



## COMPARISON OF CLONIDINE AND ATENOLOL FOR PROVIDING OPTIMAL SURGICAL FIELD IN NASAL SURGERIES UNDER GENERAL ANAESTHESIA: A RANDOMIZED, DOUBLE BLIND, PLACEBO STUDY

### Anaesthesiology

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### ABSTRACT

**Aim:** To evaluate the role of oral clonidine and atenolol in providing optimal surgical field in nasal surgeries under general anaesthesia.

**Material & Methods:** 90 patients of ASA grade I & II posted for elective nasal surgeries were randomly divided into 3 groups (n=30). Group A received 50mg oral atenolol, Group B 100 ug oral clonidine and identical looking placebo tablet in group C two hours before surgery. Induction & maintenance of anaesthesia was performed similarly. Hemodynamic parameters were measured. The surgeon, blinded to group allocation, evaluated the quality of surgical field using Average Category Scale. Total blood loss was recorded.

**Results:** Hemodynamic parameters were within normal range from induction to the end of the surgery in the both groups A and B but were on higher side in group C. The difference in blood loss between groups was highly significant being less in group B ( $117.77 \pm 7.59$  ml) as compared to group A ( $155.73 \pm 14.90$  ml) & group C ( $180.86 \pm 18.6$ ). This resulted in a better surgical field in group B.

**Conclusion:** Oral clonidine provided better surgical field than atenolol in nasal surgeries under GA.

### KEYWORDS

Atenolol, Clonidine, Nasal Surgery, Blood Loss

### INTRODUCTION:

Over the past two decades, number of patients undergoing nasal surgeries for pathological and cosmetic reasons has increased. But blood loss has been a limiting factor in these surgeries<sup>1</sup> which can result in serious complications due to impaired visibility.<sup>2</sup> For avoiding such complications, nasal surgeries have traditionally been performed either with local anaesthesia,<sup>3</sup> vasoconstrictors (e.g. epinephrine, cocaine and phenylephrine)<sup>4,5</sup> or under general anaesthesia.<sup>6</sup> To avoid discomfort associated with topical anaesthesia; general anaesthesia is preferred.<sup>3</sup> General anaesthesia is advantageous in terms of providing an immobile surgical field, effective protection of the respiratory tract, adequate analgesia and ventilation. Various drugs like beta blockers, alpha-2 agonists etc that potentiate the effect of inhalational anaesthetic agents to reduce bleeding by virtue of inhibiting sympathetic stimulation have been used. Although clonidine and atenolol have been compared in terms of intraoperative bleeding and the need for antihypertensive drugs; but there is no study which compares the effect of these two commonly used drugs for assessing the quality of surgical field in nasal surgeries.

This study was conducted for comparing the efficacy of oral clonidine and oral atenolol given as premedication in patients undergoing nasal surgeries for judging adequacy of surgical field as primary outcome and intra operative blood loss and hemodynamic variables as secondary outcome.

### MATERIAL AND METHODS:

A randomized, double blind study was conducted on 120 patients of ASA grade I & II of either sex aged 18 to 60 years, undergoing rhinoplasty, septoplasty, and functional endoscopic sinus surgery after approval from hospital ethics committee.

Patients who had bronchial asthma, chronic obstructive pulmonary disease, diabetes mellitus, hypertension, ischaemic heart disease and who had history of hypersensitivity reaction to study drugs were excluded from the study. After taking informed written consent, patients were randomly divided into three groups of 30 patients each. The number of patients was determined by power analysis (93%) to find the quality of surgical field between the two groups. Patients received oral atenolol 50mg in group A, oral clonidine 100ug in group B and similar looking placebo tablets in group C 2hr before induction of anaesthesia by number coded envelopes which contained either atenolol, clonidine or placebo. The hemodynamic parameters were checked in the preoperative room. On arrival in the operating room after attaching standard monitoring, appropriate sized cannula was inserted and intravenous line started with Ringer's lactate. Pre-oxygenation with 100% oxygen was done for 3 minutes.

All patients were premedicated with inj. glycopyrrolate 0.01mg/kg and inj butorphenol 0.02 mg/kg before induction of anaesthesia with

inj. propofol 2-3 mg/kg. After checking for ventilation inj. vecuronium 0.12mg/kg was used to facilitate orotracheal intubation with a cuffed endotracheal tube of appropriate size. Oropharyngeal packing was done. Local infiltration of surgical site was done using 10 ml of inj 2% xylocaine with adrenaline (1: 200000). Heart rate, systolic blood pressure, diastolic blood pressure, oxygen saturation were recorded before ( $T_0$ ) and after ( $T_1$ ) induction, immediately after intubation ( $T_0$ ), every 1 minute for 5 minutes ( $T_1$ - $T_5$ ), then every 5 minutes for 15 minutes and then every 15 minutes till end of surgery. Anaesthesia was maintained with halothane (1 MAC) in a mixture of nitrous oxide (60%) in oxygen (40%) and inj. vecuronium. Controlled mechanical ventilation with initial tidal volume of 8ml/kg and respiratory frequency of 12 breaths/min was adjusted to maintain end tidal carbon dioxide between 30-35 mm Hg. (Aestiva Workstation, GE, USA)

Intra-operative bleeding was measured by collecting blood in a marked container of 25 ml capacity with the precision of 0.5 ml. The blood soaked by gauge pieces and nasal pack was measured by weighing the gauge pieces before autoclaving and after the surgical procedure.

