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ORIGINAL ARTICLE

EVALUATION OF CLINICAL EFFICACY OF CLONIDINE AS AN ADJUVANT TO GENERAL ANAESTHESIA IN ELECTIVE FACIOMAXILLARY AND AESTHETIC FACE SURGERY- THE PROSPECTIVE RANDOMIZED SINGLE BLIND CONTROLLED STUDY

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ABSTRACT: AIM AND OBJECTIVES: The present study aims to evaluate the clinical efficacy of clonidine as an adjuvant to General anaesthesia in elective faciomaxillary surgery. Faciomaxillary surgery is generally long duration surgery. Bleeding is expected to be more. As an anesthetist our main aim is to reduce the bleeding and make the patient more hemodynamically stable, so there is always a need to decrease heart rate(H.R.), blood pressure (B.P.) and prevent hemodynamic stress response to intubation, extubation and intraoperatively. **MATERIAL AND METHODS:** This prospective, randomized, double-blind controlled study was conducted on 60 male adults of ASA Grade I & II scheduled for elective faciomaxillary surgery under General anaesthesia. After taking consent from the institutional ethical committee patients were divided into 2 groups comprising 30 patients in each group. Group I received 2µg/kg of clonidine in 100ml normal saline 30 min before surgery and Group II received 100ml normal saline. H.R., non-invasive B.P (N.I.B.P.), oxygen saturation in arterial blood (SpO_2) were recorded as base line, after induction, after intubation, then at 15 min internal intraoperatively and finally after extubation. H. R. and B. P. were assessed after 30 min, 2hr and 6hr postoperatively. Any complication, side effect and adverse effect upto 24 hrs postoperatively were noted. **RESULTS AND CONCLUSION:** In Group I, compared to Group II, there was significant decrease in B.P. and H.R. during intubation, intraoperatively, extubation and post operatively and the concentration of isoflurane used was also reduced. Blood loss and incidence of shivering was less and also tube tolerance ability was better when tube was left in situ after surgery Clonidine, 2µg/kg IV in 100ml normal saline, 30min before is safe and effective in preventing the hemodynamic surgical stress response as well as intubation, extubation stress response.
KEYWORDS: Clonidine, General Anaesthesia, Faciomaxillary.

INTRODUCTION: Faciomaxillary surgery is generally long duration surgery. Bleeding is expected to be more. As an anaesthetist our main aim is to reduce the bleeding and make the patient more hemodynamically stable, so there is always a need to keep the B.P. and H.R. on lower side.

Clonidine, an alpha2 agonist, is a very promising drug in faciomaxillary surgery. It reduces bleeding, keep the B.P. and H.R. on lower side, blunts the laryngoscopic intubation response, reduces the requirement of anaesthetic agent, decreases post-operative nausea vomiting, has sedative, anxiolytic, analgesic effect, decreases plasma catecholamines concentrations and increases tube tolerance if the patient has to remain intubated post operatively.

It is a centrally acting selective partial $alpha_2$-adrenergic agonist that acts as an antihypertensive drug by virtue of its ability to decrease sympathetic nervous system output from the

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central nervous system. In addition, alpha2 receptor within spinal cord modulate pain pathways resulting in analgesia. Clonidine as an anaesthetic adjuvant provide postoperative sedation without depression of ventilation.

The present study aims to evaluate the clinical efficacy of clonidine as an adjuvant to General anaesthesia in elective faciomaxillary surgery.

MATERIAL AND METHODS: Following approval by the Board of Studies, Department of Anaesthesiology, & Ethical committee, of the institution, 60 male patients of ASA grade I and II between 20-50 yrs, weighing 50-80 kg were selected for elective faciomaxillary and aesthetic face surgery. The patients were randomly divided into two groups I and II group. Group I received 100ml of normal saline and group II received 2microgram/kg of clonidine in 100ml normal saline 30 mins before surgery. Any patient having compromised cardio-pulmonary or renal status or on any medications like beta blocker, antihypertensive, antianginal drugs, anxiolytics or analgesics, obese patient (wt more than 80 kg), or patient hypersensitive to any drug used in the study, were excluded from the study.

