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Original Research Paper

Anaesthesiology

A COMPARATIVE EVALUATION OF INTRANASAL KETAMINE AND INTRANASAL DEXMEDETOMIDINE FOR PREMEDICATION IN PAEDIATRIC SURGERIES.

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ABSTRACT Any surgical procedure and the preoperative phase is very stressful for both the parents and the children. Premedication in children should aim at relieving this stress and anxiety. Several drugs have been used to find the best sedative agent and the best route of administration of these drugs in children. Both the drugs ketamine and dexmedetomidine are effective for premedication in children undergoing surgery. Comparison of the efficacy of intranasal ketamine (6mg/kg) and intranasal dexmedetomidine (1mcg/kg) as premedication in pediatric patients undergoing elective surgeries was done. This was a randomized, comparative, double blinded, prospective, single center study conducted in a tertiary care institute. It was found that Intranasal injection of ketamine (6mg/kg) as premedication proved better to relieve the Parental separation anxiety and for better mask acceptance in pediatric patients between 2-9 years of age. Ketamine showed significantly better response than dexmedetomidine in context to no fear and anxiety and aggression to intravenous cannulation, and good behavioral response, and children were calm during parental seperation while taking them to OR, and also, parents were highly satisfied by this clinical outcome.

KEYWORDS : Pediatric patients, Premedication, Ketamine, Dexmedetomidine, Parental Separation Anxiety.

INTRODUCTION

Any surgical procedure and the preoperative phase is very stressful for both the parents and the children. Most of the preschool children suffer from anxiety and appreciation when they are separated from their parents before induction of anaesthesia[1]. Anxiety and fear leads to increased levels of chatecholamines in the body this results in tachycardia, hypertension and tacypnoea[2]. Premedication in children should aim at relieving this stress and anxiety. There is increased risk of stormy induction and postoperative emotional reactions and behavioural changes [3]. The preoperative period is a stressful event for the majority of individuals undergoing surgery more so in the children. An effort should be made to make the whole procedure tolerable and pleasant to the children. Anesthesiologists who allow parental presence during induction of anesthesia or use sedative premedication least frequently, and vice versa. The non-pharmacological ways that can be used to relieve the anxiety are as following

a. A friendly visit by the anesthesiologist to build a rapport with the child.[4]
b. Giving a brief idea about the procedure.
c. Allowing parents inside the operation theatre.
d. Sedative premedication may be more effective in this regard.[5]

Pharmacological ways like giving sedation as, premedication can be used.

A premedication drug must have an acceptable, non-traumatic route of administration in order to avoid extra stress to the child.Many studies have shown that intranasal route is an effective way to administer premedication and sedation to children. Intranasal route has many advantages. Due to the high mucosal vascularity in the nasal cavity, this route has rapid and almost complete absorption within one to two hour in the systemic circulation. Intranasal medication delivery offers an alternative method of drug delivery that is often as fast in onset as intravenous medication, usually painless, inexpensive, easy to deliver, and effective in a variety of acute pediatric medical conditions. Ketamine has been used for preanesthetic sedation by many routes like oral, intramuscular, rectal, and intranasal. Intranasal ketamine permits pleasant and rapid separation of children from their parents, cooperative acceptance of mask, inhalational induction and of monitoring probe. It does not cause prolonged post anesthetic recovery or delayed discharge. Dexmedetomidine is an alpha 2 agonist with a more selective action on the alpha 2- adrenoceptor and a shorter half-life - 2hr, its bioavailability is 72.6–92.1% through nasal mucosa, when administered via intranasal route. It has analgesic and sedative action with no risk of respiratory depression and has been used as premedication. Ketamine at dose of 6mg/kg proves better than dexmedetomidine at dose of 1mcg/kg in terms of parental separation anxiety and mask acceptance. Intranasal ketamine permits pleasant and rapid separation of children from their parents, cooperative acceptance of mask inhalation induction and of monitoring probe. It does not cause prolonged post anesthetic recovery or delayed discharge.[6]

AIM-

To compare the efficacy of intranasal ketamine (6mg/kg) and intranasal dexmedetomidine (1mcg/kg) as premedication in pediatric patients undergoing elective surgeries.

