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Research Article

A COMPARISON OF EFFICACY OF INTRANASAL FENTANYL AND INTRANASAL DEXMEDETOMIDINE AS PREMEDICATION IN PEDIATRIC PATIENTS

PREMGEETH RISHIKESH, ELIZABETH JOSEPH, THOMAS JOSEPH

Department of Anaesthesiology, Government Medical College, Kottayam, Kerala, India. Email: premgeeth104@gmail.com

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ABSTRACT

Objective: The objective of the study was to determine the effects of intranasal fentanyl compared to intranasal dexmedetomidine, when used for relieving pre-operative anxiety in children on the basis of onset and quality of anxiolysis, parental separation, hemodynamic stability, and cooperation to mask holding.

Methods: A prospective observational study was conducted in Government Medical college Kottayam for a period of 12 months from December 2021 to December 2022, randomly assigned a total of 40 pediatric patients (the American Society of Anesthesiologists I and II) in the age group 3–6 years, undergoing elective surgeries requiring general anesthesia who received either intranasal fentanyl (group F) or intranasal dexmedetomidine (group D). Onset and quality of anxiolysis was compared using modified Yale pre-operative anxiety scale. Parental separation score, hemodynamic stability, and cooperation to mask holding were compared. Data collected were analyzed using SPSS version 25.

Results: Children who received intranasal fentanyl as premedication had better quality and onset of anxiolysis as compared to dexmedetomidine group. In parent-child separation, intranasal fentanyl was found to be better than intranasal dexmedetomidine.

Conclusion: We conclude that intranasal fentanyl is superior to intranasal dexmedetomidine in relieving pre-operative anxiety in pediatric population of age 3–6 years.

Keywords: Intranasal fentanyl, Intranasal dexmedetomidine, Pediatric premedication.

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INTRODUCTION

Surgery and pre-operative period is a very stressful experience for patients of all age groups. Adults and children encounter with anxiety and fear even before minor surgical procedures. Pediatric population are much more susceptible to pre-operative fear and anxiety due to sudden parent–child separation before surgery. Administration of premedication in pediatric population and smooth induction is a difficult task for most of the anesthesiologists. It is easy to manage a calm, cooperative child compared to a crying irritable one. Induction of anesthesia also will be an easy task in a calm child. Hence, relieving pre-operative anxiety is an important concern in most of the pediatric procedures and various surgeries. Majority of children are premedicated through oral and intravenous route. Oral route may not be successful always especially in an uncooperative, irritable child. Moreover, for giving drug through intravenous route, we need an iv line. However, an iv line may not be available always. All these led to search for an alternate route, which is more easy and patient friendly. Intranasal route is a popular option as it allows relatively rapid delivery of drug to bloodstream and central nervous system with minimal patient discomfort [1].

Fentanyl is a synthetic opioid analgesic with rapid onset and short duration of action. Opioids act as agonists at specific opioid receptors at presynaptic and postsynaptic sites in the CNS (mainly the brainstem and spinal cord) as well as in the periphery [2]. Dexmedetomidine is a highly selective alpha 2 agonist. It can achieve its effects such as anxiolysis, analgesia, and sedation without causing much respiratory depression [3]. We conducted this study to compare the efficacy of fentanyl and dexmedetomidine given through intranasal route as pediatric premedication and thereby making induction of anesthesia an easy task in pediatric population.

METHODS

After getting permission from SRC, IRB, Institutional Ethics Committee, Department of Anesthesiology, Department of Pediatric surgery, Government Medical College, Kottayam, an informed consent obtained from parents or guardians of the patients. The present study was conducted prospectively in 40 patients in the age group of 3–6 years of either sex of the American Society of Anesthesiologists (ASA), Physical status Class I and II admitted in Government Medical College Kottayam scheduled to undergo elective surgery under general anesthesia.