Thorough preanesthetic check-up was done and informed written consent was taken. Tab Ranitidine 150mg and alprazolam 0.25mg was given orally the night before surgery.

On the day of surgery i.v. drip was started 30 min before surgery. Monitors were attached and H.R., B.P., SpO_2, electrocardiogram (E.C.G.) and end-tidal carbondioxide (Et-CO_2) were recorded throughout the surgery. Baseline H.R. and B.P. readings were taken. Then 2microgram/kg clonidine in 100ml of normal saline was started and finished in 15minutes in group A and in group B 100ml normal saline was infused.

Normal saline drip was prepared by an anaesthetist who was not aware of the proceedings. Patient was pre-medicated with Inj. Ranitidine 50mg, Inj. Ondansetron 4 mg, Inj. Glycopyrrolate 0.2mg and Inj. Butraphenol 1mg. Induction was done with propofol 2.5mg/kg and succinylcholine1.5mg/kg and intubation was done with 7.5 or 8.0 mm I.D. spiral reinforced tube and tube was connected to the ventilator. Throat pack was placed. Heart rate, systolic and diastolic B. P. were recorded to see the intubation response.

Maintenance was done with O_2 and N_2O in the ratio 40:60 and 1% Isoflurane was started. Bolus dose of vecuronium(0.1mg/kg) was given. 1mg of vecuronium was given as top up during surgery. Ventilator setting of tidal volume and respiratory rate was adjusted to keep the $EtCO_2$ 30-35mmHg. Respiratory rate was kept between 12 to 14/min.

At the end of the surgery reversal was done with neostigmine 0.05mg/kg and glycopyrolate 0.008mg/kg. Throat pack was removed, pharyngo-tracheal suction was done and then extubation was done. Reading of B.P. and heart rate was taken at this time. After the patient was able to keep his eyes open, elevate head and breathe normally, he was shifted to ward. B.P. Heart Rate, sedation score and requirement of analgesic were assessed after 30min, 2hr and 6 hr. Any complication, side effect and adverse effect up to 24 hrs postoperatively was noted.

STATISTICS: Data was summarized as mean ± standard deviation or as percentages. Statistical analysis was performed by SPSS-15 version. Numerical variables were normally distributed and was compared by Student's unpaired 't'-test.

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RESULT: All the patients (n=60) completed the study. Hemodynamic variables were recorded in both the groups as shown in table no. 1, 2 & 3.

In group I there was increase in systolic B.P., diastolic B.P. & H.R during intubation, extubation and postoperative period upto 4 hr (P value <0.05 i.e. significant). Diastolic B.P. during intraoperative period did not increased significantly i.e. P value >0.05

In group II there was significant decreased (P value<0.05) in systolic B.P., diastolic B.P. & H.R. during intubation, extubation, intraoperative period and postoperative period upto 4 hrs.

Table No. 1

	Group I	Group II	t-value	P-value
Baseline	130.44±8.69	132.47±8.67	0.6405	P>0.05 Not Significant
At induction	128.2±13.57	103.93±11.18	5.3461	P<0.05 Extremely Significant
After Intubation	148.93±9.07	125.53±10.69	6.4645	P<0.05 Extremely Significant
Mean 15 min Intra operative	114.67±19.09	97.8±12.2	2.884	P<0.05 Very Significant
After extubation	149.73±14.82	115.07±9.6	7.6022	P<0.05 Extremely Significant
Post operative 30 min	136±11.33	118.6±6.06	5.2448	P<0.05 Extremely Significant
Post operative 2 hr	130.47±9.96	120.6±6.81	3.8102	P<0.05 Extremely Significant
Post operative 4 hr	129.87±7.18	122.93±6.28	2.8178	P<0.05 Extremely Significant
Post operative 6 hr	131±6.9	127.07±98	1.5508	P>0.05 Not Significant

