduced as an effective method of premedication in paediatrtic population. Nebulisation of a drug converts the liquid drug into tiny droplets, which are easily inhaled by the child through a mouth piece or a mask. This leads to better acceptance of the drug by child and good bioavailability. (4)

Dexmedetomidine is a selective alpha 2A adrenoreceptor agonist used in premedication for sedation, analgesia and anxiolysis without unwanted hemodynamic effects from activation of alpha1 receptor and respiratory depression. All these properties render dexmedetomidine suitable for use in the perioperative period.[5] Ketamine is a non-barbiturate cyclohexamine derivative which causes dissociation of the cortex from the limbic system. The production of balanced sedation with less respiratory depression is one of the most important advantages of ketamine premedication.[6]

Hence, this study was planned with the aim to compare premedication with nebulized dexmedetomidine and ketamine in paediatric patients undergoing elective surgery. The primary objective of this study was to compare the level of sedation on arrival in the operating room (OR) in paediatric patients undergoing elective surgery. Secondary objectives were to compare parental separation, mask acceptance and recovery parameters like recovery time, emergence agitation and postoperative pain.

Methods

This prospective, randomized trial was registered at Clinical Trial Registry on 3/11/2020 for a period of two years. The study was conducted after obtaining Institutional Ethics Committee approval. Sixty American Society of Anesthesiologists (ASA) physical status I and II children (3 to 10 years) undergoing elective surgery under general anesthesia were randomly allocated into group K (nebulized Ketamine 3mg/kg) and group D (nebulized Dexmedetomidine 2µg/kg) by using block randomization method. Patients with active upper respiratory tract infection, known allergy to study drug, significant organ dysfunction, cardiac dysrhythmias, congenital heart disease, on psychotropic medication and intellectual disability were excluded from the study.

After obtaining written informed consent from the parent and appropriate fasting, all patients received pre-medication with nebulized Dexmedetomidine (2µg/kg diluted in 4ml 0.9% saline) or Ketamine (3mg/kg diluted in 0.9% saline) 30 min before surgery. Sedation score was recorded at 5, 10, 20 and 30 min after administration of study drug. Parental separation anxiety scale (PSAS) was recorded at the time of wheeling in to the OR. The standard an aesthetic protocol consisted of an inhalational induction with 8% sevoflurane in 50% nitrous oxide and oxygen, followed by intravenous access with 24/22-gauge cannula, fentanyl 2µg/kg and propofol 1 mg/kg was administered intravenously, if required. Airway was secured with appropriate size proseal laryngeal mask airway (LMA). Anesthesia was maintained with isoflurane in nitrous oxide and oxygen (70:30) and supplemental vecuronium bromide and fentanyl as per the standard protocol. Isoflurane was

switched off 5 minutes prior to completion of surgery. At the end of surgery, neuromuscular blockade was reversed with neostigmine (0.05 mg/kg) and glycopyrrolate (0.01 mg/kg) intravenously. LMA was removed after pharyngeal suctioning, when the patient is fully awake, and responding to verbal commands.

Recovery time was taken as time from discontinuation of isoflurane till the sedation returned to baseline. Postoperative parameters monitored were: Emergence agitation using emergence agitation scale (EAS) and post-operative pain using Wong Baker FACES scale.

Statistical analysis

With reference to previous study done by Abdel Ghaffar et al [7], taking these values as reference, (mean1=2.25, mean2= 2; SD1=0.104167, SD2=0.33333) the minimum required sample size with 80% power of study and 5% level of significance is 16 patients in each study group. To reduce margin of error, and to increase the power of the study, total sample size taken was 60.

For comparing mean of two groups

$$N>=2\frac{(\text{standard deviation})^2*(Z_\alpha + Z_\beta)^2}{(\text{Mean difference})^2}$$

Where Z_α is value of Z at two-sided alpha error of 5% and Z_β is value of Z at power of 80% and mean difference is difference in mean values of two groups.

Results

The two groups were comparable in terms of age, gender, weight, height, ASA physical status and duration of surgery, [Table 1]. The sedation scores at 10min, 20min, and 30min after premedication were significantly higher in dexmedetomidine group (2.13 ± 0.57, 2.23 ± 0.57, 2.37 ± 0.61 respectively) than ketamine group (1.80 ± 0.41, 1.93 ± 0.58 1.90 ± 0.71 respectively) (p = 0.014, 0.05, 0.011 respectively). [Table 2] The mean sedation score on arrival in operation room of Group K was 1.90 ± 0.71, which was significantly lower than that of Group D (2.37 ± 0.61) (p = 0.011)

Parent Separation Anxiety Scale (PSAS) (p = 0.384) and Mask acceptance scale (MAS) (p = 0.232) was comparable in both the groups. The recovery time was significantly shorter when nebulized with dexmedetomidine (7.43 ± 2.27minutes) than with ketamine (9.57 ± 1.94minutes) (p = 0.001). The EAS was significantly higher with ketamine as compared to dexmedetomidine at baseline and at 15min postoperatively (p = 0.038, 0.001). This is depicted in figure 1. Pain was significantly lower in the dexmedetomidine group than ketamine group till one hour in the postoperative period. This is shown in figure 2 as comparison of Wong Baker's Faces Scale.

