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RESEARCH ARTICLE

COMPARISON OF INTRANASAL DEXMEDETOMIDINE V/S MIDAZOLAM AS A PREMEDICATION IN CHILDREN WITH CONGENITAL HEART DISEASE UNDERGOING CARDIAC SURGERY

Sanjay Kumar Morwal, Ajit Singh, C. K. Vyas and Neelu Sharma

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Abstract

Background: The intranasal route is a reliable way to administer preanaesthetics and sedatives to children. The aim of present study was to compare the anxiolytic and sedative effects of intranasal dexmedetomidine and midazolam as a premedication in children with congenital heart disease undergoing cardiac surgery.

Patients and Methods: Fifty children 2-12 years of age group of either sex with congenital heart disease undergoing cardiac surgery were randomly allocated into two groups.

Group A (n=25) - received intranasal dexmedetomidine as premedication (0.1 µg/kg diluted in 2ml NS)

Group B (n=25) - received intranasal midazolam as premedication (0.2 mg/kg diluted in 2ml NS)

Heart rate, mean arterial blood pressure and oxygen saturation were monitored upto 30 minute after drug administration. The sedation score, anxiety score and child separation score were recorded until the child taken to the OR. The postoperative agitation score was also observed.

Results and Conclusion: Premedication with intranasal dexmedetomidine attained significant and satisfactory sedation with better parental separation and lower anxiety levels without any adverse effects as compared with intranasal midazolam in children with congenital heart disease undergoing cardiac surgery.

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Introduction:-

Premedication means administration of drugs before induction of anaesthesia for promotion of short-term amnesia & anxiolysis, enhancing the hypnotic effects of general anaesthesia. Premedication is required to make the child calm and cooperative as most of the children suffer from severe anxiety and apprehension when they are separated from their parents or family members for the surgery under anaesthesia{1}. Various routes of drug administration- oral, intramuscular, rectal, nasal, intravenous & sublingual have been tried. There is still no ideal premedication or route of administration. The non-invasive (oral & intranasal) route is generally preferred because it is less traumatic than intramuscular & intravenous injection{2}. Intranasal route is convenient, non painful, atraumatic, easily accepted and has good absorption rate. Intranasal premedication provides good condition for induction of anaesthesia in preschool children{3}. The intranasal route is a reliable way to administer preanaesthetics and sedatives to children and is a relatively easy noninvasive route with rapid onset of action and high bioavailability comparable to that of IV administration because of bypassing the first pass metabolism and the high vascularity of the airway mucosa{4}.

Corresponding Author:- Sanjay Kumar Morwal

There is great variation in the recommendations for premedication of pediatric patients. Children who appear likely to exhibit uncontrollable separation anxiety should be given a sedative, such as midazolam (0.3–0.5 mg/kg, 15 mg maximum) or dexmedetomidine (0.2-1mcg/kg).

Dexmedetomidine is a newer highly selective α_2 -adrenergic agonist, approved by FDA in 1999. It possesses hypnotic, sedative, anxiolytic, sympatholytic and analgesic properties without producing significant respiratory depression{5}. It also diminishes intra operative requirement of analgesics and anaesthetics{6}. Dexmedetomidine increases the hemodynamic stability by altering the stress induced sympatho-adrenal responses to intubation{7}. Dexmedetomidine (0.2-1mcg/kg) is tasteless, odourless & painless when administered by intranasal route. It produce sedation, facilitate parental separation, and improve conditions for induction of general anesthesia, while preserving airway reflexes.

Midazolam is the most commonly used premedication in children. Midazolam has sedative, anxiolytic, hypnotic & anterograde amnesic properties. It has been shown to be more effective than parental presence or placebo in reducing anxiety and improving compliance at induction of anesthesia. It can be given for premedication via intranasal route, have rapidly absorbed from nasal mucosa and onset of sedation and analgesia is fast{8}.

Anxiety and psychological trauma due to maternal deprivation are major challenges in childrens during administration of anaesthesia. Preanaesthetic medication in children should be aimed to decrease the anxiety and psychological trauma and also to facilitate the induction of anesthesia without delaying the recovery. The most commonly used drugs are midazolam, dexmedetomidine, ketamine, transmucosal fentanyl and mepredine, promethazine, diazepam, morphine{9}.

The aim of present study was to compare the anxiolytic and sedative effects of intranasal dexmedetomidine and midazolam as a premedication in children with congenital heart disease(eg;-ASD,VSD) undergoing cardiac surgery.