Systolic B.P. of Both groups, mean ± standard deviation

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Table No. 2

	Group	Group II	t-value	P-value
Baseline	80.93±11.58	81.93±11.3	0.2394	P>0.05 Not Significant
At Induction	76.67±13.62	76.8±12.21	0.0275	P>0.05 Not Significant
After Intubation	94.67±9.88	75.87±11.72	4.75	P<0.05 Extremely Significant
Mean 15 min Intra operative	67.2±17.01	58.53±12.19	1.6046	P>0.05 Not Significant
After extubation	97.09±8.87	71.13±10.23	7.3903	P<0.05 Extremely Significant
Post operative 30 min	83.33±9.59	73.8±7.15	3.0856	P<0.05 Very Significant
Post operative 2 hr	81.87±8.33	71.4±9.57	3.0961	P<0.05 Very Significant
Post operative 4 hr	80.93±5.74	74.27±11.04	2.073	P<0.05 Significant
Post operative 6 hr	80.67±7.43	75.33±7.86	1.9122	P>0.05 Not Significant

Diastolic B.P. of Both groups, mean ± standard deviation

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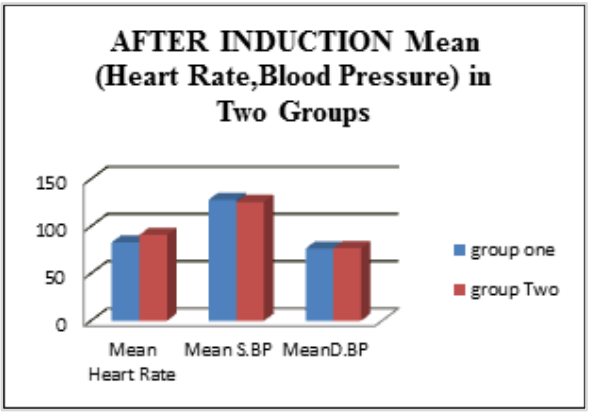
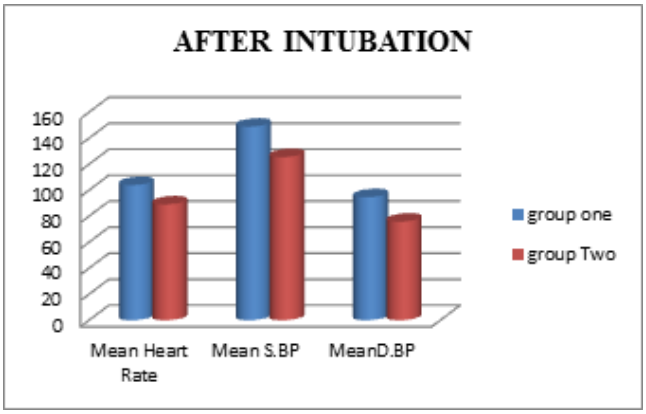
Table No. 3

	Group	Group II	t-value	P-value
Baseline	83.27±11.18	99.27±12.79	3.6478	P>0.05 Not Significant
At Induction	82.93±10.55	90.93±13.89	1.7764	P>0.05 Not significant
After Intubation	104±6.81	89.13±16.12	3.291	P<0.05 Very Significant
Mean 15 min Intra operative	89.13±8	78.73±12.38	2.7327	P>0.05 Significant
After extubation	108.13±14.13	83.27±11.58	5.2703	P<0.05 Extremely Significant
Post operative 30 min	97.73±13.01	80.47±10.88	3.9415	P<0.05 Extremely Significant
Post operative 2 hr	92±9.81	72.33±12.84	4.7146	P<0.05 Extremely Significant
Post operative 4 hr	90.4±9.93	79.33±12.75	2.653	P<0.05 Significant
Post operative 6 hr	88.33±7.51	82.8±12.38	1.4791	P>0.05 Not Significant

