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COMPARISON OF INTRANASAL CLONIDINE VERSUS DEXMEDETOMIDINE AS PREMEDICANT FOR GENERAL ANAESTHESIA IN HEAD AND NECK SURGERIES: A RANDOMISED DOUBLE BLIND STUDY

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ABSTRACT

INTRODUCTION: Alpha-2 agonists such as Clonidine and Dexmedetomidine have emerged as an alternative for premedication in anaesthesia for blunting the stress response of laryngoscopy. Intranasal route has good compliance and adequate absorption of drug.

METHODS: Seventy four patients posted for head and neck surgeries, of ASA grade I-II were divided into two groups (37 each). Group-A received intranasal clonidine 3mcg/kg and Group-B received intranasal Dexmedetomidine 2mcg/kg. Each drug diluted to 1.5ml with normal saline and given 45min before induction. Perioperative haemodynamic parameters and sedation scores were recorded. Statistical analysis was done.

RESULTS: Both groups showed decrease in Heart Rate (HR) and mean arterial pressure (MAP) but group-B had statistically significant lower HR and MAP ($p<0.05$) and more number of sedated patients.

CONCLUSION: Dexmedetomidine 2mcg/kg intranasal was better sedative premedicant and hemodynamic response suppressor than intranasal clonidine 3mcg/kg during laryngoscopy and intubation without significant side effects.

KEYWORDS : Intranasal, dexmedetomidine, clonidine, haemodynamic suppression.

INTRODUCTION:

Laryngoscopy and tracheal intubation are noxious stimuli to evoke a transient, but marked sympathetic response manifests as increase in heart rate (HR), blood pressure and arrhythmias, can leads to adverse cardiovascular events like myocardial ischemia and even infarction which affects post-operative recovery. Sedative premedication in general are considered to be an effective option for reduction of preoperative anxiety. Alpha-2 agonists such as clonidine and dexmedetomidine have emerged as an alternative for premedication in anaesthesia with the properties to blunt the stress response of laryngoscopy also.

Oral premedication having drawbacks of slow onset, non-compliance in vomiting and nil oral patients.[1] Even parenteral injections also causes anxiety, pain, higher resources consumption and the risk for contaminated needle-stick injury and needs trained staff and more time. The intranasal method of drug administration is easy, painless, faster onset than oral and relatively inexpensive with good patient acceptance and comfort.[2,3] Clonidine is a sedative and analgesic. It has been successfully used by oral, intravenous, intrathecal, epidural, intramuscular and intranasal route in the doses of 1-5mcg/kg[4]. Dexmedetomidine is a tasteless, colourless and odourless agent that acts as a more selective alpha-2 agonist with both sedative and analgesic effects via actions in the central nervous system and with the benefit of not decreasing the respiratory rate or tidal volume.

This study was conducted to compare the efficacy of intranasal clonidine and dexmedetomidine to in terms of sedation, respiratory depression and to compare the haemodynamic response to laryngoscopy and tracheal intubation.

MATERIAL AND METHODS:

This hospital based randomized double-blind comparative observational study was conducted with the permission of institutional ethical committee on the patients of either sex, 30-50 years of age, ASA grade I-II, Mallampatti grade I-II with body weight of 45-65 kg and without any acute or chronic systemic illness, undergoing elective head and neck surgeries of 45-60 min under general anaesthesia. Expecting minimum detectable difference in mean HR in both groups to be 9.8±14.78 based on study done by Lakshmi jayaraman et al[5], the sample size was calculated to be 37 subjects for each group at an alpha error 0.05 and power 80%. Routine pre-anaesthetic check-up was done a day before the surgery and the patient having allergy/contraindication to the study drug, rhinopharyngitis and recent upper respiratory tract infection were excluded. Group-A patients received intranasal clonidine 3mcg/kg diluted to 1.5ml with normal saline and Group-B received intranasal dexmedetomidine 2mcg/kg diluted to 1.5ml with normal saline. An equal volume (0.75ml each nostril) of drug was instilled into each nostril (by using 2ml of syringe without needle) with the patient in supine position at 45min before induction.

After confirming fasting status and obtaining written informed consent, patients were randomly divided into 2groups (37 patients each) by sealed envelope method. Blinding was done as the medications were prepared by one colleague and observations done by other. The patient lying supine with attached standard monitoring. The baseline values of HR, systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), SpO_2, respiratory rate and Ramsay sedation score were recorded. Ramsay sedation scale (Score1- Anxious or agitated or both, score2- Cooperative, oriented and tranquil, score3- Responds to commands only, score4- Sleep, but with brisk response to light glabellar tap or loud auditory stimulus, score5- Asleep, sluggish response to light glabellar tap or loud auditory stimulus, score6- Asleep, no response) was used to assess sedation level.

