

## CLONIDINE PREMEDICATION AS A DESIRABLE PART OF HYPOTENSIVE ANAESTHESIA FOR FUNCTIONAL ENDOSCOPIC SINUS SURGERY

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### ABSTRACT

#### BACKGROUND

Clonidine an ideal agent for hypotensive anaesthesia, also attenuates stress response to laryngoscopy, decreases requirement of inhalational anaesthetic agents, decreases postoperative analgesic requirements, prevents post-operative shivering.

#### MATERIAL AND METHODS

60 patients under 16-60 years age group posted for functional endoscopic sinus surgery (FESS) were randomly divided into 2 groups of 30 each. Placebo group (Group P) received 20 mL normal saline intravenously and Clonidine group (Group C) received 2.5 micrograms Clonidine per kilogram body weight in 20 mL saline intravenously 20 mins before surgery. Haemodynamic variability during surgery, intraoperative inhalational agent requirement and perioperative bleeding as assessed by surgeon, postoperative analgesic requirement and post-operative shivering were compared between two groups.

#### RESULTS

There was statistically significant reduction in heart rate, systolic blood pressure, diastolic blood pressure and mean blood pressure in Group C compared to Group P. There was statistically significant decrease in requirement of Isoflurane, decreased bleeding from surgical site, decreased analgesic consumption and nil incidence of postoperative shivering in Group C compared to Group P.

#### CONCLUSION

Clonidine is an ideal agent for hypotensive anaesthesia as it has got other favourable effects along with controlled hypotension, as it was observed in this study.

#### KEYWORDS

Clonidine, Hypotensive Anesthesia, Inhalational Agents, Shivering, Analgesia.

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#### INTRODUCTION

Anaesthesia for functional endoscopic sinus surgery is a challenging job. The surgeons operating field itself is very small and surrounded with mucous membranes. It is imperative for the surgeons to look at a clear surgical field in order to identify the diseased tissue properly.<sup>1</sup> By inducing hypotension, bleeding from surgical field can be reduced thereby providing a clear surgical field.<sup>2</sup> Clonidine is drug which is well known for its hypotensive property within good safety profile.

In our study, we have studied the other effects of Clonidine along with the hypotensive property.<sup>3</sup> The effects of Clonidine on requirement of Isoflurane, requirement of other vasodilators, bleeding from surgical site, analgesic consumption and post-operative shivering were compared with the placebo group.

#### MATERIAL AND METHODS

This study was conducted after getting Institute's Scientific and Ethical Committee approval. 60 participants were included in the study after obtaining informed consent. They were randomly divided into two groups of 30 each. Patients belonging to American Society of Anaesthesiologists (ASA) class 1 and 2, patients between ages 16 to 60 and patients undergoing FESS were included in the study. Patients with history of hypertension, cerebrovascular accident, ischaemic heart disease, poor respiratory reserve, hepatic and renal dysfunction were excluded from the study.

Two 18G IV lines were started. Patients were monitored with ECG, pulse oximeter, non-invasive blood pressure, temperature and end-tidal carbon dioxide. All the patients were preloaded with 500 mL normal saline before induction. Nasal packing was done with 4% lignocaine with 1:200000 adrenaline. Patients in Group P received normal saline 20 mL intravenously and patients in Group C received 2.5 micrograms (mcg) per kg body weight of Clonidine in 20 mL saline intravenously. Patients were pre-oxygenated for 5 minutes. Anaesthesia was induced with glycopyrrolate 0.2 mg, fentanyl 2 mcg/kg, Xylocard 1 mg/kg, propofol 2.5 mg/kg and vecuronium 0.1 mg/kg. Endotracheal intubation was done orally with appropriate size tube. Anaesthesia was maintained with 66% nitrous oxide, 33% oxygen, 0.75% isoflurane and vecuronium.