Heart Rate in beat per minute (bpm) of Both groups, mean ± standard deviation





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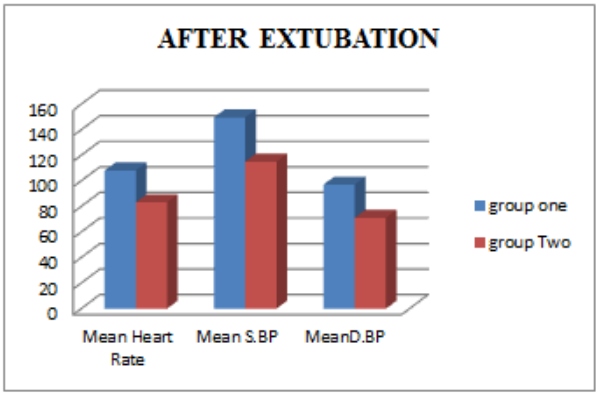

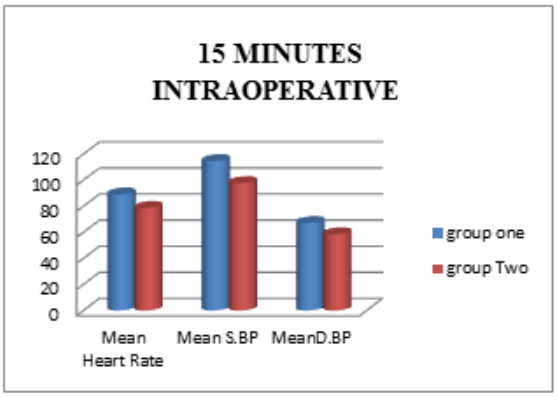

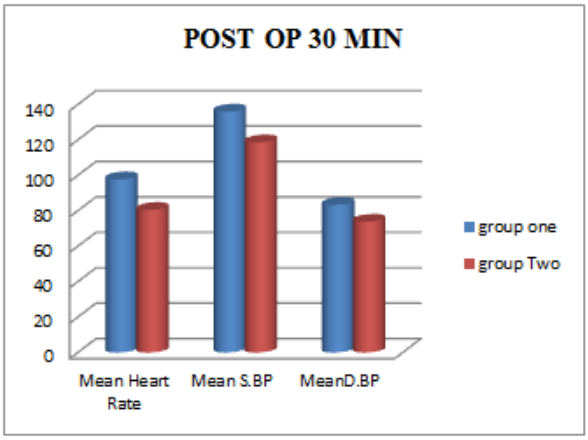

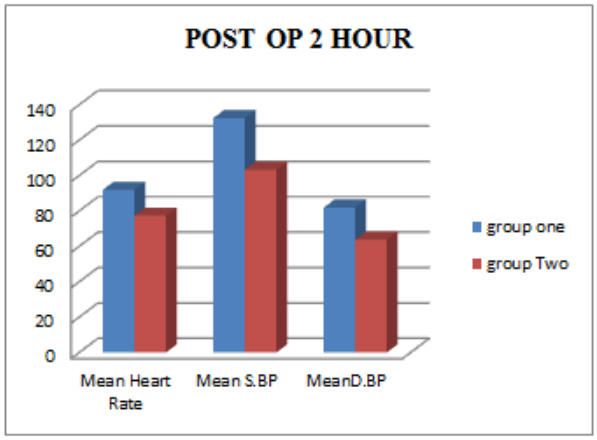

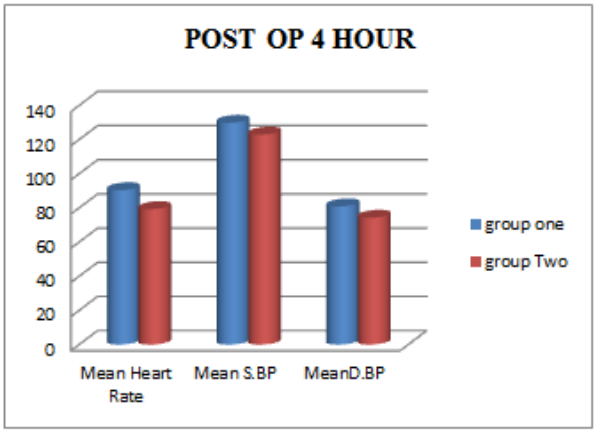

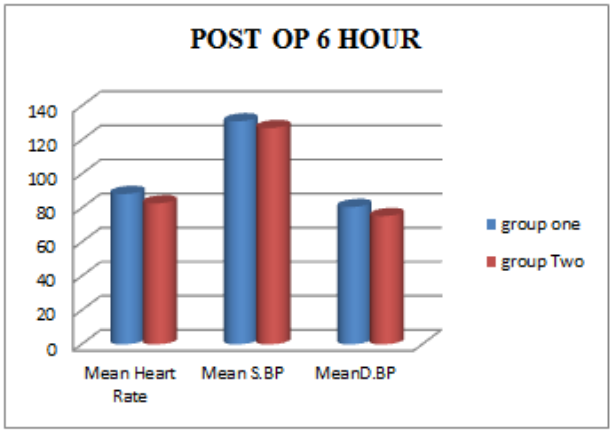

In group I 26 patients required 1% of isoflurane concentration whereas none of the patient in group II required isoflurane concentration above 0.5% and at times isoflurane was stopped due to decrease in systolic B.P.

There was less bleeding in group II as compared to group I.

DISCUSSION: The choice of anaesthetic technique for faciomaxillary surgery is limited to general anesthesia with muscle paralysis, tracheal intubation and intermittent positive pressure ventilation. Our study was conducted in 60 adult male patients belonging to ASA grade I and II, to evaluate the

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efficacy of clonidine premedication on hemodynamic stress response during intubation, extubation, intraoperative period and anaesthetic sparing. In the present study we evaluated the effect of i.v. premedication with clonidine for haemodynamic stability during laryngoscopy. It was shown in table no. 1 and 2 and graph no. 2 where baseline systolic B.P in group I was 130.44±8.69 and diastolic baseline B.P. was 80.93±11.53 mmHg and in group II systolic B.P. was 132.47±8.67 and diastolic B.P. was 81.93±11.3mmHg. After intubation in group I systolic BP was 148.93±9.07 and diastolic B.P. was 94.7±9.88mmHg B.P. and group II systolic B.P. was 125.53±10.69 and diastolic B.P. was 75.87±11.72mmHg so B.P. was significantly higher in group I incomparision to group II. This difference is extremely significant (P<0.05).

