

Comparison of two doses of intranasal dexmedetomidine as premedication in children

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Keypoints

Intranasal administration of dexmedetomidine as premedication in children is a relatively noninvasive and easy route of administration. The purpose of this study was to evaluate the preoperative sedative effects, anxiety level changes, ease of child-parent separation (as a primary end-point), perioperative hemodynamics, and the recovery profile of preoperative intranasal dexmedetomidine sedation.

Abstract

Introduction

In this study we are comparing two different doses 1 µg/kg and 2 µg/kg of intranasal dexmedetomidine for sedative efficacy and analgesia as a premedication in children (6-12 years of age). This prospective, randomized study is designed to evaluate efficacy of 2 different doses of intranasal dexmedetomidine as a premedication in children. To assess the patient preoperatively and its importance in anesthetic management. To evaluate the sedative, anxiolytic, and analgesic effects of dexmedetomidine at dose of 1 µg/kg and 2 µg/kg when administered through intranasal route in paediatric patient. To compare efficacy of these two different doses as a premedication. To study hemodynamic variations that occurs after administration of intranasal dexmedetomidine.

Materials and Methods

Patients were categorized in 2 groups: Group A: Intranasal Dexmedetomidine 1 µg/kg (n = 25) Group B: Intranasal Dexmedetomidine 2 µg/kg (n = 25) Group A and B received the drug at 45 minutes before induction of anesthesia. Various parameters were recorded. A value of $p < 0.05$ was considered as a statically significant difference with ANOVA being done along with krushual-wall's test. Sedation and hemodynamic

data were analysed by mixed model analysis of crossover. Bonferroni-T-test was used for pair wise comparison.

Results and conclusions

The group which was administered 2 mcg/kg of intranasal dexmedetomidine showed better results in terms of sedation and behavioural scores, intraoperative hemodynamics, post-operative recovery as compared to the group given 1 mcg/kg of the drug.

Keywords: Intranasal, dexmedetomidine, pediatric, sedation, premedication

Introduction

Surgery and anesthesia induce considerable emotional stress upon children. Preoperative anxiety stimulates sympathetic, parasympathetic and endocrine system leading to an increase in heart rate, blood pressure and cardiac excitability. Children aged two to five years are especially vulnerable to this problem, since their understanding is limited.

Preoperative anxiety in unpremedicated children is two-fold. Hence all pediatric patients need to be premeditated in order to decrease preoperative anxiety.

The premedicant should be pleasant, acceptable, rapid and reliable in onset with little adverse effects. Many drugs have been tried for premedication in children.

There is no single premedicant with all the ideal characteristics.

New drugs, such as the α_2 -agonists, have emerged as alternatives for premedication in pediatric anesthesia. Dexmedetomidine is a highly selective α_2 -adrenoceptor agonist that has sedative and analgesic effects. Clinical investigations have demonstrated its sedative, analgesic and anxiolytic effects after IV administration to volunteers and postsurgical patients.

Preliminary experience in children has demonstrated its efficacy for the sedation of infants and children during mechanical ventilation. It has also been used to sedate children undergoing radiological imaging studies.

Intranasal application is a relatively noninvasive and easy route of administration which has the additional benefit of not requiring patient cooperation as would be the case for swallowing the medication or retaining it sublingually. It is well tolerated and does not have an unpleasant taste/pungency.

Therefore, the purpose of this study was to evaluate the preoperative sedative effects, anxiety level changes, ease of child-parent separation (as a primary end-point), perioperative hemodynamics, and the recovery profile of preoperative intranasal dexmedetomidine sedation.

Interactions with medical providers are stressful experiences for children. Because of this stress and the anxiety it provokes, minor procedures often require mild to moderate sedation.

Intravenous route in a child is time and resource consuming for minor procedures. It also leads to an increased risk of respiratory depression due to the very high levels of medication that are achieved with bolus injection therapy.

Starting an intravenous line is painful and frightening for many. Intranasal and oral transmucosal (buccal, sublingual) delivery of sedative medications offers an alternative that provides some advantages over the above methods in properly selected minor procedure: they are faster than oral or rectal forms and less painful than injectable forms.

Situations where investigators have found them to be useful include dental procedures, minor pediatric laceration repairs, and anxiolysis prior to radiologic procedures such as MRI, pediatric preoperative sedation to assist with separation anxiety as well as sedation before other minor procedures including intravenous starts, biopsies, esophagogastroduodenoscopy and ophthalmologic procedures.