An intravenous access was secured using 20G cannula. Inj. Ringer Lactate infusion was started. The study drug was administered in both nostrils. Ramsey sedation score and haemodynamic parameters were recorded after 10,20,30,45 minutes. After taking the patient on the operation table, inj. Glycopyrrolate 0.004mg/kg, inj. Midazolam 0.02mg/kg and inj. Fentanyl 2mcg/kg were given. After pre-oxygenation with 100%O_2, anaesthesia was induced with inj. Thiopentone sodium 5mg/kg slow intravenously and intubation was facilitated with inj. Atracurium 0.5mg/kg. The laryngoscopy and tracheal intubation were performed using adequate size cuffed endotracheal tube. The patient requiring more than one attempt at

intubation and/or more than 30sec laryngoscopy were excluded. Anaesthesia was maintained with 0.6-1.2% isoflurane inhalation, 40%O_2+60%N_2O and Atracurium 0.1mg/kg injections. Intraoperative haemodynamic parameters and complications if any, were recorded just after premedication, after induction, after intubation and 3, 5 and 10min after intubation (end point of the study).

Hypotension was defined as 25% decrease in MAP from base line and managed by inj. mephentermine 6mg boluses. Bradycardia was defined as HR<60 beats/min and managed by inj. atropine 0.6mg boluses if further goes below 50beats/min.

STATISTICAL ANALYSIS:

Data were compiled in Microsoft Excel™ and analysed using Statistical Package of Social Sciences (SPSS, version20) software. The quantitative data (Mean HR, SBP, DBP, and MAP) were expressed as Mean±SD and their significance was analysed by unpaired student t-test. Mann-Whitney test applied for median sedation score comparison and qualitative data were analysed using chi-square. The 'p' value<0.05 was considered significant.

RESULTS:

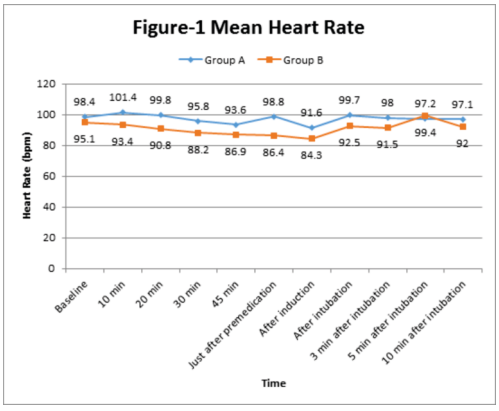
Demographic profile of both the groups was analysed. The mean age in group-A and B (35.1±4.5 years versus 39.9±9.3 years), mean weight (54.6±6.0 kgs versus 52.0±6.7 kgs), sex distribution, ASA physical status were statistically comparable (p>0.05).

Dexmedetomidine had statistically significant and better obtundation over increase in HR. Intra-group comparison as depicted in Table-1 and figure-1, shows that in Group-A, the mean HR was significantly lower than the baseline values at 10min, 45min and lowest at soon after induction (91.6±9.9, p<0.05). In Group-B, the mean HR was significantly lower than the baseline values at 10min, 30min, 45min, at premedication and lowest at soon after induction (84.3±15.4,p<0.05). Inter-group comparison as depicted in Table-1 and figure-1, shows that the baseline mean HR was statistically comparable in both the groups. Group-B (Dexmedetomidine) showed a better response (lower mean HR) in comparison to Group-A (Clonidine) from 10 min to 5 min after intubation (p<0.05).

Table-1 TREND OF MEAN HEART RATE

Time	Group A		IntraP value	Group B		Intra P value	P value	Significance
	Mean	SD		Mean	SD			
Baseline	98.4	12.8		95.1	15.2		0.308	N.S.
10 min	101.4	12.9	0.000	93.4	15.3	0.000	0.017	S
20 min	99.8	11.5	0.4344	90.8	13.8	0.665	0.003	S
30 min	95.8	11.7	0.1289	88.2	14.2	0.0070	0.0142	S
45 min	93.6	10.3	0.0115	86.9	14.3	0.004	0.0231	S
Just after premedication	98.8	12.7	0.8197	86.4	17.2	0.0063	0.0008	S
After induction	91.6	9.9	0.0003	84.3	15.3	0.0015	0.0172	S
After intubation	99.7	7.8	0.4791	92.5	18.4	0.4502	0.0338	S
3 min after intubation	98	9.3	0.8663	91.5	14.5	0.2491	0.0259	S
5 min after intubation	97.2	9.5	0.6389	99.4	12.8	0.1615	0.0108	S

N.S.=Nonsignificant, S=Significant



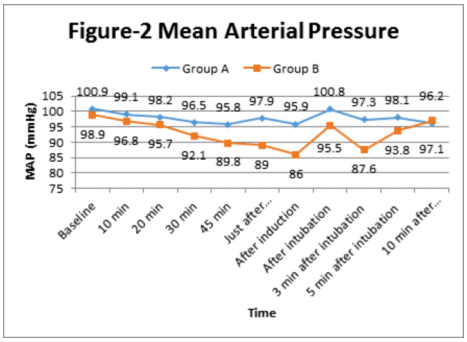
Mean SBP and DBP were lesser than the baseline value all throughout the study period in both groups. Inter-group comparison as shows that the baseline mean SBP and DBP were statistically comparable in both the groups. Group-B (Dexmedetomidine) showed a better response (lower mean SBP and DBP) in comparison to Group-A (Clonidine) from 20min to 3min after intubation (p<0.05).