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The plan was to maintain the mean arterial pressure (MAP) of 70 mmHg. If the MAP goes above, then to increase the isoflurane up to 1%. If still high, then to switch over to nitroglycerin (NTG) infusion to achieve target MAP. Intraoperative hypotension was managed with fluids, ephedrine after cutting off NTG infusion. Intraoperative tachycardia was controlled using intravenous metoprolol 1-5 mg. Intravenous bradycardia was managed with Inj. Atropine 0.6 mg. At the end of the procedure, standard reversal with neostigmine 50 mcg/kg and glycopyrrolate 8 mcg/kg was done. Patients were extubated on table.

**The Following Parameters were Studied:**

1. Heart rate, systolic blood pressure, diastolic blood pressure, mean blood pressure were recorded during 5 perioperative stages i.e. before induction, after induction, after intubation, intraoperative average, immediate postoperative period.
2. Requirement of isoflurane and nitroglycerin to achieve target hypotension. High requirement-patients requiring 1%, Moderate - 0.75 to 1%, Low <0.75%.
3. Postoperative sedation score.
4. Incidence of postoperative shivering.
5. Intraoperative problems (hypotension, hypertension, arrhythmias, tachycardia, bradycardia, ischaemia).
6. Assessment of operating condition by surgeon.
7. Postoperative analgesic request time.
8. Post anaesthesia discharge criteria.

**Statistical Analysis and Results**

The age, sex, weight parameters were comparable.

Heart Rate in Beats Per Minute			
	Group p	Group c	p Value
Before induction	100±17	79±20	0.001
After induction	98±17	72±13	0.000
After intubation	102±17	72±14	0.000
Average intra-op	83±4	70±3	0.000
Immediate post-op	102±6	78±3	0.003

**Table 1: Heart Rate**

There is statistically significant reduction in heart rate in the group C compared to group P in all the 5 perioperative stages. i.e. before induction, after induction, after intubation, intraoperative average, immediate postoperative period.

Systolic Pressure in mmHg			
	Group P	Group C	p Value
Before induction	130±17	108±14	0.000
After induction	113±17	95±14	0.004
After intubation	107±20	95±6	0.078
Average intra-op	91±4	89±5	0.482
Immediate post-op	127±8	107±3	0.030

**Table 2: Systolic Blood Pressure**

There is statistically significant reduction in systolic blood pressure in the group C compared to group P before induction, after induction, and immediate postoperative period.

Diastolic pressure in mmHg			
	Group P	Group C	p Value
Before induction	89±12	71±11	0.000
After induction	75±12	64±13	0.001
After intubation	81±13	62±4	0.059
Average intra-op	62±3	61±3	0.293
Immediate post-op	85±5	75±3	0.046

**Table 3: Diastolic Blood Pressure**

There is statistically significant reduction in diastolic blood pressure in the group C compared to group P before induction, after induction, and immediate postoperative period.

Mean Arterial Pressure in mmHg			
	Group P	Group C	p Value
Before induction	101±15	82±11	0.000
After induction	86±22	73±13	0.085
After intubation	90±15	74±5	0.066
Average intra-op	69±3	72±3	0.382
Immediate post-op	100±7	85±3	0.044

**Table 4: Mean Arterial Pressure**

There is statistically significant reduction in mean arterial pressure in the group C compared to group P before induction and in immediate postoperative period.

	High Requirement	Moderate Requirement	Low Requirement
Placebo Group	60%	40%	0
Clonidine Group	0	10%	90%

**Table 5: Intraoperative Requirement of Isoflurane**

In group P, 40% of the patients had moderate and 60% had high requirement of isoflurane. In the group C, there were only 10 % who had moderate requirement of isoflurane and 90% of the patients had only low requirement.

Placebo Group	60%
Clonidine Group	0%

**Table 6: Intraoperative Requirement of Nitroglycerin**

60% of the patients in group P required nitroglycerin intraoperatively and none of the patients in group C required nitroglycerin intraoperatively.