Providing anesthesia to children undergoing for different surgery is challenging and adequate premedication administered non-invasively, would make the procedure smoother.

Most of the Pediatrics patients receive analgesic and sedative agents as a premedication to optimize patient comfort and safety. Benzodiazepines, propofol, ketamine and opioids are the sedatives that have in recent years most often been used for this purpose. Preoperative anxiety and emergence delirium in children continue to be common with these medications.

Oral Midazolam is the most commonly used drug for this purpose till now. There is no single ideal sedative or analgesic drug for these patients.

As an alternative, dexmedetomidine, a highly selective α_2 -adrenoceptor agonist; is tasteless, odorless and painless when administered by intranasal route. Intranasal administration is relatively easy and convenient, it also reduces first pass metabolism and has been used successfully for fentanyl, ketamine, and midazolam premedication.

Several routes of parenteral administration (intravenous, intramuscular, subcutaneous and intranasal) have been utilized. The bioavailability of intranasal dexmedetomidine was relatively good (65%) and higher than oral route, but interindividual variation was large. The possibility of potentially altered potency and effect duration should be taken into account when administering dexmedetomidine to pediatric, elderly or hypoalbuminaemic patients.

Dexmedetomidine produces sedation, analgesia, facilitate parental separation, and improve conditions for in-

duction of general anesthesia, while preserving airway reflexes.

Intranasally administered dexmedetomidine was efficacious and well tolerated, making it appropriate for clinical situations requiring light as well as deep sedation.

Separation anxiety and acceptance of the mask during induction of general anesthesia are issues that lead many clinicians to prefer sedating children in the pre-operative phase before they take them from their parents into the operating theatre.

Oral medications are commonly used but have considerable delays in onset, whereas IV and IM medications are painful and frightening. This has led several investigators to consider intranasal medications as an alternate method of achieving smoother separation and mask acceptance.

The option of intranasal preoperative sedation might be most useful in situations where the prior case ends quickly and the next patient has not had sufficient time for their oral medication to take effect (or has not even received it). In this case, nasal sedatives are rapidly effective (5-10 minutes), reliable and possibly titratable.

Advantages of these drugs over nasal midazolam appear to be due to the fact that no transient nasal burning occurs, reduced confused state is present after the procedure and there is no respiratory depression risk from the medication.

In this study we are comparing two different doses 1 µg/kg and 2 µg/kg of intranasal dexmedetomidine for sedative efficacy and analgesia as a premedication in children (6-12 years of age).

This prospective, randomized study is design to evaluate efficacy of 2 different doses of intranasal dexmedetomidine as a premedication in children.

1. To assess the patient preoperatively and its importance in anesthetic management.
2. To evaluate the sedative, anxiolytic, and analgesic effects of dexmedetomidine at dose of 1 µg/kg and 2 µg/kg when administered through intranasal route in paediatric patient.

3. To compare efficacy of these two different doses as a premedication.
4. To study hemodynamic variations that occurs after administration of intranasal dexmedetomidine.
5. To study complications occurring during perioperative period.

Materials and methods

After ethical committee approval fifty patients of paediatrics age group of physical status ASA I-II aged between 6-12 years undergoing different surgeries were randomly selected from the civil hospital, asarwa Ahmedabad.

Inclusion criteria: Age of the patient: 6-12 year, Male or female child, Written informed consent of patient's relative, ASA-PS grades I & II.

Exclusion criteria: Age < 6 years or >12 years, Patient's refusal, Recent upper respiratory tract infection, Allergy or hypersensitivity to drugs, Pre-existing cardiovascular, respiratory or cerebrovascular disease, History of congenital abnormality, diabetes or other systemic abnormalities. Known hypersensitivity to dexmedetomidine.

A Preoperative visit was made on the day prior to surgery. A cannulation sites were noted. All routine investigations were done. Parents explained about the concerned technique & informed consent taken. No sedative premeditations ordered on the day prior to surgery. Parents were also instructed to keep the children fasting for 6-8 hours depending on the age. All the resuscitation and monitoring equipment were kept ready before administration of pre-medication, for management of any adverse reactions.

On the day of surgery, Children were shifted along with one of the parents to the Preoperative holding room. Baseline HR, RR, SpO₂, BP was recorded. The 22-gauge or 24-gauge venous cannula was inserted.