OBJECTIVES-

1. To study the effects of intranasal ketamine as premedication
2. To study the effects of intranasal dexmedetomidine as premedication
3. To evaluate the effects by parental separation anxiety score and mask acceptance scale in children
4. To assess the hemodynamic changes.

MATERIALS AND METHODS-

Sample Size Estimation- Sample size calculation for this study was done by using α (type 1error) = 0.05 and (1-β) i.e.study power is set at 80 %. The non inferiority margin of 20 % for mask acceptance score was assumed. The aim of this study was "To evaluate and compare the effect of intranasal Dexmedetomidine and intranasal Ketamine for premedication in pediatric anesthesia" .Mask acceptance score was one of the criteria used to compare the effect of intranasal dexmedetomidine and intranasal Ketamine. Using the data from randomized control trial by Bhat eta al. mask was acceptable in 18 (66.6%) patients in dexmedetomidine and Ketamine group and 14 (52%) in group dexmedetomidine only. Thus we used assumed proportion in Ketamine =0.666 and Assumed proportion in dexmedetomidine = 0.52. Then considering formula for sample size calculation by

Sample Size Calculation:

$$n = 2.\left(\frac{Z_{1-\alpha} + Z_{1-\beta}}{\delta_0}\right)^2 .p(1-p)$$

n = 30 IN EACH GROUP

Study Designs: This was a randomized, comparative, double blinded, prospective, single center study conducted in a tertiary care institute. The study was carried out after obtaining approval from the ethical committee of the institute.

Selection of cases:

Inclusion Criteria:

1. Total 60 children
2. Age 2 years to 9 years
3. Sex: Male or Female
4. ASA Grade I & II.
5. Scheduled to undergo elective surgery under General Anesthesia lasting for 1 to 2 hrs duration were enrolled in this prospective randomized control study. Surgeries Like: Herniotomy, Circumcision, Skin grafting, Colostomy, Hydrocoele repair, Upper limb and lower limb surgeries and ear surgeries.

Exclusion Criteria:

1. Parent or children refusal
2. ASA grade III and above
3. Known allergy or hypersensitivity to Dexmedetomidine and Ketamine
4. Patient with upper respiratory tract infection
5. History of any nasal pathologies or surgeries
6. Major organ dysfunction
7. Psychological disorder
8. Congenital heart disease

After getting approval from the institutional ethics committee and taking a written informed consent from the parents of the child, the child was enrolled for the study.60 pediatric patients between age 2-9 years who are fit according to the inclusion criteria were chosen. These patients were then randomly divided into two groups of 30 each, namely Group D, receiving dexmedetomidine and Group K, receiving ketamine were given these drugs through insulin syringe directly into the nostrils, before induction. GROUP K (n=30): -Patients receiving ketamine at dose of 6mg/kg, intra-nasally. GROUP D (n=30):- Patients receiving dexmedetomidine at dose of 1mcg/kg, intra-nasally.

Patients were kept NBM for at-least 6 hours and were assessed in the pre-op room, all monitors attached and baseline heart rate, blood pressure and spO2 were recorded before giving the premedication drugs intra-nasally through the insulin syringe. Patients were monitored for heart rate, blood pressure and spO2 at 10mins, 30mins, 45 mins till the patient is taken in the operating room. Group D patients received intranasal dexmedetomidine (1μg/kg) and Group K patients were given intranasal ketamine (6 mg/ kg) before induction of anesthesia, using insulin syringe. Both the drugs used were free of any kind of preservative. Children were made to lie on one side (lateral position) and the calculated dose of drug diluted in distilled water to a total volume of 1 ml was administered, 0.5 ml in each nostril, with the help of an insulin syringe.

Vital signs (heart rate, blood pressure, oxygen saturation) were recorded before administering the intranasal drug and again at an interval of every 10 minutes, 30 minutes, 45 minutes, meanwhile the patient is taken in the operating room. Intravenous line was taken with intracath. size 22 or 24. The Parental separation anxiety scale (PSAS) (Table 1) was used and scoring done after taking the child in the operating room. The Mask acceptance scale (Likert scale) (Table 2) was used to score the child after starting of bag mask ventilation.