Intraoperative Problems	Placebo (P)		Clonidine (C)		P-Value
	NO.	%	NO.	%	
Arrhythmia					
Yes	0	0	0	0	
No	30	100	30	100	
Hypotension					
Yes	6	20	10	33	0.04
No	24	80	20	67	
Hypertension					
Yes	6	20	4	13	1.0
No	24	80	24	87	
Tachycardia					
Yes	28	94	0	0	0.60
No	2	6	30	100	
Bradycardia					
Yes	2	7	2	7	0.60
No	28	93	28	93	

**Table 7: Intraoperative Adverse Events**

In the group C, five cases developed hypotension and two developed hypertension. The incidence of bradycardia

was one in both the groups. Intraoperative tachycardia, arrhythmias and ischaemia were not seen in both the groups.

Operating Field	Placebo Group(P)	Clonidine Group (C)	Total
Excellent	14	16	30
Good	16	14	30
<b>Total</b>	<b>30</b>	<b>30</b>	<b>60</b>

**Table 8: Evaluation of Operating Condition by Surgeons**

	Value	Degree of freedom	P value
Pearson Chi-Square	1.616	2	.446
Likelihood Ratio	1.628	2	.443
No of valid Cases	60		

**Table 9: Evaluation of Operating Condition by Surgeons: Chi Square**

21 patients in group C and 9 patients in group P had excellent operating conditions as assessed by the surgeon.

		Placebo Group(p)	Clonidine Group(c)	Total
Postoperative Shivering	No	21	30	51
	Yes	9	0	9
<b>Total</b>		<b>30</b>	<b>30</b>	<b>60</b>

**Table 10: Post-operative Shivering**

	Value	Degree of Freedom	p value
Pearson chi-square	8.445	2	.015
Likelihood ratio	12.386	2	.002
No. Of valid cases	60		

**Table 11: Post-operative Shivering**

35% of patients in group P and none in group C developed postoperative shivering.

		Placebo Group (p)	Clonidine Group (c)	Total
Post-op sedation score	2	8	5	13
	3	4	10	14
	4	16	15	31
	5	2	0	2
<b>Total</b>		<b>30</b>	<b>30</b>	<b>60</b>

**Table 12: Post-operative Sedation Score**

	Value	Degree of Freedom	P Value
Pearson chi-square	10.526	6	.104
Likelihood ratio	11.863	6	.065
Linear-by-linear association	.164	1	.685
No. of valid cases	60		

**Table 13: Post-operative Sedation Score**

There was no statistical difference in postoperative sedation score between two groups.

Analgesia Request	Placebo Group(p)	Clonidine Group(c)	P-value
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No. of cases	30	30	<0.001
Mean	0.2	6.4	
S.D.	0.37	1.54	
Median	0	7	
Mode	0	7	
Range	0-1	2-8	

**Table 14: Time for Analgesia Request: (Hours After Extubation)**

The median time for request of analgesics was 7 hours in group C compared to less than one hour in group P.

PADSS - 6 PM on day of Surgery	Placebo(p)		Clonidine(c)		P-value
	No.	%	No.	%	
6	0	0	5	16.6	<0.001
7	8	26.6	25	83.4	
8	18	60	0	0	
9	4	13.4	0	0	

**Table 15: PADSS - 6 Hours Post-operative**

PADSS - 6 AM	Placebo (P)		Clonidine (C)		p-Value
	No.	%	No.	%	
7	3	10	3	10	0.01
8	0	0	0	0	
9	18	60	27	90	
10	9	30	0	0	

**Table 16: PADSS - 18 Hours Post-operative**

Only 10% of cases in group P were fit to get discharged on the day of surgery, but majority of the patients in both the group were fit to be discharged in the next day. There was no statistical difference in these criteria. So, Clonidine provides satisfactory hypotension, better operating condition, attenuates intubation response, prevents postoperative shivering, prolongs analgesia, decreases requirement of Isoflurane and nitroglycerin, without affecting the recovery.

