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COMPARATIVE EVALUATION OF THE HYPOTENSIVE EFFECTS OF CLONIDINE TO DEXMEDETOMIDINE DURING FUNCTIONAL ENDOSCOPIC SINUS SURGERY IN THE INDUCTION OF HYPOTENSION: AN INTERVENTIONAL STUDY

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ABSTRACT

Background: Decreasing MAP (mean arterial blood pressure) using controlled hypotension, is introduced to improve visibility of the surgical site by reducing blood loss during FESS.

Aims: The present study was conducted to compare and assess the hemodynamic stability and hypotensive efficacy of Clonidine and Dexmedetomidine in FESS.

Materials and Methods:40 subjects were randomly divided into two groups of 20 subjects each. Subjects from Group I received 1 μg/kg dexmedetomidine, whereas, Group II subjects received 2 μg/kg Clonidine. Postoperative complications and Haemodynamic parameters were assessed at baseline, following the loading dose, 1- and 5-minutes following intubation, and every 10 minutes till recovery. These parameters were mean arterial pressure, systolic and diastolic blood pressures, oxygen saturation, and heart rate (HR).

Results:MAP and HR decreased significantly from baseline at all the time intervals of assessment ($p<0.001$). These values were statistically significant for both intragroup and intergroup for Group I and Group II. Also, statistically non-significant results were seen concerning the visibility of the surgical field. Emergence time was significantly higher for Group I (7.38±0.58 min) than Group II (6.44±0.72 min) with $p=0.001$. Sedation scores were higher significantly for group I (1.88±1.23) than Group II (1.37±0.12) with $p=0.001$. VAS scores were significantly lower for Group I (2.24±0.78) than Group II (3.01±0.14) at all time intervals with $p=0.001$. First rescue analgesia was significantly higher for Group I (110.45±12.25 min) than Group II (84.31±10.06) with the p-value of <0.0001

Conclusion: Present study concludes that, better hemodynamic stability was seen with dexmedetomidine compared to Clonidine. However, decreased blood loss and intraoperative

visibility were comparable for both dexmedetomidine and Clonidine. Sedation and prolonged anesthesia were also better with dexmedetomidine.

Keywords: Clonidine, Dexmedetomidine, induced hypotension, FESS, Functional Endoscopic Sinus Surgery.

INTRODUCTION

Nasal and sinus pathologies are treated surgically using FESS (Functional endoscopic sinus surgery), which is an important surgery conducted frequently. However, bleeding at the site of the surgery is a major limitation concerning visibility during Functional endoscopic sinus surgery. Owing to this challenge encountered, decreasing MAP (mean arterial blood pressure) using the controlled hypotension, is introduced to improve visibility of the surgical site by reducing blood loss during FESS. This reduction is achieved by hypotensive anesthesia, where mean arterial pressure can be reduced to 65-70mmhg or by 30% from the baseline values. However, various side effects are seen associated with induced hypotension including cerebral hypoperfusion, acidosis, acute kidney injury, and/or vital organs ischemia, and these side effects need to be managed.[1]

The agents used for induced hypotension are beta-blockers, sodium nitroprusside and like vasodilators, inhaled anesthetics in a higher dose, and/or nitroglycerine. These agents are either used alone or in combination with each other for induced hypotension. The ideal agent for achieving hypotension has not been established yet. However, the desirable properties of an ideal agent for induced hypotension are rapid onset, easy administration, dose-dependent effect, acceptable half-life, and rapid elimination.[2]

The two commonly used total anesthetic agents and sedative-analgesic agents are Clonidine and Dexmedetomidine.Dexmedetomidine is approved by the USFDA (United States Food and Drug Administration) as a total anesthetic agent and sedative-analgesic agent in both pediatric and adult subjects with acceptable potency.Dexmedetomidine works on central a-2A and imidazoline type 1 receptors.[3] Decrease in heart rate and blood pressure is reported owing to norepinephrine release reduction via the action of dexmedetomidine on these receptors. The mode of action for Clonidine is via a-1 agonist properties as it is a selective a-2 adrenergic agonist. Clonidine functions by reducing the output of the sympathetic nervous system from the CNS (Central Nervous System).Considerable data in literature have shown that mucosal bleeding is reduced by administering Clonidine preoperatively in FESS, which in turn, helps in improving visibility and decreasing intra-operative duration.[4]