Inclusion criteria

The following criteria were included in the study:

1. Children in the age group 3–6 years
2. ASA I and II
3. Patients undergoing elective surgery under general anesthesia.

Exclusion criteria

The following criteria were excluded from the study:

1. Children with ASA physical status Classes III and IV
2. Allergy to the drugs under study
3. Patients with any intranasal pathology/congenital anomaly of upper airway tract
4. Patients undergoing emergency surgeries
5. Children with bradycardia.

Methodology

No sedatives were given in children who were included in the study. Patients were kept fasting in the pre-operative period according to ASA fasting guidelines (clear fluids = 2 h, semi-solid food = 6 h, and solid foods = 8 h). Patients were randomly allocated into two groups, consecutively until the sample size of 40 is reached, without any specific criteria. The first group (group F) was given intranasal fentanyl and the second group (group D) received intranasal dexmedetomidine. A detailed pre-anesthetic checkup was conducted in patients chosen on the basis of inclusion criteria, a day before surgery and was documented which included a thorough history taking and physical examination. Mother/parent was explained in detail about the study and verbal consent was

obtained. Patients were investigated for blood tests such as CBC, PT, INR, APTT, RFT, serum electrolytes, and other necessary investigations.

On the day of surgery, child along with mother/parent was taken in to the recovery room after getting an informed consent from parent after confirming patient identity. ECG, SpO2, and blood pressure (BP) monitors were attached and baseline values were noted. Mother/parent was counseled regarding the study, and informed consent was obtained. Patients were given calculated doses of drugs instilled into both nostrils equally. Group F patients were premedicated with intranasal Fentanyl 1.5 mg/kg as nasal drops 30 min before surgery. Group D patients were given intranasal dexmedetomidine 1 mg/kg as nasal drops 30 min before surgery. Heart rate, BP, Spo2, and respiratory rate were noted at the time of administration of drug and patients were monitored every 5 min for the next 30 min. Anxiety scoring was done every 5 min. Child was taken to operation theater after 30 min of administration of drug.

Level of pre-operative anxiolysis was calculated using modified YALE pre-operative anxiety scale (mYPAS). The mYPAS was developed in 1995 and modified in 1997 [4].

The mYPAS score

Activity

1. Looking around, curious, playing with toys, reading (or other age appropriate behavior); moves around holding area/treatment room to get toys or go to parent; and may move toward OR equipment.
2. Not exploring or playing may look down, may fidget with hands or suck thumb (blanket), may sit close to parent while waiting, or play has a definite manic quality.
3. Moving from toy to parent in unfocused manner, non-activity derived movements; frenetic/frenzied movement or play; and squirming, moving on table, may push mask away, or clinging to parent.
4. Actively trying to get away, pushes with feet and arms, may move whole body; in waiting room, running around unfocused, not looking at toys or will not separate from parent, and desperate clinging.

Vocalizations

1. Reading (non-vocalizing appropriate to activity), asking questions, making comments, babbling, laughing, and readily answers questions but may be generally quiet; child too young to talk in social situations or too engrossed in play to respond
2. Responding to adults but whispers, "baby talk," only head nodding
3. Quiet, no sounds, or responses to adults
4. Whimpering, moaning, groaning, and silently crying
5. Crying or may be screaming "no"
6. Crying, screaming loudly, and sustained (audible through mask).

Emotional expressivity

1. Manifestly happy, smiling, or concentrating on play
2. Neutral, no visible expression on face
3. Worried (sad) to frightened, sad, worried, or tearful eyes
4. Distressed, crying, extreme upset, may have wide eyes.

State of apparent arousal

1. Alert, looks around occasionally, notices watches what anesthesiologist does with him/her (could be relaxed)
2. Withdrawn child sitting still and quiet may be sucking on thumb or face turned into adult
3. Vigilant looking quickly all around may startle to sounds, eyes wide, body tense
4. Panicked whimpering may be crying or pushing others away, turns away.