Discussion

Optimum premedication in children has been an area of research in the past. Several drugs have been evaluated for this purpose. Ketamine and dexmedetomidine have been used for the same via various routes. Our study highlights that inhaled dexmedetomidine is associated with better sedation scores, early recovery and better postoperative pain control along with decreased incidence of emergence agitation as compared with inhaled ketamine.

Similar results were obtained by Qiao et al[8], the sedation scores of the three groups (dexmedetomidine group, ketamine group and dexmedetomidine combined with ketamine group) showed no significant difference at 10 min however, they were significantly higher with dexmedetomidine and its combination with ketamine than with ketamine, at 20 and 30 min ($p < 0.001$). [7] In yet another study, Abdel Ghaffar et al compared nebulised ketamine, dexmedetomidine and midazolam and reported that children nebulized with dexmedetomidine had more satisfactory sedation on arrival in OR.[9]

The children in both the groups had acceptable parental separation scores (1.90 ±1.03) in Group K and (2.03±0.85) in Group D. However, there was no significant difference in the scores between the two groups in our study. Our findings were consistent with previous studies, where the observed parental separation anxiety between the groups was comparable.[8,9]

During the intraoperative period, sedation scores and mask acceptance were compared between the groups. The sedation scores on entering the operating room was 1.90 ± 0.71 in group K and 2.37 ± 0.61 in group D (p = 0.011). The children in dexmedetomidine group were calmer and sitting or lying comfortably as per the sedation scale. Those in ketamine group were more alert and not crying.

Dexmedetomidine, being a selective α_2 receptor agonist, leads to a normal sleep like, cooperative and arousable sedation with little effect on respiration. Ketamine, on the other hand, causes sedation by binding preferentially to the NMDA receptors on the inhibitory interneurons in the cortex, limbic system and hippocampus. Ketamine also has little effect on respiration.[6]

In a similar study, Sabry et al comparing nebulized dexmedetomidine (3 µg/kg), nebulized ketamine (3mg/kg) and their combination (1.5µ/kg of nebulized dexmedetomidine +1.5mg/ kg of nebulized ketamine) given 30 min prior to surgery, in 75 children aged 3 to10 years, observed that nebulized dexmedetomidine provides better sedation on arrival in the operating room as compared with nebulized ketamine (p = 0.039).[10]

The children in both groups of our study had satisfactory mask acceptance (2.33 ± 1.06 with ketamine and 2.03 ± 0.85 with dexmedetomidine) and were comparable. Easy mask acceptance leads to a smoother inhalational induction. Conversely in a study by Sabry et al[10], mask acceptance was significantly better with dexmedetomidine (3 µg/kg) than ketamine (3mg/kg) (*P*=0.037). Difference in dose of dexmedetomidine (2 µg/kg) might be the reason for this difference in mask acceptance scale between the groups.

In our study, the recovery time was defined as the time from discontinuation of isoflurane till the sedation returns to baseline. It was significantly shorter when nebulized with dexmedetomidine than with ketamine (p = 0.001). This implies early recovery and transfer to ward and resumption of daily activities. Our findings are consistent with a study by Ghaffar et al[9], who compared nebulized dexmedetomidine, ketamine, and midazolam, wherein they concluded that children premedicated with nebulized dexmedetomidine had a shorter recovery time from anaesthesia than with ketamine and midazolam (p = 0.000).

In our study, the Emergence Agitation scale was significantly higher with ketamine as compared to dexmedetomidine at baseline and at 15min postoperatively (0.038, 0.001). The mild dissociative type of sedation caused by ketamine is probably the reason for the higher incidence of emergence agitation.[11] Children nebulised with dexmedetomidine were calmer, whereas, those nebulised with ketamine were comparatively more restless but settled on reassurance. Our findings were similar in a study by Kim et al, who compared 90 patients scheduled for closed reduction of nasal bone fracture.[12] The control group received saline infusion and the other group received 1µg/kg of intravenous dexmedetomidine 30 min prior to induction of anaesthesia. They compared the Aono's four-point scale scores after anaesthesia (primary end point) and recovery time (secondary end point). They concluded that preoperative administration of dexmedetomidine decreased the incidence, duration and severity of post-

operative emergence agitation compared to saline infusion.

In our study, pain was significantly lower in the dexmedetomidine group than ketamine group till one hour in the postoperative period (p = 0.000, 0.000, 0.003, 0.003, 0.016 at baseline, 15min, 30min, 45min, 60 min respectively). The Wong bakers FACES scale was significantly lower with dexmedetomidine than ketamine till one hour postoperatively.

Hence, dexmedetomidine offers better postoperative analgesia, reduced opioid and non-opioid analgesic requirement. It may also lead to decrease in the incidence of postoperative nausea, vomiting and early acceptance of oral feeds.

The heart rate was significantly lesser with dexmedetomidine compared to ketamine during the intraoperative period. MAP was significantly lower with dexmedetomidine than ketamine in the preoperative (from 5 to 30 min), intra operative (at baseline, 5min, 15min, 30min, 45min and 60min) and postoperative periods (at 30min and 45 min) (p = 0.000,0.000,0.003,0.003,0.016 respectively). Overall, the heart rate and blood pressure in both the groups were well within the normal range.