Both Clonidine and Dexmedetomidine have been widely used for decreasing hemodynamic response to tracheal intubation and laryngoscopy. However, data in the literature concerning the comparison of the efficacy of induced hypotension using Dexmedetomidine and Clonidine during Functional Endoscopic Sinus Surgery (FESS) is scarce in the literature.Hence, the present study was conducted to compare and assess the hemodynamic stability and hypotensive efficacy of Clonidine and Dexmedetomidine in FESS.

MATERIALS AND METHODS

The present prospective clinical interventional study was conducted to compare and assess the hemodynamic stability and hypotensive efficacy of Clonidine and Dexmedetomidine in FESS. The study was conducted atShyam Shah Medical College And Sanjay Gandhi

Memorial Hospital, Rewa, Madhya Pradeshafter obtaining clearance from the concerned Ethical committee.The study included a total of 40 subjects from both genders. The subjects were enrolled after obtaining the informed consent verbally as well as in the written format.

The inclusion criteria for the study were subjects who had to undergo FESS of a duration between 1 hour to 70 minutes, subjects from both the genders, weight range of 45-65 kgs, subjects within the age range of 20 years to 54 years, and the subjects willing to participate in the study. The exclusion criteria for the study were subjects allergic to either clonidine or dexmedetomidine, recurrent sinus allergy, hypertension, heart blocks, autonomic neuropathy, coronary artery disease, renal dysfunction,rhinorrhoea, coagulation abnormalities, cerebral insufficiency, and/or hepatic dysfunction.

The study was blinded where the recording of the study parameters and administration of the anesthesia was done by two different anaesthesiologists. Before the surgery, a pre-anesthetic evaluation was done. All 40 subjects were randomly divided into two groups of 20 subjects each. Subjects from Group I received 1 μg/kg dexmedetomidine, whereas, Group II subjects received 2 μg/kg Clonidine. Before administering the anesthesia, fasting status was confirmed for all the subjects followed by anesthesia induction with 1.5mg/kg succinylcholine and 5mg/kg thiopentone sodium which was maintained throughout the surgery. 10 minutes before the general anesthesia induction, the loading dose of the study drug was given which was maintained till surgery completion. The dose was not maintained in cases where hypotension was below the threshold.

Hemodynamic parameters were assessed at baseline, following the loading dose, 1- and 5-minutes following intubation, and every 10 minutes till recovery. These parameters were mean arterial pressure, systolic and diastolic blood pressures, oxygen saturation, and heart rate (HR). Frequent suction need and bleeding severity at the surgical site were assessed using Fromme and Boezaart.[5]Loss of blood was estimated by counting blood-soaked gauges and by measurement of suction container volume after subtracting the volume of irrigation fluid. Emergence time was estimated from the time between anesthetic discontinuation to eye-opening on verbal instructions.

Postoperatively, every 30 minutes, sedation scores (Ramsay Sedation Score[6]), emergence time, and hemodynamic parameters were assessed. VAS was also assessed postoperatively at 15-minute intervals till a VAS score of 3 was reached. First rescue analgesia was also assessed after receiving iv 75mg diclofenac. Postoperative complications including bradycardia (HR<50/min), hypotension, mouth dryness, shivering, vomiting, and nausea were also assessed. Mean arterial pressure of <65mmHg was considered as hypotension, which was managed.All other complications were also managed using appropriate drugs.

The collected data were subjected to the statistical evaluation using SPSS software version 21.0 (Chicago, IL, USA) and t-test. The data were expressed in percentage and number. The level of significance was kept at $p<0.05$.