Patients were categorized in 2 groups :

Group A: Intranasal Dexmedetomidine 1 µg/kg (n = 25)

Group B: Intranasal Dexmedetomidine 2 µg/kg (n = 25)

Group A received 1 µg/kg intranasal dexmedetomidine in a total volume of 0.5 mL normal saline at 45 minutes

before induction of anesthesia, and Group B received 2 µg/kg intranasal dexmedetomidine in a total volume of 0.5 mL normal saline at 45 minutes before induction of anesthesia. In both group intranasal dexmedetomidine was dripped into both the nostrils using a 1ml tuberculin syringe with the child in the recumbent position.

The heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP) and oxygen saturation (SpaO₂), respiratory rate (RR) were measured before administration of the study drug (baseline values) and every 5 min after that until the children were transferred to the operating room (OR). Sedation and anxiety levels were assessed before administration of the study drug (baseline values) and at the time of transferring to the OR.

Also, the ease of child-parent separation at the time of transferring to the OR, wake-up behaviour score and parental satisfaction was assessed.

Sedation level was assessed using a 6-point sedation scale, which was modified from the observer assessment of alertness and sedation scale.

Both groups also received Inj. Glycopyrrolate 0.004mg/kg i.v. and Inj Ondansetron 0.15mg/kg i.v. as a premedication just before induction.

At 45 min, response to mask placement assessed & recorded. Based on the body weight, children <20 kgs paediatric circuit consisting of Jackson Ree's modification of Ayre's T – piece and >20 kgs, Bain's circuit was used with appropriate fresh gas flows. Patient preoxygenated for 3-5 mins & induced with Inj Propofol 2.5-3.5mg/kg i.v. or Inj. Thiopentone 3-5 mg/kg and Inj. Scoline 2mg/kg i.v. was given and patient intubated with appropriate portex cuffed endotracheal tube. Anesthesia was maintained by 50% oxygen + 50% N₂O and Inj. Atracurium IV or Inj vecuronium IV in a standard doses. IV fluids calculated and administered based on the NPO period and degree of surgical trauma.

At the end of surgery all the inhalational anaesthetic agents were discontinued and residual effect of relaxants were reversed with Neostigmine & glycopyrrolate, ex-

tubation done after thorough suctioning of the oral cavity and return of protective reflexes.

Children shifted to PACU after confirmation of adequate clinical recovery. Closed Observation was done for respiratory depression. The presence or absence of complication at any time from emergence from anesthesia until 2 hour postoperatively was noted.

Arterial BP, HR, and SaO₂ were measured every 15 min during the 2-h postoperative observation period. Occurrence of hypotension, bradycardia or desaturation was recorded.

A value of p < 0.05 was considered as a statically significant difference with ANOVA being done along with krushual-wall's test. Sedation and hemodynamic data were analysed by mixed model analysis of crossover. Bonferroni-T-test was used for pair wise comparison.

See Table A for scoryng systems.

ALERTNESS OR SEDATION SCALE

6	Does not respond to noxious stimulus
5	Does not respond to mild prodding or shaking
4	Responds only after mild prodding or shaking
3	Responds only after name is called loudly or repeatedly
2	Lethargic response to name spoken in normal tone
1	Appears asleep but responds readily to name spoken in normal tone
0	Appears alert and awake, responds readily to name spoken in normal tone

BEHAVIOUR SCORES

4	Calm And Cooperative
3	Anxious but reassurable
2	Anxious and not reassurable
1	Crying or resisting

WAKE UP BEHAVIOUR SCORES

4	Calm and cooperative
3	Not calm but could be easily calmed
2	Not easily calmed, moderately agitated or restless
1	Combative, excited, disoriented

MASK ACCEPTANCE

1	Combative, crying
2	Moderate fear of mask, not easily calmed
3	Cooperative with reassurance
4	Calm, cooperative
5	Asleep

PARENTAL SATISFACTION

1	Not satisfied
2	Good, satisfied
3	Excellent

SCALES	SEDATION SCORE	MASK ACCEPTANCE	PARENTAL SATISFACTION	BEHAVIOUR	WAKE UP BEHAVIOUR	REMARKS
SCORES						

Table A. Scoryng systems

Results

A study of 50 paediatric patients aged between 6-12 years undergoing different day care surgery were randomized into 2 groups with 25 patients in Group A (Intranasal Dexmedetomidine 1µg/kg) and 25 patients in Group B (Intranasal Dexmedetomidine 2µg/kg).