Table 1: Parental separation anxiety scale (PSAS)

Behavior of the child during separation from parents	Criteria	Score
Excellent	Patient unafraid, cooperative, or asleep	1
Good	Slightly afraid/ Good crying, quiet with reassurance	2
Fair	Moderately afraid and crying, not quiet with reassurance	3
Poor	Crying, need for restraint	4

Table 2: Mask Acceptance Scale (Likert Scale)

Behaviour of child during mask ventilation	Criteria	Score
Excellent	Unafraid, cooperative, accepts mask readily	1
Good	Slight fear of mask, easily reassured	2
Fair	Moderate fear of mask, not calmed with reassurance	3
Poor	Terrified, crying, or combative	4

Score of 1-2 was satisfactory
Score of 3-4 was unsatisfactory

Randomization was done by computer generated random numbers.

Blinding: The insulin syringes were loaded with either Ketamine or Dexmedetomidine by different anesthetist other than the one who conducted the study. Nil by mouth for 8 hours was confirmed pre-operatively. Monitors Electrocardiogram (ECG), Noninvasive blood pressure (NIBP), Spo2 were attached. After making note of baseline parameters, drug either ketamine or dexmedetomidine was instilled inside the nares of the child by the anesthetist without informing the parents about the drug which is being given.

PARENT SEPERATION ANXIETY SCORE was noted. Child was taken inside the operation theatre. Intravenous line was taken with intracath. size 22 or 24, slowly intravenous fluid started. Child was monitored for every 10 mins inside the operation theatre for all the parameters like HR, SBP, DBP, SPO2, MASK ACCEPTANCE SCORE. Preoxygenation with 100% oxygen done for 3 mins.

Anesthesia Technique: Patients undergoing this study went thorough preoperative assessment including detailed case history, physical examination and all necessary investigations. Patients were kept NBM (nil by mouth) for at least 4 hours prior to procedure. Sedative premedication by intranasal route was given 45 minutes prior to the induction according to the group allocated. Monitoring of HR, SBP, DBP, SPO2, PARENT SEPARATION ANXIETY SCORE for every 10 minutes and at baseline, MASK ACCEPTANCE SCALE after taking the patient in the operation theatre, Occurrence of side effects, if any were noted. Patients were shifted to the O.T. Intravenous line was taken with intracath size 22 or 24. Monitors were attached.HR, NIBP, SPO2 and ECG were recorded.

Premedication in Operation Theatre: Inj. Ondansetron 0.08 mg/kg intravenously, IV fluids slowly started in both group of patient according to patients weight. General anesthesia using balanced anesthesia technique was given in both group. Operating room temperature was kept between 21-23°C.Perioperatively HR, SBP, SPO2, ECG, sedation and, any side effects were recorded. Patients were monitored for nausea, vomiting, hypotension and/or hypertension, Bradycardia and/or tachycardia, Dry mouth, skin rash, sedation, excessive secretions, dissociation.

Monitoring Chart Was Recorded For Data Analysis: HR, SBP, DBP, SPO2, PARENT SEPARATION ANXIETY SCORE were recorded for every 10 mins and at baseline, MASK ACCEPTANCE SCALE was recorded after taking the patient in the operation theatre.

Statistical Analysis was done using Unpaired-t test for comparison of age, weight, HR, SBP, DBP, SPO2, PARENTAL SEPERATION ANXIETY SCORE, MASK ACCEPTANCE SCALE values. Statistical analysis for comparison of sex and ASA Grade was done by Chi square test. P value < 0.05 was considered as statistically significant.

RESULT TABLES AND GRAPHS

Table 3: Comparison of Mean Age between Groups.

Group	No of patients	Mean Age (In years)	Standard deviation	P Value
KETAMINE	30	5.27	2.21	0.6956
DEXMEDETOMIDINE	30	5.50	2.32	

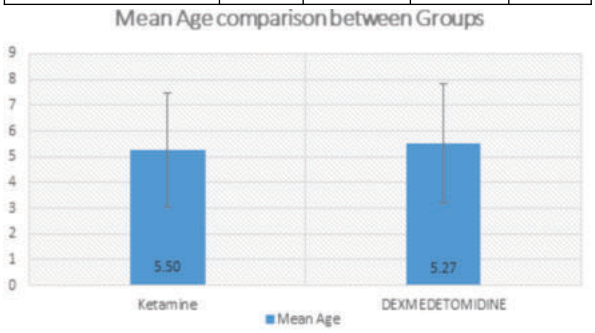

Figure 1: Column Chart Showing mean age distribution

Table 4: Gender Distribution between Groups.