Use of parents

1. Busy playing, sitting idle, or engaged in age appropriate behavior and does not need parent; may interact with parent if parent initiates the interaction
2. Reaches out to parent (approaches parent and speaks to otherwise silent parent), seeks and accepts comfort, may lean against parent
3. Looks to parents quietly, apparently watches actions, does not seek contact or comfort, accepts it if offered or clings to parent
4. Keeps parent at distance or may actively withdraw from parent, may push parent away or desperately clinging to parent, and will not let parent go.

Note: The use of parents is only scored when parent is present.

Scoring: Divide each item rating by the highest possible rating (i.e., 6 for the "vocalizations" item and four for all other items), add all of the produced values, divide by 5 (or 4 if E is not rated), and multiply by 100.

Total adjusted score = (A/4+B/6+C/4+D/4+E/4)100/5.

Ranges from 0 to 100.

Onset of anxiolysis = score ≤40.

Parental separation of the child was noted with child-parent separation score.

1. Patient fearful and crying, not quieted with reassurance
2. Patient slightly fearful and/or crying, quieted with reassurance
3. Patient unafraid, cooperative or asleep.

Score ≥ 3 considered satisfactory.

Cooperation to mask holding was assessed as,

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

Score ≥4 considered satisfactory.

The surgery was carried out and after surgery the patients were reversed and extubated. They were observed for 1 h postoperatively for full recovery, and then, the patients were shifted to post-operative wards for further management. No complications were noted in either of the groups.

Data management and statistical analysis

Data were numerically coded and entered into Microsoft Excel spread sheet. Analysis of data was done using SPSS 25 software. Categorical variables were expressed as proportions and quantitative variables were expressed as mean and standard deviation. For qualitative data, frequency and percentage along with Chi-square test were used. For quantitative variables, t-test was used and was considered statistically significant whenever p≤0.05.

RESULTS

The study was conducted in the Department of Anesthesiology, Government Medical College, Kottayam from December 30, 2021, to December 29, 2022. The study population included 40 pediatric patients aged between 3 and 6 years belonging to ASA class I and II undergoing elective surgeries under general anesthesia. The participants were the patients who satisfied the inclusion criteria.

The baseline mYPAS score was assessed initially and reassessed periodically at 5 min, 10 min, 15 min, 20 min, 25 min, and 30 min after administration of drugs in both groups and was compared. Baseline values of mYPAS score showed no statistically significant difference between the two groups with p=0.399. It was observed that at 15, 20, 25, and 30 min after giving the drug, there was a statistically significant difference in anxiolysis between group F and Group D. P-value obtained was 0.002, 0.000, 0.000, and 0.000, respectively (Table 1). Hence the data was found to be statistically significant. The mean onset of anxiolysis in group F was 15 min, whereas the mean onset of anxiolysis in group D

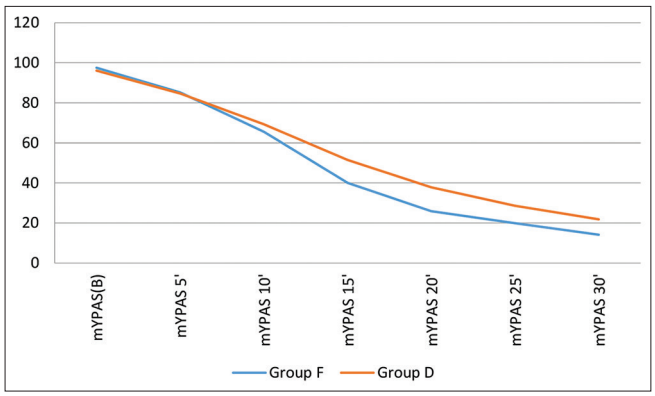

Fig. 1: Comparison of study participants based on m YPAS scores (baseline, 5 min, 10 min, 15 min, 20 min, 25 min, and 30 min)