After the end of the procedure reversal of neuromuscular blockade was achieved using inj. neostigmine 0.05 mg/kg & inj. glycopyrrolate 0.01mg/kg. After oropharyngeal suctioning, the pack was removed. The same surgeon, unaware of the group, was asked to evaluate the quality of the operative field using a pre-defined average category scale (ACS) adapted from Fromme et al<sup>7</sup> (Table 1) at the beginning of surgical procedure and in the end. Surgical field was graded as Good -- ACS 0 or 1, Fair -- ACS 2 or 3, Poor-- ACS 4 or 5. When patient started obeying commands, extubation was done and shifted to recovery room. Blood pressure & heart rate were recorded every 15 minutes for 4 hours in recovery room. After shifting to the ward, heart rate and blood pressure were again recorded every 2 hours for next 8 hours, then at 16th hour and 24 hours.

**Table 1: Average Category Scale (ACS) Grading**

| GRADE | BLEEDING                                                                                                                                                         |
|-------|------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 0     | No bleeding                                                                                                                                                      |
| 1     | Slight bleeding- no suctioning required                                                                                                                          |
| 2     | Slight bleeding- occasional suctioning required. Surgical field not threatened.                                                                                  |
| 3     | Slight bleeding- frequent suctioning required. Bleeding threatens surgical field a few seconds after suction is removed.                                         |
| 4     | Moderate bleeding- frequent suctioning required. Bleeding threatens surgical field directly after suction is removed.                                            |
| 5     | Severe bleeding- constant suction required. Bleeding appears faster than can be removed by suction. Surgical field severely threatened and surgery not possible. |

During the intraoperative and postoperative period (upto 24 hrs) the occurrence of side effects like hypotension and bradycardia were noted. Hypotension, defined as 20% decrease in systolic blood pressure from baseline and bradycardia less than 60 bpm; if occurred, were treated appropriately.

At the end of study decoding of groups and the data compilation was done. Statistical analysis was done by using Chi Square test for non-parametric data and student's t test for parametric data using SSPS I or III software. Wilcoxon Signed Rank Test was used for intragroup comparison of quality of surgical field with Z value more than 5 considered as significant. For intergroup comparison of surgical field quality Chi Square test was used. P value of less than 0.05 was considered significant and less than 0.001 as highly significant.

## RESULTS:

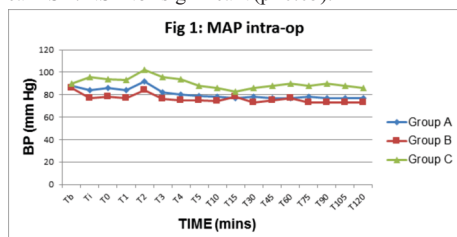
There was no statistically significant difference between groups with regard to age, sex, weight, ASA physical status and duration of surgery as shown in Table 2.

Haemodynamically blood pressure showed transient response to intubation. Mean Arterial Pressure (MAP) varied between  $82.03 \pm 4.5$  mm of Hg in group A,  $78.06 \pm 5.5$  mm of Hg in group B and  $88.15 \pm 8.5$  mm of Hg in group C. (Fig. 1)

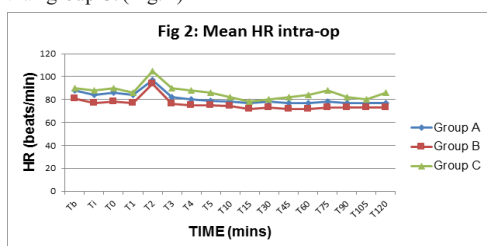
**Table 2: DEMOGRAPHIC DISTRIBUTION**

|                            | Group A              | Group B              | Group C            | Significance |
|----------------------------|----------------------|----------------------|--------------------|--------------|
| Age (years)                | 27.8<br>$\pm 10.416$ | 31.4<br>$\pm 11.773$ | $28.8 \pm 9.614$   | NS           |
| Sex (F:M)                  | 9:21                 | 7:23                 | 10:20              | NS           |
| ASA (I: II)                | 26:4                 | 25:5                 | 24:6               | NS           |
| Weight (kg)                | $58.1 \pm 8.6$       | $58.2 \pm 10.2$      | $57.2 \pm 10.4$    | NS           |
| Duration of surgery (mins) | $118.80 \pm 30.80$   | $120.00 \pm 30.68$   | $117.80 \pm 20.41$ | NS           |

Data: mean $\pm$ SD. NS- Non significant ( $p > 0.05$ ).