Materials And Methods:-

Subject:

Pediatric patients with congenital heart disease posted for cardiac surgery under general anaesthesia.

Materials required:

Weighing machine, Multipara monitor having pulseoxymeter, NIBP, ECG, IV infusion set, blood transfusion set, IV Cannula(20G, 22G, 24G) IV extension line, IV Fluids: crystalloids(including normal saline, ringer lactate) and colloids, Disposable syringes(2ml, 5ml, 10ml), Suction machine, stethoscope, laryngoscope, ET tubes of different sizes, ECG electrodes, Anatomical face mask of different sizes, Pediatric bain's circuit.

Drugs :

ALL EMERGENCY DRUGS, ANAESTHESIA DRUGS(Ranitidine, metoclopramide, glycopyrrolate, midazolam, thiopentone, propofol, sch, atracurium, sevoflurane, diclofenac sodium, ondansetron, neostigmine)

Study Drugs:

Dexmedetomidine (0.1 µg/kg), Midazolam (0.2mg/kg)

Study Location:

After attaining ethical committee approval, the study was conducted on children with congenital heart disease undergoing cardiac surgery at Cardiac OT in the Department of Anaesthesiology, S.M.S. Medical College & attached Group of Hospitals, Jaipur after obtaining the written informed consent from all patients.

Study Design:

Hospital based, prospective, randomized, double blind, interventional study.

Sample Size:

The sample size was calculated to be a minimum of 17 subject in each group at alpha error 0.05 and study power 90% to detect expected minimum difference of 1.4 ± 1.2 (as per reference article) in VAS score after 30 minutes of drug administration among the two study groups. Hence for study purpose sample size was enhanced and rounded off to 25 subjects in each of the two groups as per seed article{10}.

Sampling Technique:

The subjects were randomized into the two groups by simple random sampling using sealed envelope method.

Blinding:

This trial was so planned that neither the doctor nor the participant were aware of the group allocation and the drug received. Study drug was prepared by one anaesthetist and after the completion of the procedure he or she has disclosed the name of the study drug. All the observations were noted as proforma.

Study Universe:

The study included 50 patients undergoing cardiac surgery under general anaesthesia.

Study Groups :

Group A(n=25) = received intranasal dexmedetomidine as premedication. (0.1 µg/kg diluted in 2ml NS via prefilled syringe attached to mucosal drug atomizer.).

Group B (n=25)= received intranasal midazolam as premedication. (0.2 mg/kg diluted in 2ml NS via prefilled syringe attached to mucosal drug atomizer.)

Eligibility Criteria:**Inclusion criteria :**

Patients having congenital heart disease, Age group between 2 to 12 years, Patients belonging to ASA class- II & III, weight: up to 30 kg

Exclusion criteria :

Parent not ready to give consent for study, Allergy to study drugs, Any nasal disorder [recurrent nasal bleeding or nasal masses] ,Obstructive pharyngeal or laryngeal pathology ,Mental retardation .

Outcome Variables

Anxiolytic effect	-4 point scale
Sedative effect	- Ramsay scale (6 point sedation score)
Hemodynamic variables	-HR, SBP, DBP, MAP, SpO ₂ , RR
Complications	-Nausea, Vomiting

Pre Anaesthetic Check Up:

All Patients were visited one day prior to surgery and explained about the anaesthetic technique. Each patient had a pre-anaesthetic check up which includes: Any significant present/past medical/surgical history. History of any previous surgery with significant anaesthetic complications, History of present or past medication and history of drug allergy, Physical examination including assessment for difficult intubation. Vital parameters- B.P., Pulse, Respiratory rate, Systemic examination. Routine investigation – Hb, TLC, DLC, Platelet count, Bleeding time, Clotting time, Fasting blood sugar, Serum Urea and Creatinine, SGOT, SGPT, Chest X ray, ECG, 2D Echo, Angiography. Written informed consent was obtained for performance of general anaesthesia after complete explanation about the study protocol and the procedure.

Procedure:-

On arrival in the operation theatre, fasting status, written informed consent and PAC was checked. Routine non invasive monitors attached and baseline parameters i.e. heart rate (HR), Systolic blood pressure (SBP), Diastolic blood pressure (DBP), Mean arterial pressure (MAP), and SpO₂ were noted. ECG & ETCO₂ were attached to the patient. General assessment for mental status, weight, pulse was recorded.