In table no. 3 and graph 2 suppression of pressor response during intubation was also reflected on heart rate which was 83.27±11.18 bpm as a baseline in group I & 99.27±12.7 bpm in group II. After intubation in group I was 104±6.81 bpm and 98.13±16.12 bpm in group II Here also heart rate was higher in group I incomparision to group II and P value <0.05 which is very significant. We observed the anxiolytic and sedative effects of i.v. premedication without significant respiratory depression. Haemodynamic responses of laryngoscopy were attenuated by i.v. premedication with clonidine due to its central sympatholytic action.

Near stable haemodynamic variable and absence of any sympatho-somatic response with i.v. premedication after clonidine is shown in the present study. Clonidine effectively attenuated the rise of heart rate and mean arterial blood pressure indicating inhibiton of catecholamine. Clondine posesses several properties to make it valuable premedicant to attenuate the hemodynamic response of laryngoscopy. Bernard J M et al; described the same effect of clonidine in premedication on hemodynamic and adrenergic response during laryngoscopy recovery from anesthesia.[11]

Montazerik et al; showed the effect of clonidine as a premedication in attenuating the presssor response to direct laryngoscopy and tracheal intubation.[12] This effect is demonstrated in many other studies also like Gupta K et al; Gupta D et al; Kumar B etal; Fuji Y etal.[13],[14],[15],[18]
Haemodynamic response to laryngoscopy should be attenuated due to associated risk of myocardial ischemia or cerebral haemorrhage. The haemodynamic changes can be detrimental in elderly and haemodynamicaly compromised patients. Clonidine activated alpha$_2$ adrenergic receptors in the brain and spinal cord to decrease sympathetic outflow, causing sedation, analgesia and decrease in B.P. and HR without significant respiratory depression.