	KETAMINE	DEXMEDETOMIDINE	Total	P Value
Male	18(60)	17(56.67)	35.00	0.7953
Female	12(40)	13(43.33)	25.00	
Total	30(100)	30(100)	60.00	

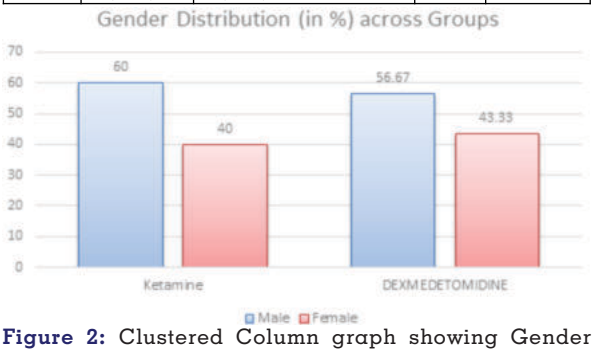

Figure 2: Clustered Column graph showing Gender Distribution.

Table 5: Comparison of Mean weight between Groups.

Group	No of patients	Mean	Standard deviation	P Value
KETAMINE	30.00	13.77	3.83	0.2367
DEXMEDETOMIDINE	30.00	12.63	3.55	

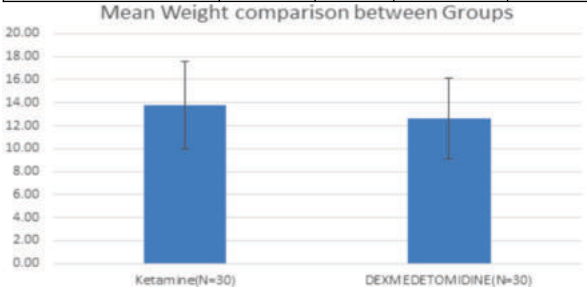

Figure 3 : Column graph showing mean weights.

Table 6: Comparison of Heart rate at Different Time points

Heart rate in beats/Minutes	Ketamine (N=30)		Dexmedetomidine (N=30)		
	Mean	Standard Deviation	Mean	Standard Deviation	P-value
baseline	108.30	5.93	110.00	7.21	0.3227
drug instillation (0 min)	110.03	7.34	108.57	6.12	0.4062
10 min	112.47	5.07	105.13	4.53	<0.0001
30 min	112.00	6.01	101.93	4.57	<0.0001
45 min	112.10	7.38	94.50	3.10	<0.0001

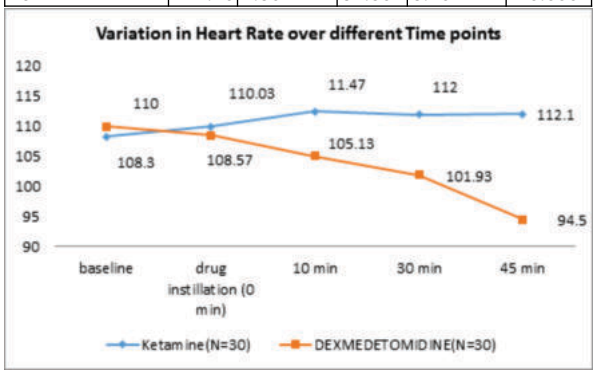

Figure 4 : Line with markers chart showing Heart rate at different Time points.

Table 7: Comparison of Systolic Blood Pressure at different Time points

Systolic Blood Pressure in mm Hg	Ketamine (N=30)		Dexmedetomidine (N=30)		
	Mean	Standard Deviation	Mean	Standard Deviation	P-value
baseline	101.13	5.22	101.13	6.65	0.7964
drug instillation (0 min)	106.07	4.74	106.07	8.77	0.5123
10 min	107.60	4.65	107.60	6.93	0.0007
30 min	109.20	4.54	109.20	4.74	<0.0001
45 min	108.07	4.77	108.07	4.96	<0.0001

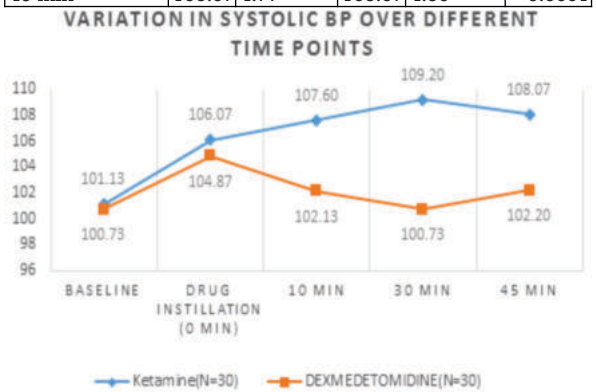

Figure 5 : Line with markers chart showing Systolic Blood Pressure at different Time points.