The study was undertaken to compare two different doses of intranasal dexmedetomidine as premedication.

The two groups were comparable in age, weight, sex, and ASA physical status.

Table-1 and Figure 1 are showing the mean age in both the groups. The mean age in Group A was 9.40 ± 2.14 years and in group B was 9.48 ± 2.47 years with p value >0.05 & found to be statistically not significant.

Table-1 and Figure 1 are showing the mean weight in both the groups. The mean weight in Group A was 24.2± 4.71kg and in group B was 24.64 ± 5.20 kg with p value >0.05 & found to be statistically not significant.

Table-1 and Figure 2 are showing the gender distribution in both the groups. Gender distribution in Group A was found to be 12 males &13 females. In group B it was 15 male & 10 females. The P value observed was >0.05 & was found to be statistically not significant. Table-1 and Figure 2 are showing the ASA-PS in both the groups. ASA-PS distribution in Group A was found to be 17 with ASA-PS I& 8 ASA-PS II. In group B it was 18 ASA-PS I & 7 ASA-PS II. The P value observed was >0.05 & was found to be statistically not significant.

In both groups, pulse rate decreased from baseline.

At 15 min pulse rate decrease by 10-15%from baseline with mean value of 97 ± 7.9 in group A and 97.2 ± 8.0in group B. (p > 0.05)

At 30 min pulse rate decrease by 15-25% from baseline with mean value of 86± 7.1 in group A and 85.7 ± 7.1in group B. (p > 0.05)

At 45 min pulse rate decrease by 20-30%from baseline with mean value of 75 ± 6.5 in group A and 68.24 ± 5.9 in group B.

In both groups, systolic blood pressure decreased from baseline.

At 15 min SBP decrease by 5-10 %from baseline with mean value of 107.92 ± 9.66 in group A and 107.92 ± 9.7 in group B. (p > 0.05)

At 30 min SBP decrease from baseline with mean value of 100.88 ± 8.60 in group A and 101.36 ± 8.1 in group B. (p > 0.05)

At 45 min SBP decrease by 20-30%from baseline with mean value of 90.96 ± 9.71 in group A and 91.04 ± 7.8 in group B. (p > 0.05)

On comparison in both the groups SBP decreases but no significant difference found stastically.

In both groups, diastolic blood pressure decreased from baseline.

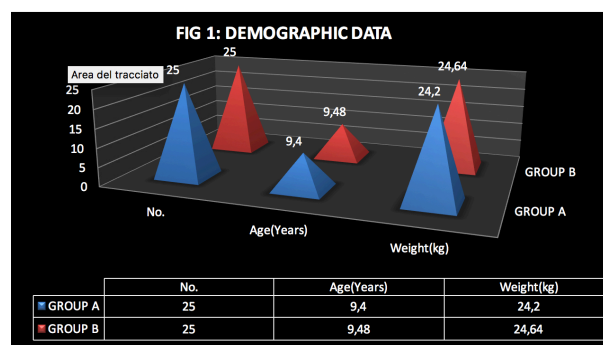
At 15 min DBP decrease from baseline with mean value of 66.08 ± 7.22 in group A and68.48 ± 9.8 in group B. (p > 0.05)

At 30 min DBP decrease from baseline with mean value of 60.56 ± 66.3 in group A and 60.48 ± 66.3 in group B. (p > 0.05)

At 45 min DBP decrease by 20-30%from baseline with mean value of 55.60 ± 4.08 in group A and 54.4 ± 4.08 in group B. (p > 0.05)

On comparison in both the groups SBP decreases but no significant difference found stastically.

See the following figures 1-6 and tables 1-6 for data analysis.