RESULTS

The present prospective clinical interventional study was conducted to compare and assess the hemodynamic stability and hypotensive efficacy of Clonidine and Dexmedetomidine in FESS. The study included a total of 40 subjects from both genders. weight range of 45-65 kgs, subjects within the age range of 20 years to 54 years. All 40 subjects were randomly

divided into two groups of 20 subjects each. Subjects from Group I received 1 μg/kg dexmedetomidine, whereas, Group II subjects received 2 μg/kg Clonidine. The demographic characteristics of the two groups are compared and depicted in Table 1. The mean age of the study subjects of Group I and Group II was 27.25±7.73 and 27.51±8.66 years respectively. This difference was statistically non-significant with a p-value of 0.9207. All the demographic characteristics were comparable and statistically non-significant between the two groups. The p-values for gender, ASA status, weight, and surgery duration were 0.812, 0.753, 0.4450, and 0.5188 respectively.

On assessing the heart rates and mean arterial pressure in the study subjects, it was seen that both the parameters were statistically insignificant in both the groups at baseline with p-values of 0.6881 and 0.5432 respectively for group I and Group II. The study results showed that mean arterial pressure and heart rates both decreased significantly from baseline at all the time intervals of assessment ($p<0.001$). These values were statistically significant for both intragroup and intergroup for Group I and Group II (Table 2). Also, statistically non-significant results were seen concerning the visibility of the surgical field.

The blood loss in the two groups during FESS was 128.16±6.52ml and 129.73±6.83ml respectively, which was statistically non-significant with p=0.4617. Emergence time was significantly higher for Group I (7.38±0.58 min) than Group II (6.44±0.72 min) with p=0.001. Sedation scores were higher significantly for group I (1.88±1.23) than Group II (1.37±0.12) with p=0.001. VAS scores were significantly lower for Group I (2.24±0.78) than Group II (3.01±0.14) at all time intervals with p=0.001. First rescue analgesia was significantly higher for Group I (110.45±12.25 min) than Group II (84.31±10.06) with the p-value of <0.0001 (Table 3).

The study also assessed the postoperative complications in the two groups of study subjects. It was seen that dry mouth was seen in 20% (n=4) subjects from Group I and 5% (n=1) subject from Group II. Nausea and vomiting were seen in 15% (n=3) of study subjects from Group I and in 5% (n=1) subjects from Group II. Hypotension and bradycardia were seen in 10% (n=2) subjects from Group I and 10% (n=2) subjects from Group II (Table 4). Hypotension and bradycardia were corrected spontaneously after stopping and restricting the study drug infusion. Severe adverse effects were not encountered in any subject. Any encountered side-effect was managed effectively.

DISCUSSION

The study results showed that heart rates and mean arterial pressure were statistically insignificant in both the groups at baseline with p-values of 0.6881 and 0.5432 respectively for group I and Group II. The study results showed that mean arterial pressure and heart rates both decreased significantly from baseline at all the time intervals of assessment ($p<0.001$). These values were statistically significant for both intragroup and intergroup for Group I and Group II. Also, statistically non-significant results were seen concerning the visibility of the surgical field. These results were consistent with the studies by Bajwa S et al[7] in 2016 and Jiwanwall M et al[8] in 2017 where heart rate and mean arterial pressures were significantly decreased from baseline.

Concerning study parameters, blood loss in the two groups during FESS was 128.16±6.52ml and 129.73±6.83ml respectively, which was statistically non-significant with p=0.4617. Emergence time was significantly higher for Group I (7.38±0.58 min) than Group II

(6.44±0.72 min) with p=0.001. Sedation scores were higher significantly for group I (1.88±1.23) than Group II (1.37±0.12) with p=0.001. VAS scores were significantly lower for Group I (2.24±0.78) than Group II (3.01±0.14) at all time intervals with p=0.001. First rescue analgesia was significantly higher for Group I (110.45±12.25 min) than Group II (84.31±10.06) with the p-value of <0.0001. These findings were in agreement with the findings of and Kumar NR et al[9] in 2020and Suggala KK et al[10] in 2020 where comparable parameters to the present study were reported by the authors.

The study also assessed the postoperative complications in the two groups of study subjects. It was seen that dry mouth was seen in 20% (n=4) subjects from Group I and 5% (n=1) subject from Group II. Nausea and vomiting were seen in 15% (n=3) of study subjects from Group I and in 5% (n=1) subjects from Group II. Hypotension and bradycardia were seen in 10% (n=2) subjects from Group I and 10% (n=2) subjects from Group II. Hypotension and bradycardia were corrected spontaneously after stopping and restricting the study drug infusion. Severe adverse effects were not encountered in any subject. Any encountered side-effect was managed effectively. The complications seen in the present study were similar to what was reported by Guven DG et al[11] in 2011 and Moshiri E et al[12] in 2017 where authors reported dry mouth, nausea, vomiting, bradycardia, and hypotension following drug administration.