After initial response to intubation MAP remained stable throughout the study period. But at all point of time MAP in group B was lower than that in group B and C. Heart rate in both groups A and B neither showed reduction nor fluctuation throughout study period but was lower than group C. (Fig. 2)



Total blood loss was  $155.73 \pm 14.90$  ml in group A,  $117.77 \pm 7.59$  ml in group B and  $180.86 \pm 18.6$  in group C. (Table 3).

**Table 3: Showing Total blood loss**

|          | Group A            | Group B           | Group C           | Statistical Significance               |
|----------|--------------------|-------------------|-------------------|----------------------------------------|
| TBL (ml) | $155.73 \pm 14.90$ | $117.77 \pm 7.59$ | $180.86 \pm 18.6$ | B to A- HS<br>B to C- HS<br>A to C- HS |

Data: mean $\pm$ SD. NS- Non significant ( $p > 0.05$ ).

Blood loss seen at the end of surgery was significantly less in group B, this provided better surgical field compared to group A and C. On intragroup comparison of quality of surgical field, a significant

improvement (clinically and statistically) was found in both the groups A and B but not in group C at end of surgery as compared to start (Z value  $> 5$ ) as depicted in Table 4

**Table 4: Quality of surgical field**

| ACS GRADE | START |      |      | END  |      |      | INTRAGRO UP ANALYSIS |              |
|-----------|-------|------|------|------|------|------|----------------------|--------------|
|           | GOOD  | FAIR | POOR | GOOD | FAIR | POOR | Z VALUE              | SIGNIFICANCE |
| GROUP A   | 0     | 6    | 24   | 7    | 23   | 0    | 5.07                 | S            |
| GROUP B   | 0     | 9    | 21   | 15   | 15   | 0    | 5.07                 | S            |
| GROUP C   | 0     | 2    | 28   | 0    | 5    | 25   | 3.10                 | NS           |

## DISCUSSION:

Several methods have been designed to reduce bleeding during surgery. The basic method to reduce the bleeding from the nasal mucous membranes operated on is to constrict the capillaries of the area involved. This can be accomplished by local anemization of the mucosa with vasoconstrictors, preoperative use of steroids, positioning the patient in the anti-Trendelenburg position, pharmacological cardiodepression, heart rate stabilization within lower physiological limits and the reduction in mean arterial pressure (MAP).<sup>8</sup>

Various studies have shown reduced heart rate and mean blood pressure with either atenolol or clonidine, but in all the studies multiple other drugs were used perioperatively to reduce blood pressure to a desired level of MAP.<sup>9</sup> Premedication with oral clonidine reduced intraoperative bleeding and decreased isoflurane, fentanyl or urapidil requirement for achieving controlled hypotension in patients undergoing middle ear surgery.<sup>10</sup>

With clonidine premedication in spine surgery intra-operative blood loss was found to be less as compared to placebo group even at the same level of MAP. It implies that the decreased bleeding and improved surgical field is not just limited hypotensive action of clonidine. Thus, it is possible that clonidine produces the same effect even at higher blood pressure, which can reduce the need for hypotensive anesthesia.<sup>11</sup>

In a similar study by Amr et al, premedication with oral atenolol in spinal surgeries decreased the requirement of sodium nitroprusside along with decreased intraoperative bleeding inspite of comparable MAP intraoperatively.<sup>12</sup>

In this study, we compared clonidine and atenolol as oral premedication to evaluate their effect on surgical field without any additional drug to decrease the MAP. This could be one of the reason for comparatively higher pulse and mean blood pressure. Secondly, submucosal infiltration of xylocaine and adrenaline may have been responsible for higher hemodynamic parameters but at the same time led to reduced bleeding. Also the dose of atenolol and clonidine used was much less compared to other studies. This may again be the cause of for higher haemodynamic variables.

Both these drugs produced stable haemodynamics and reduced bleeding thus leading to optimal surgical field. Although in other studies optimal surgical field was due to induced hypotension. But in our study the mechanism could be due to reduction and attenuation of the excitatory effect of sudden increased catecholamine/sympathetic stimulation during surgery.<sup>2</sup>

Limitation of our study is that we did not divide the patients depending upon type of surgery like FESS, rhinoplasty, rhinoseptoplasty etc which could have further clearly defined the efficacy of study drugs.

## CONCLUSION:

Thus to conclude, both clonidine and atenolol were effective and safe, in terms of stable haemodynamic profile and reducing intraoperative bleeding; when given orally to patients as premedication in patients for nasal surgeries under general anaesthesia. However, out of the two drugs clonidine appeared to be better in terms of reduction of blood loss and providing good quality of surgical field when compared to atenolol

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