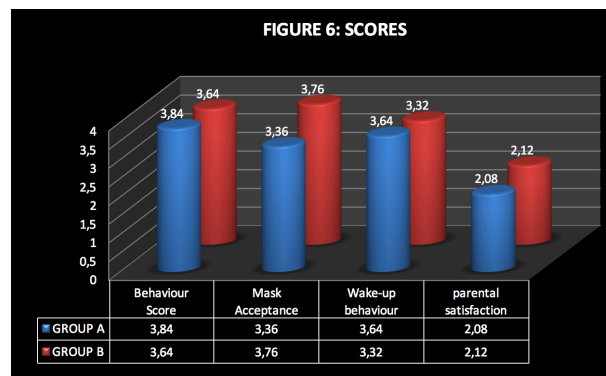
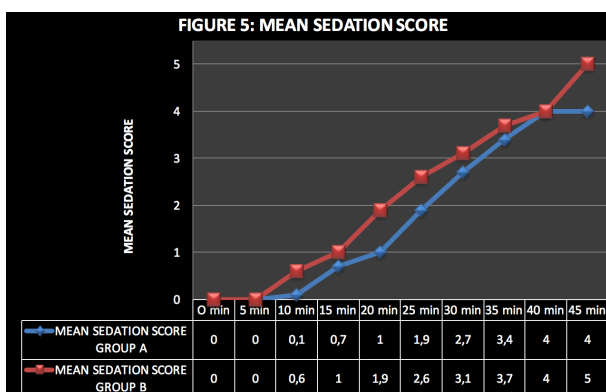
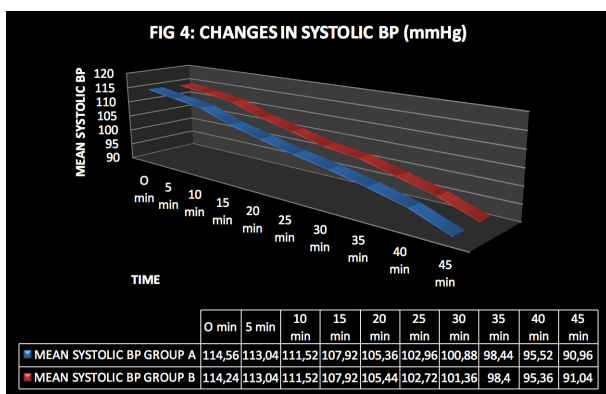
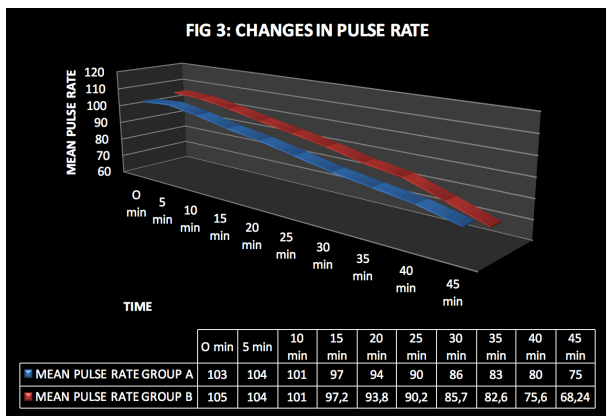
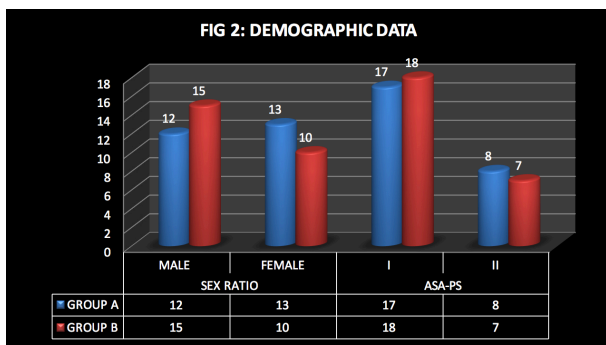


TABLE 1: DEMOGRAPHIC DATA

	GROUP A	GROUP B
No.	25	25
Age(Years)	9.40 ± 2.14	9.48 ± 2.47
Weight(kg)	24.2 ± 4.71	24.64 ± 5.20
Sex Ratio(M:F)	12:13	15:10
ASA-PS(I/II)	17:8	18:7

Values are mean ± SD or numbers.

GROUP A = Intranasal Dexmedetomidine 1µg/kg

GROUP B = Intranasal Dexmedetomidine 2µg/kg

TABLE 2: PULSE RATE CHANGES

TIME	PULSE RATE (/min)	
	GROUP A	GROUP B
0 min	103 ± 8.1	105 ± 7.7
5 min	104 ± 9.4	104 ± 9.4
10 min	101 ± 7.3	101 ± 7.3
15 min	97 ± 7.9	97.2 ± 8.0
20 min	94 ± 6.9	93.8 ± 6.9
25 min	90 ± 6.5	90.2 ± 6.5
30 min	86 ± 7.1	85.70 ± 7.1
35 min	83 ± 7.3	82.6 ± 7.3
40 min	80 ± 7.3	75.6 ± 6.2
45 min	75 ± 6.5	68.24 ± 5.9

Values are mean ± SD or numbers.