In both groups, Mean of MAP were lesser than the baseline value all throughout the study period as depicted in Table-2 and figure-2. The lowest MAP was noted after induction in both the groups (95.9±6.7mmHg in group-A and 86±9.5mmHg in group-B). Inter-group comparison shows that the baseline mean of MAP were statistically comparable in both the groups. Group-B (Dexmedetomidine) showed a better response (lower MAP) in comparison to Group-A (Clonidine) from 30min to 3min after intubation (p<0.05).

Table-2 TREND OF MEAN ARTERIAL PRESSURE

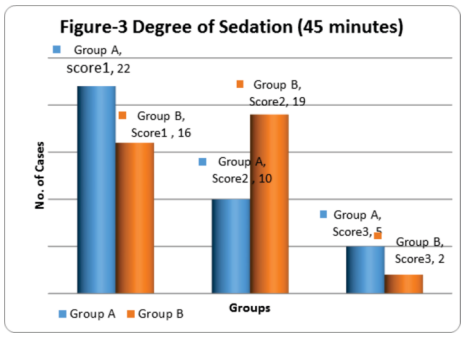
Time	Group A		Intra P value	Group B		Intra P value	P value	Significance
	Mean	SD		Mean	SD			
Baseline	100.9	3.6		98.9	8.1		0.1744	NS
10 min	99.1	4.0	0.000	96.8	8.2	0.000	0.1380	NS
20 min	98.2	5.6	0.000	95.7	6.6	0.0009	0.0784	NS
30 min	96.5	4.7	0.000	92.1	6.8	0.000	0.0023	S
45 min	95.8	7.1	0.000	89.8	8.3	0.000	0.0013	S
Just after premedication	97.9	6.3	0.0013	89.0	7.8	0.000	0.000	S
After induction	95.9	6.7	0.000	86.0	9.5	0.000	0.000	S
After intubation	100.8	6.7	0.9113	95.5	8.9	0.1082	0.0055	S
3 min after intubation	97.3	5.7	0.000	87.6	12.1	0.000	0.0001	S
5 min after intubation	98.1	6.9	0.0069	93.8	12.1	0.0163	0.0639	NS
10 min after intubation	96.2	3.7	0.000	97.1	11.7	0.4022	0.6498	NS

N.S.=Nonsignificant, S=Significant



In both the groups, Respiratory rate and SpO2 were statistically comparable and were with in normal limits all throughout the study period. No case was associated with respiratory depression.

Ramsay sedation score as shown in figure-3, was analysed. Maximum sedation was noted at 45min in both the groups but dexmedetomidine showed significantly better sedation than clonidine ($p<0.05$). In group-A, 13.5% patients achieved score-3, 27% patients achieved score-2 and no sedation occurred in 59.5% patients. While in group-B, 5.4% patients achieved score-3 and 51.4% patients achieved score-2 and no sedation occurred in 43.2% patients.



Dexmedetomidine showed more incidence of bradycardia (13.51%) and hypotension (8.11%) in compare to clonidine (5.4% bradycardia, 5.4% hypotension) but the difference was statistically insignificant ($p>0.05$).

DISCUSSION:

Increasing attention has been focused on sedative premedication as it provides sedation, anxiolysis, and reduction of emotional trauma with facilitating smooth induction and intubation by attenuating hemodynamic responses. Clonidine and dexmedetomidine induce central sympatholysis by activating presynaptic autoreceptors but dexmedetomidine is about 8-10 times more selective towards the alpha2 adrenoceptor (1600:1) especially because of its 2A subtype selectivity[6]. The highly vascularised nasal mucosa and the olfactory tissue in direct contact with the central nervous system allow nasally administered drugs to be rapidly transported into the bloodstream and brain, with onset of action approaching that of intravenous therapy.[7] The absorption, bioavailability and effectiveness can be increased by minimizing drug volume, maximizing concentration, using both nostrils and use of atomized particles.[1,2,3]

In our study dexmedetomidine produced better obtundation of the haemodynamic response to laryngoscopy and tracheal intubation in terms of better control on HR and MAP. This observation was similar to the study done by Dharmendra Kumar Yadav et al[8] on intranasal dexmedetomidine versus clonidine. There was a decrease in MAP after the peak effect of clonidine and dexmedetomidine. Dexmedetomidine produced better anxiolysis and preoperative sedation without any respiratory depression or hypoxia. Dexmedetomidine sedated more patients but mainly with Ramsay sedation score2, explaining the feature of conscious sedation by dexmedetomidine. This finding was similiar with Kumar L et al[9] and Mahmoud M et al.[10]

CONCLUSION:

Dexmedetomidine when administered intranasally in a dose of 2mcg/kg is a better anxiolytic, sedative premedicant and has better obtundation of hemodynamic responses during laryngoscopy and intubation with insignificant side effects in comparison to clonidine 3mcg/kg in patient undergoing elective surgeries under GA.

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