Demographic data including age, weight, sedation scale before premedication were recorded. The calculated dose of the study drug to the patient was administered in each nostrils divided equally 30 min before induction of anaesthesia. The study drug was administered prefilled in a syringe attached to nasal atomizer. For next 30 min patients were asked to maintain supine position with slight head low. Before induction data were collected for onset of sedation. Sedation score(six points sedation scale), anxiety score, child parent separation score & haemodynamic data(HR, NIBP, PR, RR & SPO₂) were recorded at 5, 10, 15, 20, 25 & 30 minutes. IV line secured and IV fluids RL was started at 5ml/kg/hr. IV glycopyrrolate 0.004 mg/kg was given. Induction was done with an induction agent Inj.

Etomidate 0.3mg/kg, rocuronium 0.9mg/kg was given. Hemodynamic data were collected just before intubation. Patient were intubated with appropriate size of endotracheal tube and maintained on O₂ and inhalational anaesthetic (isoflurane). Hemodynamic data were collected intraop. At the conclusion of surgery patient were shifted to cardiac ICU. Patient were observed for any side effects.

Outcome analysis:-

Qualitative data (Gender, complication) were summarized as number & percentage and analyzed using Chi square test. Continuous variable (HR, SBP etc) were summarized as mean & standard deviation and analyzed using unpaired t test. Ordinal variables (scores) were summarized as median & range and analyzed using Mann Whitney U test.

Statistical analysis:-

Data obtained from predesigned proforma was entered into MS EXCEL sheets and master chart was prepared. Statistical analysis was performed with the SPSS, version 21 for Windows statistical software package (SPSS inc., Chicago, IL, USA). The Categorical data was presented as numbers (percent) and were compared among groups using Chi square test. The quantitative data was presented as mean and standard deviation and were compared by student t-test. Anova/Kruskal Wallis Test were used to compare the medians of more than two sample. P-value was considered to be statistically significant if less than 0.05.

Discussion:-

Preoperative anxiety (anxiety regarding impending surgical experience) in children is a common phenomenon that has been associated with a number of negative behaviors during the surgery experience (e.g., agitation, crying, spontaneous urination, and the need for physical restraint during anesthetic induction). Preoperative anxiety has also been associated with the display of a number of maladaptive behaviours postsurgery, including postoperative pain, sleeping disturbances, parent-child conflict, and separation anxiety. For these reasons, researchers had sought out interventions to treat or prevent childhood preoperative anxiety and possibly decrease the development of negative behaviours postsurgery. **Irola et al**{11} documented that administration of intranasal dexmedetomidine had a high bioavailability 65% (35%–93%) and was potentially useful sedative effects in surgical procedures. **H Gudmundsdottir et al**{12} found that Intranasal administration of midazolam had rapid and reliable onset of action and predictable effects. The absolute bioavailability of midazolam in the nasal formulation was determined to be $64 \pm 19\%$ (mean $\pm$ standard deviation). With this background 50 patients of ASA grade 2 and 3, aged between 2 to 10 years, wt up to 30 kg with congenital heart disease undergoing cardiac surgery under general anaesthesia were randomly selected after applying inclusion and exclusion criteria. These patients were divided into two groups, group A (Dexmedetomidine group) and group B (Midazolam group).

In our study, sedation score, child parental separation score, anxiety score in both the groups were compared. In addition demographical variables (such as age, gender, ASA grading, wt) and hemodynamic changes (such as heart rate, systolic blood pressure, diastolic blood pressure, mean arterial blood pressure, arterial oxygen saturation and respiratory rate) were compared. Six point sedation scale (Ramsay scale) for sedation score, four point scale for child parental separation score and four point scale for anxiety score were used to compare the groups in this study. The mean age of the patients in A group was 7.00 ± 4.34 years and in B group was 7.68 ± 3.18 years. There was no statistically significant difference between the groups with regards to age ($p > 0.05$). This helped us to judge the clinical significance of our study as the distribution, metabolism, excretion and action of drug are undoubtedly varied in different age groups. Therefore, clinically insignificant variation in age simply helped to alleviate these confounding factors.

In group A 15 patients were male and 10 patients were female. In group B 15 patients were male and 10 patients were female. There was no statistically significant difference between the groups with regards to gender ($p > 0.05$).

Mean weight of patients in A group was 17.80 ± 8.13 kg, and in B group was 17.92 ± 6.42 kg. The two groups were comparable with respect to weight. There was no statistically significant difference between the groups with regards to weight ($p > 0.05$). This helped us in alleviating a point of controversy because obesity as well as cachexia has significant effect on the clinical action of the drug.