Table 8: Comparison of Diastolic Blood Pressure at different Time points

Diastolic Blood Pressure (in mm Hg)	Ketamine (N=30)		Dexmedetomidine (N=30)		P-value
	Mean	Standard Deviation	Mean	Standard Deviation	
baseline	73.53	3.35	74.80	3.70	0.1687
drug instillation (0 min)	75.07	3.51	76.00	3.86	0.3329
10 min	76.27	3.27	72.40	3.04	<0.0001
30 min	77.07	3.74	74.13	3.71	0.0034
45 min	76.67	3.58	74.00	3.44	0.0046

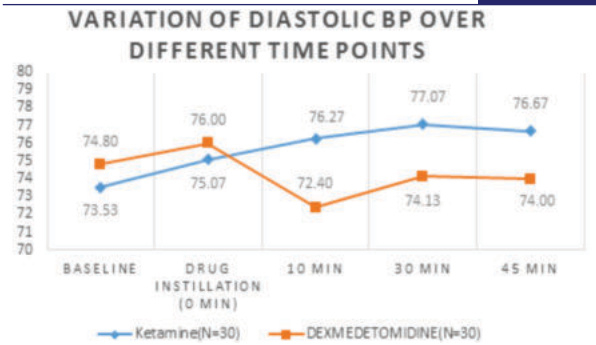

Figure 6 : Line with markers chart showing Diastolic Blood Pressure at different Time points.

Table 9: Comparison of SPO2 at different Time points

SPO2 (In %)	Ketamine (N=30)		Dexmedetomidine (N=30)		P-value
	Mean	Standard Deviation	Mean	Standard Deviation	
baseline	100.00	0.00	100.00	0.00	1
drug instillation (0 min)	100.00	0.00	100.00	0.00	1
10 min	99.57	0.77	99.47	0.78	0.6192
30 min	99.57	0.73	99.47	0.82	0.6197
45 min	99.73	0.52	99.53	0.73	0.2266

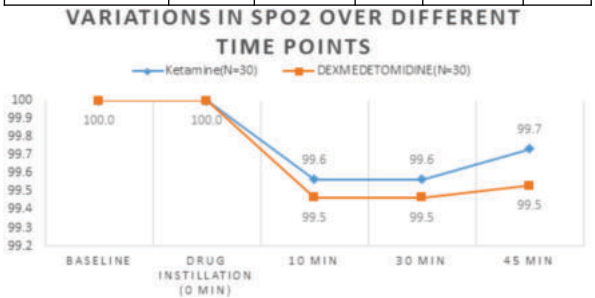

Figure 7 : Line with markers chart showing SPO2 at different Time points.

Table 10: Distribution of PSAS scores compared between Groups

PSAS Scores	Ketamine (N=30)		Dexmedetomidine (N=30)		P-value
	Frequency	Proportion	Frequency	Proportion	
1	7	23.33	0	0.00	0.0053
2	19	63.33	5	16.67	0.0003
3	4	13.33	13	43.33	0.0106
4	0	0.00	12	40.00	0.0001

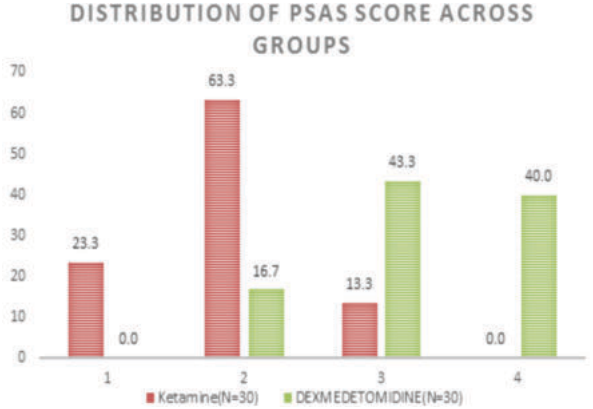

Figure 8: Clustered Column graph showing Distribution of PSAS score.