GROUP A = Intranasal Dexmedetomidine 1µg/kg

GROUP B = Intranasal Dexmedetomidine 2µg/kg

TABLE 3: CHANGES IN SYSTOLIC BLOOD PRESSURE

TIME	MEAN SYSTOLIC BP (mmHg)	
	GROUP A	GROUP B
0 min	114.56 ± 9.47	114.24 ± 9.2
5 min	113.04 ± 9.36	113.04 ± 9.4
10 min	111.52 ± 10.4	111.52 ± 10
15 min	107.92 ± 9.66	107.92 ± 9.7
20 min	105.36 ± 9.32	105.44 ± 9.6
25 min	102.96 ± 8.38	102.72 ± 8.2
30 min	100.88 ± 8.60	101.36 ± 8.1
35 min	98.44 ± 7.93	98.4 ± 8.0
40 min	95.52 ± 6.91	95.36 ± 6.9
45 min	90.96 ± 9.71	91.04 ± 7.8

Values are mean ± SD or numbers.

GROUP A = Intranasal Dexmedetomidine 1µg/kg

GROUP B = Intranasal Dexmedetomidine 2µg/kg

TABLE 4: CHANGES IN DIASTOLIC BP

TIME	MEAN DIASTOLIC BP (mmHg)	
	GROUP A	GROUP B
0 min	74.96 ± 7.53	73.6 ± 7.7
5 min	73.76 ± 7.35	73.76 ± 7.4
10 min	70.24 ± 7.77	70.24 ± 7.8
15 min	66.08 ± 7.22	68.48 ± 9.8
20 min	62.86 ± 6.97	62.56 ± 6.8
25 min	61.52 ± 6.72	61.36 ± 6.72
30 min	60.56 ± 66.3	60.48 ± 66.3
35 min	58.28 ± 10.6	59.88 ± 10.6
40 min	57.04 ± 5.91	57.2 ± 5.91
45 min	55.60 ± 4.08	54.4 ± 4.08

Values are mean ± SD or numbers.

GROUP A =Intranasal *Dexmedetomidine* 1µg/kg

GROUP B = Intranasal *Dexmedetomidine* 2µg/kg

TABLE 5: SEDATION SCORE

TIME	MEAN SEDATION SCORE	
	GROUP A	GROUP B
0 min	0.0 ±0.0	0.0±0.0
5 min	0.0±0.0	0.0±0.2
10 min	0.1±0.3	0.6±0.5
15 min	0.7±0.5	1.0±0.5
20 min	1.0±0.0	1.9±0.7
25 min	1.9±0.3	2.6±0.8
30 min	2.7±0.5	3.1±0.9
35 min	3.4±0.5	3.7±0.9
40 min	4.0±0.4	4.0±0.9
45 min	4.0±0.4	5.0±0.7

Values are mean ± SD or numbers.

GROUP A =Intranasal *Dexmedetomidine* 1µg/kg

GROUP B = Intranasal *Dexmedetomidine* 2µg/kg

TABLE 6: SCORES

	GROUP A	GROUP B
Behaviour Score	3.44 ± 0.71	3.64 ±0.56
Mask Acceptance score	3.36 ±0.48	3.76 ±0.72
Wake-up behaviour score	3.64 ±0.48	3.32 ±0.55
parental satisfaction score	2.08 ±0.27	2.12 ±0.33

Values are mean ± SD or numbers.

GROUP A =Intranasal *Dexmedetomidine* 1µg/kg

GROUP B = Intranasal *Dexmedetomidine* 2µg/kg

Discussion

This study was designed to evaluate the potential role of intranasal dexmedetomidine as premedication before the induction of anesthesia. Children of age group of 6-12 years were divided into two groups of 25 each randomly. Two doses of dexmedetomidine- 1 µg/kg and 2 µg/kg were instilled intranasally into group A and group B respectively. Children were evaluated for sedation and behaviour scores.

Satisfactory pre-operative sedation in this study was defined as a child that was asleep with a sedation score of 3 or 4 when transferred from the holding area to the operating theatre in preparation for induction of anaesthesia. If a child was drowsy and appeared sleepy the sedation status was still classified as unsatisfactory (score 1 or 2). Whilst this degree of sedation is necessary for young children, it may not be so for older children who

usually remain calm and cooperative to induction of anaesthesia when their sedation level is lighter, probably because they have a better understanding of the anaesthetic process.