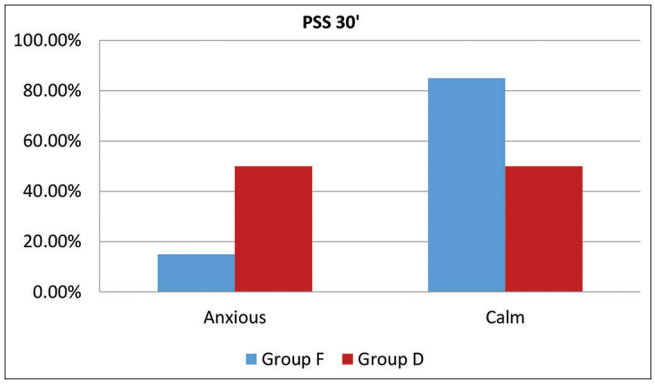

Fig. 2: Comparison of study participants based on parental separation score at 30 min

was 20 min. Group F was found to have an early onset of anxiolysis compared to group D (Fig. 1).

It was found that about 85 % of Group F patients were calm at 30 min in terms of parental separation score, whereas about 50% of patients in Group D were found to be calm at 30 min (Fig. 2). P-value was found to be 0.018 (<0.05) (Table 2). Hence, there was significant difference in parental separation score at 30 min between the two groups. Fentanyl was found to be superior to dexmedetomidine.

DISCUSSION

Pre-operative anxiety is more common in pediatric patients compared to adults. Relieving anxiety preoperatively in pediatric patients can make induction of anesthesia an easy task for the anesthesiologist. Our study was aimed at comparing the efficacy of intranasal fentanyl and intranasal dexmedetomidine when used as a premedicant in pediatric population. We conducted the study in 40 pediatric patients in the age group of 3–6 years scheduled to undergo elective surgery under general anesthesia, who received either fentanyl or dexmedetomidine intranasally and the difference in efficacy of the two drugs was compared.

Chatrath *et al.* conducted a double blinded study in a group of 75 pediatric patients comparing fentanyl and dexmedetomidine and found that fentanyl was associated with better onset and quality of anxiolysis compared to dexmedetomidine [5]. The results were similar to our study. They also concluded that there was no statistically significant difference in parental separation between the two groups, whereas, in our study, we found that fentanyl produced better parent child separation than dexmedetomidine.

Moore *et al.* did a randomized clinical trial in 33 young children scheduled for treatment of dental caries, and they found that oral

Table 1: Comparison of study participants based on mYPAS scores (baseline, 5 min, 10 min, 15 min, 20 min, 25 min, and 30 min)

Group	N	Mean	SD	t	p-value
mYPAS (B)					
Group F	20	97.5000	4.71211	0.853	0.399
Group D	20	96.1250	5.45466		
mYPAS 5'					
Group F	20	85.1750	7.28467	0.250	0.804
Group D	20	84.6375	6.26995		
mYPAS 10'					
Group F	20	65.550	8.6540	1.211	0.233
Group D	20	69.250	10.5762		
mYPAS 15'					
Group F	20	40.000	9.6341	3.413	0.002
Group D	20	51.475	11.5445		
mYPAS 20'					
Group F	20	25.875	6.8861	4.765	0.000
Group D	20	37.825	8.8515		
mYPAS 25'					
Group F	20	19.940	1.5635	5.585	0.000
Group D	20	28.600	6.7563		
mYPAS 30'					
Group F	20	14.180	2.4213	11.233	0.000
Group D	20	21.830	1.8476		

Table 2: Comparison of study participants based on parental separation score at 30 min

Group	PSS 30'		Total	χ^2	p-value
	Anxious	Calm			
Group F					
Count	3	17	20	5.584	0.018
%	15.0	85.0	100.0		
Group D					
Count	10	10	20		
%	50.0	50.0	100.0		
Total					
Count	13	27	40		
%	32.5	67.5	100.0		

transmucosal fentanyl was associated with better parental separation scores [4]. We also observed in our study that fentanyl created better parent child separation than dexmedetomidine.