Table 11: Distribution of Mass Acceptance Scores compared between Groups

Mask Acceptance Score	Ketamine (N=30)		Dexmedetomidine (N=30)		P-value
	Frequency	Proportion	Frequency	Proportion	
1	5.00	16.67	0.00	0.00	0.0205
2	20.00	66.67	4.00	13.33	<0.0001
3	5.00	16.67	13.00	43.33	0.0255
4	0.00	0.00	13.00	43.33	0.0001

Figure 9 : Clustered Column graph showing Distribution of Mass Acceptance Scores.

DISCUSSION-

Pediatric patients show anxiety and crying behavior because of numerous factors, such as separation from their parents and environmental changes before surgery. The preoperative administration of sedatives can reduce anxiety, psychological trauma, and anesthesia induction. Intranasal drug delivery entails the infusion of the drug into the highly vascularized mucosal layer of the nose to subsequently reach systemic circulation[7].The intranasal route is effective, well tolerated and convenient for administration of dexmedetomidine.[8] Intranasal medication delivery has been described as safe ,effective as it provides high patient and provider satisfaction.[9] Most drugs are applicable by the intranasal route such as glucocorticoids, nasal decongestants, naloxone, midazolam, ketamine, and dexmedetomidine. If we administer intranasal dexmedetomidine or intranasal ketamine, it avoids the need for intravenous cannulation and is unpleasant in the nasopharynx. It requires little patient cooperation and it does not have distressing side effect.[10]

Demographic Data:

Mean age was calculated between both the groups viz. Group K and Group D. Mean age in group K was calculated as 5.27±2.21 and group 2 was found to be 5.50±2.32. Gender distribution study showed that group K had 18 male and 12 females and group D had 17 males and 13 females. Comparison of mean weight between weight of children between both the groups indicated that Group K had mean weight as 13.77±3.83 and Group D had mean weight as 12.63±3.55 which was not statistically significant. Statistical analysis for the demographic data for all the parameters in two groups revealed that there was no statistically significant difference between the two groups (P value > 0.05).

Parental Separation Anxiety Score:

We determined anxiety score, when the child was separated from the parents according to **Table 1.** PSAS scores of 1 and 2 were considered "successful separation from parents." The number of children that "successfully separated from their parents" was recorded in both groups. PSAS score analysis of the two groups of children showed that 7 children with PSAS score of "1 point" in Group K and no children in Group D (P=.0053). 19 children in Group D showed PSAS score of "2 points" and 5 children in Group D (P=.0003). 4 children in Group K showed PSAS score of 3 and 13 children of Group D showed PSAS score of 2. No children in Group K showed PSAS score of 4 whereas 12 children in Group D showed PSAS score of 4 (P=.0001). The data were compared between the two groups, and we found the difference to be statistically significant in all the score categories.

Mask Acceptance Scale (MAS)

The child's acceptance of the mask presented by the anesthesiologist was rated on four scales: according to **Table 2**, and the number of children with "satisfactory" scores was recorded separately in both groups. In Group K, 5 children showed score of 1 and none of the children in Group D showed MAS of 1. We found that scores frequency was different in both the groups with Group K having more children who were not afraid, cooperative, easy to accept the mask (P= 0.0205). 20 children in Group K showed MAS score as 2 and 4 children in

Group D showed MAS score of 2. This difference was statistically significant (P<.0001). 5 children in Group K showed MAS score of 3 whereas 13 children in Group D showed MAS score of 3. No children in Group K showed MAS score of 4 and 13 children in Group D showed MAS score of 13. This difference in frequency was statistically significant (P<.0001).