Previous studies have shown a dose-dependent increase in sedation levels in adults when dexmedetomidine is given intravenously, therefore we expected an increase in the proportion of patients with satisfactory sedation when we doubled the dose of intranasal dexmedetomidine.

We administered intranasal dexmedetomidine by simply dripping the drug into both nostrils from a 1-ml tuberculin syringe. In our study, we found that at 30 minutes 60% and 75% of the children attained a satisfactory level of sedation after 1 µg/kg and 2 µg/kg intranasal dexmedetomidine respectively. But mean sedation score is less satisfactory (2.7±0.5 vs. 3.1±0.9) at 30 minute with 1 µg/kg dose. And at 45 minutes all the children attained satisfactory sedation level in both group but mean sedation score is higher with 2 µg/kg dose. Children premedicated with 2 µg/kg of intranasal dexmedetomidine (Mean value 5.0±0.7) attained more significant and satisfactory sedation score at parental separation and at induction of anesthesia than those patients who received 1 µg/kg of intranasal dexmedetomidine (Mean value 4.0±0.4).

64% of children in group A and 40% in group B allowed inhalational induction without fear of mask and remain cooperative with reassurance (Mask acceptance score is 3). 36% of children in group A and 44% in group B remain calm and cooperative (Mask acceptance score is 4). However only 16% of children in group B remain asleep (Mask acceptance score is 5) in comparison no children was fall asleep in group A. so we found that children who were administered higher dose of intranasal dexmedetomidine had better mask acceptance and allowed easy administration of inhaled anesthesia.

Our behaviour scoring system did not allow us to evaluate the anxiety level of children. We have shown in this study that the behaviour of children at separation

from parents and at induction of anesthesia were similar in children who received 1 µg/kg and 2 µg/kg intranasal dexmedetomidine based on our behaviour scale.

Hemodynamic effects

In this study, we have shown that preoperative 1 and 2 µg/kg intranasal dexmedetomidine reduces HR and blood pressure in healthy children during the first hour after drug administration. In group A who were administered 1 µg/kg intranasal dexmedetomidine, we have shown reduction in HR by 17-23 % and BP by 15-20%. In group B who were administered 2 µg/kg intranasal dexmedetomidine, we have shown reduction in HR by 18-25% and BP by 20-25%. We found significant hypotension (BP decreases >30% from base line) in one patient in Group B.

Limitations of this study

We did not evaluate the onset time and peak effect of the two doses of intranasal dexmedetomidine or the blood concentrations. In this study, the premedication period was 45 min for intranasal dexmedetomidine; however, some children were transferred to the OR slightly earlier in order not to interfere with the normal OR schedule. If a longer premedication period had been allowed, possibly more subjects could have attained satisfactory sedation at separation from parents and at induction of anesthesia.

Conclusion

Intranasal Dexmedetomidine is a technique for producing sedation in children. It causes no discomfort during administration. Intranasal drug administration is relatively quick, simple, and may have benefits over transmucosal routes or rectal administration, which requires more patient cooperation.

In this study we compared between two doses - 1 µg/kg and 2 µg/kg of Intranasal Dexmedetomidine as a premedication for children of age group 6 to 12 years .Two groups consisting of 25 children each were divided and were intranasally administered dexmedetomidine in doses of 1µg/kg and 2 µg/kg respectively.

The sedation score, behavioural score, intraoperative and post-operative hemodynamics were observed and compared between the two groups. The group which was administered 2 mcg/kg of intranasal dexmedetomidine showed better results.

The sedation and behavioural scores , intraoperative hemodynamics, post-operative recovery were found to be better in group which was given 2 mcg/kg of intranasal dexmedetomidine as compared to the group given 1 mcg/kg of the drug.

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Abbreviations

ASA-PS: American Society of Anaesthesiologist- Physical Status

CBF: Cerebral Blood Flow

CRMO₂: Cerebral Oxygen Consumption

FDA: Food And Drug Administration

HR: Heart rate

ICU: Intensive Care Unit

IM: intramuscular

IN: intranasal

IV: Intravenous

MAP: Mean Arterial Blood Pressure

MAC: Monitored Anesthesia Care

ml: Millilitre

Ng: Nanogram

PaO₂ : Partial Pressure of Oxygen

PaCO₂ : Partial Pressure of Carbon Dioxide

SD: Standard Deviation