Thus patients belonging either to group A or group B were similar in term of Demographic parameters.[Table-1].

Both groups had patients in ASA grade II & ASA grade III. In group A 22 patients were in ASA grade II and 3 patients were in ASA grade III. In group B 21 patients were in ASA grade II and 4 patients were in ASA grade III. There was no statistically significant difference between the groups with regards to ASA grading ($p>0.05$).

Table 1:- Demographic Datas.

	Group A		Group B		P value
	Mean	SD	Mean	SD	
AGE	7.00	4.34	7.68	3.18	0.530(NS)
SEX:-male Female	15 10		15 10		0.885(NS)
WEIGHT	17.80	8.13	17.92	6.42	0.954(NS)

Seperation Score:

In our study, separation score was assessed using Four point scale (Table no. 2). We found that child parent separation score was significantly higher in dexmedetomidine group (2.68 ± 0.85) than midazolam group (2.04 ± 0.79) at 30 minutes after intranasal premedication (p value 0.008). The children were satisfactorily separated from parents in dexmedetomidine group when compared to midazolam group. Similar results were observed by **Medhat M. Messeha et al{10}**. They concluded that premedication with intranasal dexmedetomidine (2.09 ± 0.51) attained significant and satisfactory parent separation without any adverse effects as compared with intranasal midazolam (1.21 ± 0.4) in children with simple congenital heart disease undergoing cardiac catheterization (p value < 0.05). Similarly **Darshna D. Patel et al{10}** did a comparison of intranasal dexmedetomidine versus intranasal midazolam as a pre anaesthetic medication in children and they found that Intranasal Dexmedetomidine as compared to intranasal Midazolam was associated with easier child-parent separation without any adverse side effects. Thus, it was concluded that intranasal Dexmedetomidine can be used effectively and safely as a preanaesthetic medication in children. Comparable results found by **Ghali AM et al{13}**.

Hence we conclude that intranasal dexmedetomidine is better as compared to intranasal Midazolam in terms of separation score.[Table-2]

Table 2:- Comparison of Separation Score Among Study Groups at 30 Minutes.

	Group A		Group B	
	No.	%	No.	%
1	2	8.00	6	24.00
2	8	32.00	13	52.00
3	11	44.00	5	20.00
4	4	16.00	1	4.00
Total	25	100.00	25	100.00
Mean±SD	2.68±0.85		2.04±0.79	
P value	0.008 (S)			

Dexmedetomidine produces sedation by stimulating α_2 -adrenergic receptors in the locus coeruleus, apart from the brain stem involved in the sleep-wake cycle, which reduce central sympathetic outflow, resulting in increased stimulation of inhibitory neurons{14}. Therefore, it causes analgesia and sedation without causing respiratory depression. It produces "cooperative sedation," which means that the sedated patient can still interact with healthcare professionals{15,16}. While midazolam stimulates gamma-aminobutyric acid (GABA) receptors in the cerebral cortex to increase the conductance of chloride ions and hyperpolarization that inhibits normal function of neurons producing sedation.

Anxiety Score:-

In our study, anxiety score was assessed using Four point scale (Table no. 3). We found that anxiety score was lower (less anxiety) in dexmedetomidine group (1.8 ± 0.76) than midazolam group (3.16 ± 0.69) at 30 minutes after intranasal premedication (p value < 0.001). Our results coincide with study by **Medhat M. Messeha et al{10}**. They

concluded that premedication with intranasal dexmedetomidine (1 ± 0.2) attained significant and satisfactory anxiety levels without any adverse effects as compared with intranasal midazolam (1.8 ± 0.4) in children with simple congenital heart disease (ASD, VSD) undergoing cardiac catheterization (p value < 0.05). **Ghali AM et al{13}** did a comparison of intranasal dexmedetomidine versus oral midazolam as a preanesthetic medication in children. Intranasal dexmedetomidine (31.59 ± 3.88) appeared to be a better choice for preanesthetic medication than oral midazolam (44.35 ± 4.51) in their study. Dexmedetomidine was associated with lower anxiety levels at the time of transferring patients to the OR than children who received oral midazolam (p value 0.036). Similar results were observed by **Patel et al{17}** and **Akin et al{18}**.

Table 3:- Comparison of Anxiety Score Among Study Groups at 30 Minutes.