Vital Signs

Heart Rate

When comparing heart rate changes after intranasal application of the drug, we observed that at the baseline the heart rate in Group K was 108.3±5.3 and Group D was 110.0±7.21. We did not found any statistically significant difference (P value > 0.05) between the two groups before giving the drug at the baseline. At 10 minutes after giving the drug, it was found that Group K showed mean heart rate as 112.47±5.07 and Group D showed mean heart rate as 105.13±4.53. It was found that there was statistically significant difference between the two groups (P value < 0.0001). At 30 min after giving the drug, there was statistically significant difference between the two groups (Group K: 112.00±6.01; Group D: 101.93± 4.57, P value < 0.0001), and also at 45 min, the difference between two groups became statistically highly significant (Group K: 112.10±7.38; Group D: 94.50±3.10; P value < 0.0001). In this study we observed, as here we observed gradual decrease in heart rate in Group D and little increase in heart rate or stationary heart rate in Group K. Intraoperatively, the change in heart rate calculated among both the groups was statistically insignificant. Postoperatively, the difference was statistically significant (P value < 0.0001).

Comparison of Systolic Blood Pressure at different Time points

At baseline, mean systolic blood pressure was found to be 101.13±5.22 in Group K and 101.13± 6.65 in Group D. We observed that the results was statistically insignificant at baseline before giving the drug (P value >0.05). At 10 minutes, we found that mean systolic blood pressure in Group K was 107.60± 4.65 and Group D was 107.60±6.93. The difference in both the groups was found to be statistically insignificant. At 30 and 45 minutes also, the results between the two groups was not statistically significant.

Comparison of Diastolic Blood Pressure at different Time points:

At baseline, there was no statistical difference between both the groups. After 10 min of drug infusion, we found that mean diastolic blood pressure in Group K as 76.27± 3.27 and Group D was 72.40± 3.04 which was statistically significant (P<.0001) with mean diastolic pressure lower in Group D than that in Group K. There was no statistically significant difference found between both the groups after 30 and 45 min of drug infusion.

Comparison of SPO2 at different Time points:

Results of the study revealed that there was no statistically significant difference between the both groups as regards to oxygen saturation (P value > 0.05) through all the stages of evaluating the drug preoperative after intranasal application of drug, intraoperative, and postoperative in recovery.

CONCLUSION-

The aim of this study was to compare the efficacy of intranasal intranasal ketamine (Group K) versus dexmedetomidine (Group D) for anxiolysis to alleviate stress, agitation, and anxiety in children before general anesthesia and for promoting sedation for them. Another aim from this study is to prove the adequacy and effectiveness of another safe, effective, easy, and rapid route of administration of drugs and to make the perioperative period non-stressful and uneventful for the pediatric population.According to this study, ketamine showed significantly better response than dexmedetomidine in context to no fear and anxiety and aggression to intravenous cannulation, and good behavioural response, and children were calm during separation from parents while taking them to OR, and also, parents were highly satisfied by this clinical outcome.

REFERENCES

1. Beeby D G,Huges JOM Behavior of unsedated children in the anesthetic room.British Journal of Anesthesia 1980:52,279-281
2. Korsch B.M.The child and operating room.Anaesthesiology 1975;431:251-257
3. Kain ZN.Perioperative psychological trauma in children. In:complication in anesthesia,1st edn.Philadelphia;W.B. Saundres,1990.
4. Yuen VM,Hul TW,Irwin MG,Yuen MKA comparison of intranasal dexmeditomidine and oral midazolam for premedication in pediatric anesthesia:a double-blinded randamized controlled trial.Anes.Analg. 2008 Jun;10696):1715-21
5. Rita L,Cox Jm,Seleny FL et al.Ketamine hydrochloride for pediatric premedication:comparison to pentazocine.Anes Analg. 1974:53:375
6. Diaz J.H. Intranasalketamine preinduction of pediatric Anesthesia 1997; 7(4):273-8
7. NISHINA K, MIKAWA K, SHIGA M, OBARA H: Clonidine in paediatric anaesthesia. Paediatr Anaesth; 1999, 9:187-202.
8. Bagatini A,Gomes CR, Masella MZ,Rezer G.Dexmeditomidine: pharmacology and clinical application.
9. Neville DN, Hayes KR, Ivan Y, McDowell ER, Pitetti RD (2016) Double-blind randomized controlled trial of intranasal dexmedetomidine versus intranasal midazolam as anxiolysis prior to pediatric laceration repair in the emergency department. Acad Emerg Med 23(8):910–917
10. Liu S, Wang Y, Zhu Y, Yu T, Zhao H (2019) Safety and sedative effect of intranasal dexmedetomidine in mandibular third molar surgery: a systematic review and meta-analysis. Drug Design Dev Ther 13:130