CONCLUSION

Within its limitations, the present study concludes that better hemodynamic stability was seen with dexmedetomidine compared to Clonidine. However, decreased blood loss and intraoperative visibility were comparable for both dexmedetomidine and Clonidine. Sedation and prolonged anesthesia were also better with dexmedetomidine. However, the present study had few limitations including a smaller sample size, geographical area biases, recall bias, and single-institution nature. Hence, more longitudinal and prospective studies with larger sample sizes, and longer monitoring periods are needed to reach a definitive conclusion.

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TABLES

Characteristics	**Group I (Dexmedetomidine)**	**Group II (Clonidine)**	**p-value**
Age range (years)	20-52	21-54	-
Mean Age (Years)	27.25±7.73	27.51±8.66	0.9207
Gender			
Females	57% (n=11)	50% (n=10)	0.812
Males	45% (n=9)	50% (n=10)	
ASA Status			
I	80% (n=16)	86% (n=17)	0.753
II	20% (n=4)	14% (n=3)	
Weight (kg)	55.08±6.22	53.75±4.55	0.4450
Surgery Duration (min)	66.73±2.65	66.22±2.29	0.5188

Table 1: Demographic characteristics of the study subjects

Time	**Group I Dexmedetomidine**	**Group II-Clonidine**	**p-value**		
			Intragroup (Group I)	Intragroup (Group II)	Intergroup
Mean Arterial Pressure (mmHg)					
At Baseline	96.72±3.43	97.33±2.83			0.5432
At loading dose	85.97±3.27	86.41±4.12	<0.001	<0.001	0.7104
At induction	80.15±3.58	85.99±6.55	<0.001	<0.001	0.0012
1 min after intubation	78.99±2.46	84.23±4.72	<0.001	<0.001	0.0001
5 mins after intubation	72.80±5.42	79.75±6.01	<0.001	<0.001	0.0005
10 mins	70.23±4.25	78.07±5.90	<0.001	<0.001	<0.0001
70 mins	70.29±2.36	77.50±4.12	<0.001	<0.001	<0.0001
Mean Heart Rate (beats/min)					

At Baseline	93.71±8.13	92.71±7.49			0.6881
At loading dose	80.31±6.81	81.91±8.18	<0.001	<0.001	0.5055
At induction	76.79±5.91	82.19±8.56	<0.001	<0.001	0.0257
1 min after intubation	74.82±4.96	79.85±7.87	<0.001	<0.001	0.0205
5 mins after intubation	69.79±5.93	78.73±7.24	<0.001	<0.001	<0.0001
10 mins	66.56±5.51	76.56±6.81	<0.001	<0.001	<0.0001
70 mins	72.54±2.44	79.70±5.54	<0.001	<0.001	<0.0001

Table 2: Mean arterial pressure and heart rate at different time intervals in the study subjects

Parameters	**Group I-Dexmedetomidine**	**Group II-Clonidine**	**p-value**
Blood Loss (ml)	128.16±6.52	129.73±6.83	0.4617
Emergence Time (min)	7.38±0.58	6.44±0.72	0.001
Sedation Scores (at 70 mins)	1.88±1.23	1.37±0.12	0.001
VAS Scores (at 70 mins)	2.24±0.78	3.01±0.14	0.001
First Rescue analgesia (min)	110.45±12.25	84.31±10.06	<0.0001

Table 3: Comparison of study parameters in the two groups of the study subjects

Complications	**Group I -Dexmedetomidine**		**Group II-Clonidine**	
	%	**n**	**%**	**n**
Dry Mouth	20	4	5	1
Nausea and Vomiting	15	3	5	1
Hypotension and Bradycardia	10	2	10	1

Table 4: Comparison of complications seen postoperatively in the two groups of the study subjects