As shown in table no. 1 and 2 and graph no. 3 to 7 patients in group I had intraoperative systolic BP 114.67 ±19.09 and diastolic BP 67.2 ±17.01mmHg, and in group II systolic BP 97.8±12.2 and diastolic BP 58.53±12.19mmHg. Post-operative systolic BP after 30 min in group I was 136±11.33 and diastolic BP 83.33±9.59mmHg and in group II post-operative systolic BP after 30 min was 118.6±6.06 and diastolic BP 73.8±7.15 mmHg. Post-operative systolic BP after 2 hrs in group I was 130.47±9.96 and diastolic BP was 81.87±8.33 mmHg and in group II systolic BP was 120.6±6.81 and diastolic BP 71.4±9.57 mmHg. Post-operative systolic BP after 4 hrs in group I was 129.8±7.18 and diastolic BP was 80.93±5.74mmHg and group II systolic BP was 122.93±6.28 and diastolic BP was 74.27±11.04mmHg. There was significant decrease in intraoperative and postoperative B.P. upto 4 hour in group II i.e. P-value <0.05.

As shown in table no.3 and graph no. 3 to 7 patients in group I had intraopertively heart rate 89.13 ±8bpm and group II 78.73±12.38 bpm. After extubation HR in group I was 108.13±14.1 bpm and in group II was 83.27±11.58 bpm. Post-operative after 30 min in group I HR was 97.73±13.01

bpm and group II HR was 80.47±10.88 bpm. Post-operative after 2 hrs HR in group I was 92±9.81 bpm and group II was 72.33±12.84 bpm and post-operative 4 hrs HR in group I was 90.4±9.93 bpm and group II was 79.33±12.75 bpm. Here also there is significant decrease in heart rate intraoperatively and postoperatively upto 4 hrs (P value <0.05) as compared to group I.

Hypertension and tachycardia were noticeably higher in group I as compared to group II. The patients who were given i.v. clonidine 30 minutes prior to surgery had more stable haemodynamic than those given i.v. normal saline. Clonidine premedication effectively blunted the cardiovascular response to intubation, extubation and surgical stress. As seen in table no. 1, 2, 3 and graph 3 to 7 compared with baseline measurement, there was significantly less increase in heart rate and blood pressure in group II compared to group I. The same hypotensive effect of clonidine is elicited by Pandazi et al; Lee J et al; Gupta K et al; Singh S et al; Hackman et al; Farah et al; Sung C S et al.[3],[19],[13],[6],[7],[5],[18]

Clonidine for premedication has been used by other authors who have documented maintenance of stable haemodynamics during intubation, extubation, intraoperative and postoperative period. Clonidine as an oral, i.v. and transdermal patch has been used. In our study we have used clonidine intravenously.

As already shown in our study Caverni V et al; also showed that the use of clonidine as premedication in 3 different groups hypotension was successfully obtained with a bloodless surgical field and there was no need for additional use of a potent hypotensive agent.[2]

In our randomized, single blinded study, we demonstrated that clonidine reduced the need of isoflurane required to produces a bloodless surgical field. Desired haemodynamic response was maintained at significantly lower concentration of isoflurane. Our finding were in concordance with other studies in which there was decrease in MAC and inhalational agent requirement.

Inomata et al; studied the effects of clonidine premedication on sevoflurane requirement and anaesthetic intubation time.[8],[9] They concluded that there was reduction in MAC and MAC for intubation after clonidine premedication. Bernad et al; studied about the preoperative use of oral clonidine followed by i.v. infusion postoperatively was found to improve the hemodynamic profile associated with anaesthetic discontinuation this further proving its anesthetic sparing effect.[11] Morris J et al; studied the effect of clonidine premedication on propofol requirements during lower extremity vascular surgery.[10]

CONCLUSION: Clonidine was found to be very useful as an adjuvant to G. A in faciomaxillary and aesthetic face surgery as it effectively reduced intubation, extubation response and decreased intraoperative B.P., heart rate thus no other hypotensive agent was required. It has anesthetic sparing effect and intraoperative blood loss was less and requirement of blood was decreased. There was reduction in nausea and vomiting. Postoperatively light sedation with analgesia was maintained and tube tolerability was better in cases where tube was left in situ postoperatively.

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