	Group A		Group B	
	No.	%	No.	%
1	10	40.00	0	0
2	10	40.00	4	16.00
3	5	20.00	13	52.00
4	0	0	8	32.00
Total	25	100.00	25.00	100.00
Mean±SD	1.80±0.76		3.16±0.69	
P value	P<0.001 (S)			

Sedation Score:

In our study, sedation score was assessed using Ramsay sedation scale (Table no. 4). We found that sedation scores were higher in dexmedetomidine group than midazolam group at 5, 10, 15, 20, 25 and 30 minutes after intranasal premedication. The children in dexmedetomidine group ($4.44\pm.65$) achieved better sedation than midazolam group (3.60 ± 0.76) at 30 minutes after intranasal premedication (p value < 0.05). **Medhat M. Messeha et al{10}** Concluded that premedication with intranasal dexmedetomidine (4.74 ± 1.2) attained significant and satisfactory sedation with better levels without any adverse effects as compared with intranasal midazolam (3.34 ± 0.9) in children with simple congenital heart disease (ASD, VSD) undergoing cardiac catheterization (p value < 0.05). **Ghali AM et al{13}** did a comparison of intranasal dexmedetomidine versus oral midazolam as a preanesthetic medication in children. Intranasal dexmedetomidine (2.94 ± 1.37) appeared to be a better choice for preanesthetic medication than oral midazolam (3.99 ± 1.58) in their study. Dexmedetomidine was associated with lower sedation levels at the time of transferring patients to the OT than children who received oral midazolam (p value 0.042). **V. M. Yuenetal{19}** found similar results that's coincide with our study.

Table 4:- Comparison of Sedation Score Among Study Groups.

	Group A		Group B		P value
	Mean	SD	Mean	SD	
Baseline	1.16	0.37	1.08	0.28	0.394
5 min	2.12	0.60	1.76	0.60	0.038
10 min	2.74	0.62	2.35	0.49	0.022
15 min	2.96	0.79	2.48	0.52	0.014
20 min	3.56	0.82	3.00	0.71	0.012
25 min	3.96	0.68	3.36	0.76	0.004
30 min	4.44	0.65	3.60	0.76	0.0001

Hemodynamic Parameters:

In our study after giving study drug; the mean heart rate decreased in both groups (Table no. 5). There was statistically significant reduction observed in heart rate in group A as compared to group B at 5, 10, 15, 20, 25 and 30 min after premedication (p value < 0.05). The mean baseline variables were comparable between both groups. The mean baseline pulse rate in group A was 122.40 ± 11.99 bpm and in group B was 121.96 ± 10.61 bpm. The difference in heart rate was not significant as shown by P value of > 0.05. Similarly the mean baseline Systolic blood pressure in group A was 115.60 ± 11.45 mmHg and in group B was 121.28 ± 15.20 mmHg (p value > 0.05). In group A mean Diastolic blood pressure was 75.96 ± 13.29 mmHg and in group B was 79.36 ± 15.09 mmHg (p

value>0.05). In group A mean of Mean arterial pressure was 92.28 ± 11.42 mmHg and in group B was 95.80 ± 13.03 mmHg (p value >0.05). Thus we find that all the baseline variables in two groups were similar and can say that the randomization was done adequately.

In our study the mean SBP, mean DBP, mean MAP decreased in both the study groups after premedication (Table no. 6,7,8). There was statistically significant reduction in systolic and diastolic blood pressure and mean arterial blood pressure in group A as compared to group B at 5, 10, 15, 20, 25 and 30 min after premedication (p value < 0.05). In our study, peripheral arterial SpO₂ and RR were compared in both groups (Table no. 9 and 10) at various time intervals till 30 min after premedication. There were no significant differences observed in both groups (p value > 0.05).

In the current study, the peripheral arterial SpO₂ and RR were well maintained throughout the perioperative observation period in both groups. Dexmedetomidine does not suppress respiratory function, even at high doses{20} while midazolam acts as GABA-mimetic drug, and therefore, it is known to decrease the respiratory drive in a dose-dependent manner{18}.

Similar results were reported by Yuen et al{21}. They did a comparison of intranasal dexmedetomidine and oral midazolam for premedication in pediatric anesthesia and found that dexmedetomidine was known to decrease sympathetic outflow and circulating catecholamine levels and was therefore be expected to cause a decrease in HR and SBP{22}.

In addition, this study demonstrated that intranasal dexmedetomidine reduced HR and SBP during the preoperative sedation period compared with the oral midazolam. Children in both groups maintained normal SpO₂ value

Results And Conclusion:-

The following observations were made

No significant difference regarding demographic data (age, gender, body weight) was observed.

No significant difference regarding ASA grading was observed.