Hence, from the observations of our study we conclude that nebulized dexmedetomidine 2 µg/kg is better than nebulized ketamine 3 mg/kg for premedication in children in terms of level of sedation, recovery time, emergence and postoperative analgesia.

References

1. Zanaty OM, El Metainy SA. A comparative evaluation of nebulized dexmedetomidine, nebulized ketamine, and their combination as premedication for outpatient pediatric dental surgery. Anesth Analg 2015; 121: 167–71.
2. Davidson A, McKenzie I. Distress at induction: prevention and consequences. Curr Opin Anaesthesiol 2011; 24: 301-6.
3. Kain ZN, Caldwell-Andrews AA, Maranets I, et al. Preoperative anxiety and emergence delirium and postoperative maladaptive behaviour. Anesth Analg 2004; 99: 1648-54.
4. Anttila M, Penttila J, Helminen A, et al. Bioavailability of dexmedetomidine after extravascular doses in healthy subjects. British J Clin Pharmacol 2003; 56: 691-3.
5. Gertler R, brown CH, Mitchell DH, et al: a novel sedative-analgesic agent. Proc BaylUniv Med Cent 2001; 14: 13-21.
6. Altiparmak B, Akça B, Yilbaş AA, et al. All about ketamine premedication for children undergoing ophtalmic surgery. Int J clin exp med 2015; 8: 21525.
7. Abdel-Ghaffar HS, Kamal SM, El Sherif FA, et al. Comparison of nebulised dexmedetomidine, ketamine, or midazolam for premedication in preschool children undergoing bone marrow biopsy. Br J Anaesth. 2018 Aug;121(2):445-452
8. Qiao H, Xie Z, Jia J. Pediatric premedication: a double-blind randomized trial of dexmedetomidine or ketamine alone versus a combination of dexmedetomidine and ketamine. BMC anesthesiol 2017; 17: 158.
9. Abdel-Ghaffar HS, Abdel-Wahab AH, Roushdy MM, et al. Preemptive nebulized ketamine for pain control after tonsillectomy in children: randomized controlled trial. Rev Bras Anesthesiol 2019; 69: 350-7.
10. Sabry MH, El Gamal NA, Elhelw N, et al. Comparison of the use of nebulized dexmedetomidine, ketamine, and a mixture thereof as premedication in pediatric patients undergoing

tonsillectomy: a double-blind randomized study. Res Opin Anesth Intensive Care 2020; 7: 70.

11. Guit JB, Koning HM, Coster ML, et al. Ketamine as analgesic for total intravenous an aesthesia with propofol. Anaesthesia 1991; 46:24-7.
12. Kim JC, Kim J, Kwak H, et al. Premedication with dexmedetomidine to reduce emergence agitation: a randomized controlled trial. BMC anesthesiol 2019; 19: 1-6.

Legends Figures and tables

Table 1: Comparison of demographic profile and duration of anesthesia between group K and D

Variables	Group K	Group D	p value
Age (in years)	6.63 ± 2.33	6.83 ± 2.15	0.771
Gender (male/female)	24/6	25/5	0.739
ASA I/II	25/5	22/8	0.347
Weight(kg)	20.70 ± 8.52	22.30 ± 7.04	0.431
Height (in cm)	117.63 ± 15.48	118.00 ± 14.40	0.925
Duration of an aesthesia (min)	54.00 ± 16.99	52.00 ± 17.05	0.600

Table 2: Comparison of Sedation Scores post-nebulization between the two groups

Sedation score	Group K	Group D	p value
Baseline	1.33 ± 0.48	1.30 ± 0.47	0.783
5 min	1.33 ± 0.48	1.43 ± 0.50	0.43
10 min	1.80 ± 0.41	2.13 ± 0.57	0.014*
20 min	1.93 ± 0.58	2.23 ± 0.57	0.05*
30 min	1.90 ± 0.71	2.37 ± 0.61	0.011*

Figure 1: Comparison of Emergence Agitation Scale (EAS) between the Groups

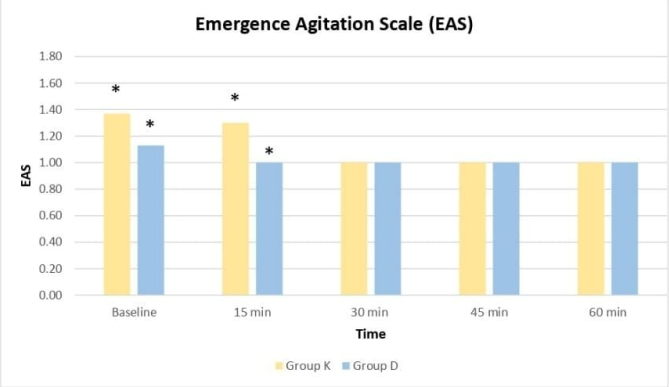

Figure 2: Comparison of Wong Bakers Faces Scale (WBFS) between the Groups