**DISCUSSION**

Functional endoscopic sinus surgery (FESS) is associated with significant bleeding that impairs recognition of fine structures which negatively affects outcome. Hypotensive anaesthesia decreases blood loss, reduces surgical time and improves operation theatre resources.<sup>4</sup>

The primary goal of hypotensive anaesthesia is not only to provide bloodless surgical field but also to conduct a balanced anaesthesia and prompt recovery. Sodium nitroprusside, nitroglycerin, trimetaphan, adenosine, remifentanyl, beta-blockers, ACE inhibitors, alpha-2 adrenergic agonists were tried for hypotensive anaesthesia so far in which alpha-2 adrenergic agonists has got proven safety and recovery profile.<sup>5</sup> Dexmedetomidine and clonidine are common alpha adrenergic agonists used for hypotensive anaesthesia. But compared to clonidine, dexmedetomidine is costlier and has got side effects like bradycardia, dry mouth and sedation.<sup>6</sup> Clonidine has been tried in oral as well as intravenous route for premedication in hypotensive anaesthesia.

Oral clonidine premedication was tried in some surgeries to achieve hypotensive anaesthesia for reduction of blood loss. But the results were unsatisfactory.<sup>7</sup>

Intravenous clonidine given in dose up to 4 micrograms per kilogram body weight/kg B.W (mics/kg B.W.) had produced satisfactory and reliable hypotension in patients undergoing middle ear and nasal surgeries.<sup>2</sup> Studies have

compared three doses of intravenous clonidine. 2 mics/kg, 3 mics/kg B.W, 5 mics/kg B.W. 2 mics/kg doses provided less analgesia and stable haemodynamics. 5 mics/kg dose provided intense analgesia but hypotension in the postoperative period. 3 mics/kg dose has provided optimum analgesia with stable haemodynamics.<sup>8</sup> In our study, we have used 2.5 mics/kg B.W. of clonidine with which we had reliable hypotension and decreased blood loss from surgical field. The effects are titratable and the side effects of Clonidine are easily manageable. Clonidine also produces lesser episodes of tachycardia and hypertension and provides lower heart rate and blood pressure.<sup>9</sup>

Clonidine apart from an adjuvant for hypotensive anaesthesia had also got other advantages. Clonidine compared to placebo group attenuates pressor response to laryngoscopy.<sup>10</sup> Preoperative clonidine premedication also reduces the requirement of narcotics and inhalational anaesthetics significantly. Without Clonidine it is mandatory to go up on concentrations of inhalational anaesthetics and narcotics to achieve desired hypotensive levels.<sup>11,12</sup> In our study, there was significant decrease in requirement of inhalational anaesthetics compared to placebo group.

Clonidine premedication also decreases the need for vasodilators along with inhalational agents to achieve desired hypotension.<sup>13</sup> In our study, the placebo group required vasodilators to achieve hypotension in few cases. But none of the patients in clonidine group required vasodilators. Clonidine is a safe agent for hypotensive anaesthesia as it does not cause myocardial ischaemia or arrhythmias. There were no significant intraoperative adverse effects in patients who had received intravenous Clonidine in our study.<sup>14</sup> There was minimal bleeding from the surgical site and the field was clear for the surgeon to operate. This parameter was assessed in our study by the surgeon. Clonidine, if used in appropriate doses, has no effect on recovery from general anaesthesia.<sup>15</sup> Alpha-2 adrenergic agents has got another advantage in prevention of shivering in the postoperative period due to intraoperative hypothermia.<sup>16</sup> In our study, there was no incidence of shivering in the postoperative period in the Clonidine group. Clonidine also prolongs the postoperative analgesia.<sup>17,18</sup> In our study, there was significant increase in duration of postoperative analgesia and decreased analgesic requirements in clonidine group compared to placebo group. Studies show that there was no significant change in post-anaesthesia discharge time in patients who had received intravenous Clonidine which was analysed using Aldrete score.<sup>19</sup> In our study, there was no significant difference in mean discharge time for both the groups.

#### CONCLUSION

Clonidine apart from its hypotensive property, attenuates pressor response to laryngoscopy, decreases requirement of inhalational anaesthetics, prolongs postoperative analgesia and prevents postoperative shivering without much effect on recovery from anaesthesia.

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