Study conducted by Feld *et al.* compared oral transmucosal fentanyl versus placebo and they found that oral fentanyl produced significantly less anxiety compared with placebo [6]. In our study, also we could find that fentanyl was associated with good anxiolysis than dexmedetomidine.

Study done by Rajan *et al.* observed that fentanyl and dexmedetomidine have comparable hemodynamic stability [7]. In our study, also we found that both fentanyl and dexmedetomidine were not associated with any significant hemodynamic fluctuations and both the drugs were comparable in terms of hemodynamic stability. We observed in our study that, that there was no significant deviation from the base line vitals such as HR, SBP, DBP, and SpO2 in the two groups.

Yadav *et al.* compared fentanyl-midazolam and dexmedetomidine-midazolam combinations and concluded that both are effective for awake fiberoptic intubation under topical anesthesia [8]. They found that dexmedetomidine was associated with more stable hemodynamics. In our study, we found that both the drugs were comparable in terms of hemodynamics.

In our study, we found that there was no significant difference between the two groups in terms of cooperation to mask holding. Chatrath *et al.* also obtained results similar to our study.

Mason *et al*. conducted a study in 2008, 250 pediatric population were studied and were found that intravenous dexmedetomidine sedation was associated with modest fluctuations in HR and blood pressure [9].

Another study conducted in a group of 60 people in 2007 by Bayrak *et al*. compared oral tramadol, oral midazolam, and intranasal sufentanyl showed that intranasal sufentanil and oral midazolam are more appropriate premedication options than tramadol drops in children [10].

In 1992, Stanley and Ashburn conducted a study on novel delivery routes and sufentanil and they found that easy separation from parents was achieved in 86% of the children 10 min following administration of the premedication. They concluded that nasal transmucosal drug delivery may have value, especially in frightened or uncooperative children [11].

The baseline characteristics of the population in terms of age, gender, weight, and ASA grades were compared in our study and no significant differences were seen. Among the total 40 participants chosen 55% belonged to age group of 3–4 years, rest 45% were from age group of 5–6 years. Of the total 40 children studied, there were 20 males and 20 females. Majority of children (72.5%) were having a weight between 10 and 20 kg. About 15% patients were having a weight <10 kg and 12.5 % of population were having a weight more than 20 kg. Among the participants, 92.5% were ASA1 patients, and the rest were ASA 2.

The base line mYPAS score was found to be comparable in both the groups. The onset of anxiolysis was found to be early in the fentanyl group compared to dexmedetomidine group. Fentanyl had early onset with mean onset of anxiolysis of 15 min, whereas dexmedetomidine had mean onset of anxiolysis at 20 min.

In our study, we found that fentanyl has better quality of anxiolysis compared to dexmedetomidine as evidence by significant reduction in mYPAS score at 15 min, 20 min, 25 min, and 30 min with $p<0.05$. Fentanyl was found to have better pre-operative anxiolysis compared to dexmedetomidine group.

In our study, the baseline parental separation score was found to be comparable in both groups. Moreover, we observed that at the end of 30 min, there was statistically significant difference in parental separation score between the two groups. At the end of 30 min, 85 % patients who received fentanyl intranasally were found to be calm, whereas only 50% patients from the dexmedetomidine group were found to be calm. Fentanyl was found to be superior to dexmedetomidine in child-parent separation. No adverse effects were noted in any of the patients who received drugs intranasally.

Limitations

1. Drug dropper caused anxiety in some children.

CONCLUSION

The results of this study suggest that children who received intranasal fentanyl as premedication had better quality and onset of anxiolysis, and better parent-child separation as compared to children who received intranasal dexmedetomidine. Hence, we conclude that intranasal fentanyl is superior to intranasal dexmedetomidine in relieving pre-operative anxiety in pediatric population.

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