Children in dexmedetomidine group achieved significant higher sedation score and lower anxiety score (more sedated) up to 30 min after drug administration in comparison to midazolam group. Furthermore, the children were satisfactorily separated from parents in dexmedetomidine group when compared to the midazolam group.

Hemodynamic data showed that SBP, DBP, MAP and HR were significantly decreased 5, 10, 15, 20, 25 and 30 min after drug administration in the dexmedetomidine group when compared with the midazolam group.

Peripheral arterial SpO₂ and RR displayed no significant difference between the studied groups throughout the study period.

Finally we conclude that intranasal dexmedetomidine appears to be a better choice for preanesthetic medication than intranasal midazolam in our study. Premedication with intranasal dexmedetomidine attained significant and satisfactory sedation with better parent separation and lower anxiety levels without any adverse effects as compared with intranasal midazolam in children with congenital heart disease undergoing cardiac surgery.

Table 5:- Comparison of Heart Rate (bpm) Among Study Groups.

	Group A		Group B		P value
	Mean	SD	Mean	SD	
Baseline	122.40	11.99	121.96	10.61	0.891
5 mins	111.32	13.63	119.12	10.20	0.026 *
10 min	107.40	13.54	114.36	9.79	0.042 *
15 min	105.24	12.68	114.44	10.79	0.008 *
20 min	103.00	11.74	111.96	10.56	0.006 *
25 min	101.64	10.83	109.76	8.25	0.004 *
30 min	101.08	10.53	108.40	8.45	0.009 *

Table 6:- Comparison of Systolic Blood Pressure (mmHg) Among Study Groups.

	Group A		Group B		P value
	Mean	SD	Mean	SD	
Baseline	115.60	11.45	121.28	15.20	0.142
5 min	108.16	11.82	117.24	14.65	0.019 *
10 min	107.40	11.18	115.92	14.59	0.024 *
15 min	105.00	6.49	113.00	10.68	0.002 *
20 min	102.36	14.85	110.04	12.33	0.049 *
25 min	98.52	8.85	105.80	9.35	0.006 *
30 min	96.40	10.17	103.28	9.72	0.018 *

Table 7:- Comparison of Diastolic Blood Pressure (mmHg) Among Study Groups.

	Group A		Group B		P value
	Mean	SD	Mean	SD	
Baseline	75.96	13.29	79.36	15.09	0.402
5 min	66.36	11.27	76.92	14.39	0.005 *
10 min	63.84	11.54	72.08	13.12	0.022 *
15 min	64.44	10.57	72.16	10.95	0.014 *
20 min	58.72	12.96	67.04	12.95	0.027 *
25 min	52.12	9.03	64.40	14.68	0.0008*
30 min	55.84	10.67	62.04	12.79	0.048 *

Table 8:- Comparison of Mean Arterial Pressure (mmHg) Among Study Groups.

	Group A		Group B		P value
	Mean	SD	Mean	SD	
Baseline	92.28	11.42	95.80	13.03	0.314
5 min	80.29	10.80	93.44	12.63	0.002 *
10 min	78.36	10.41	90.68	12.55	0.004 *
15 min	77.96	8.03	88.92	8.85	0.003 *
20 min	73.27	12.89	85.24	10.98	0.006 *
25 min	67.59	7.25	81.88	11.64	0.009 *
30 min	69.36	9.05	79.48	10.77	0.007 *

Table 9:- Comparison of SpO₂ (%) among Study Groups.

	Group A		Group B		P value
	Mean	SD	Mean	SD	
Baseline	88.60	8.20	89.32	8.01	0.754
5 min	87.60	8.82	86.38	8.66	0.835
10 min	87.20	8.71	87.00	8.56	0.935
15 min	86.92	8.64	86.72	8.48	0.934
20 min	86.36	8.75	86.16	8.60	0.935
25 min	86.56	8.78	86.36	8.63	0.935
30 min	86.20	8.91	85.64	8.40	0.820

Table 10:- Comparison of Mean Respiratory Rate of Study Groups.

	Group A		Group B		P value
	Mean	SD	Mean	SD	
Baseline	27.48	2.62	26.52	2.60	0.199
5 min	26.64	2.23	25.64	2.23	0.120
10 min	26.60	2.63	25.60	2.63	0.185

15 min	26.32	2.72	25.32	2.72	0.199
20 min	26.28	2.44	25.28	2.44	0.154
25 min	25.88	2.20	24.88	2.20	0.115
30 min	26.00	2.52	25.00	2.52	0.166

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