

Research Article – Medicine

Limiting blood loss in orthognathic surgery with Esmolol as a hypotensive agent

Sailesh Kumar Mukul*, Amit Kumar, Ejaz Ahmad Mokhtar, Shweta Pandey

Department of Dentistry, AIIMS Patna, Patna, Bihar – 801507, India

Abstract

Orthognathic surgery may be complicated by difficulty in achieving hemostasis because unlike soft tissue, the vessels traversing bone cannot be identified and isolated before osteotomy. In this study we evaluated the amount of blood loss and duration of surgery under deliberate hypotensive anesthesia in comparison to amount of blood loss and duration of surgery under normotensive anesthesia on patients undergoing orthognathic surgical procedures. A total of 16 cases undergoing orthognathic surgery were included in this clinical study. Patients were randomly grouped under normotensive (group I) or hypotensive group (group 2). Patients in hypotensive anesthesia group were given Esmolol to maintain mean arterial pressure in the range of 70-80 mm of Hg till osteotomy segments were fixed. There was more than 40% reduction in blood loss in orthognathic surgical procedures when induced hypotension was used, but there was not statistically significant ($p=0.91$) reduction in the operative time. Based on surgeons and anesthetist's assessment fast acting agents like Esmolol can be used intraoperatively to induce hypotension as and when required.

Key words: Orthognathic Surgery, Blood loss, Hypotensive anesthesia, Normotensive anesthesia, Esmolol.

Introduction

Orthognathic surgeries are frequently performed to correct dentofacial deformities stemming from hereditary and acquired causes. Although the procedure performed is standardized and yields predictable results, it is associated with considerable blood loss. In these surgeries bleeding occurs from soft tissue, intrabony capillaries and vessels. Although several methods directly limit the inflow of blood to the operative site; the predictability and relative safety associated with execution of induced hypotension makes it a widely recommended method for controlling blood loss in orthognathic surgeries (1). Controlled hypotension was first proposed by Cushing in 1917 and it developed to be an acceptable method. Induced hypotension is defined as “a reduction of the systolic blood pressure to 80–90 mm of Hg, a reduction of mean

arterial pressure (MAP) to 50–65 mm of Hg or a 30% reduction of baseline MAP” (2). Controlled hypotension not only reduces blood loss, but also improves the surgical field and decreases operative time (3), and may obviate the need for blood transfusion. This can avoid potential risk of transfusion reactions or transmission of blood borne pathogens, which are significant factors when considering elective procedures like orthognathic surgeries (3). Careful selection of agents limits the major risks, risks that are generally less important than those of transfusion or alternatives to transfusion (4).

Hypotensive agents used successfully alone include inhalation anesthetics like Isoflurane, Sodium nitroprusside, Nitroglycerin, Trimethaphan, Camsilate, Alprostadil, Adenosine, Remifentanyl and agents used in spinal anesthesia. Agents that can be used alone or in combination include calcium channel antagonists (e.g. Nicardipine), adrenoceptor antagonists [e.g. Propranolol, Esmolol] and Fenoldopam (4).

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*Corresponding Author

Sailesh Kumar Mukul, *Department of Dentistry Room No. 223, Department of Dentistry, Ayush PMR Building, AIIMS Hospital Campus, All India Institute of Medical Sciences Patna, Patna, Bihar, India*

Hypothesis and Objectives

The study hypothesis was “If blood loss and operating time can significantly reduce in orthognathic surgery when hypotensive anesthesia using Esmolol is adopted”.

The objectives of the study were:

1. To evaluate the amount of blood loss between normotensive and hypotensive groups in orthognathic surgical procedures.
2. Duration of surgery under hypotensive anaesthesia using Esmolol as hypotensive agent when compared to normotensive anesthesia in orthognathic procedures.

Methodology

A total of 16 cases undergoing orthognathic surgery were included in this clinical study. These patients underwent standard orthognathic surgical procedures. Consent was obtained from institutional ethical committee, the patient and respective guardians or relatives.

Data included age, sex, chief complaint, medical and dental history, clinical findings, radiographic findings, cephalometric findings, blood investigations including pre and post-operative hemoglobin, hematocrit, pre and post-operative blood pressure (B.P.) records, blood loss during surgery and duration of surgery.

Inclusion Criteria

Young and healthy adults who were fit under the category of American Society of Anesthesiologists, Physical Status I (ASA-I) undergoing orthognathic surgery.

Exclusion Criteria

Patients not fulfilling ASA I criteria e.g. cardiovascular, renal and hepatic disorders, uncontrolled hypertension, myocardial infarction within 6 months, hypovolemia, previous cerebro vascular accidents and pregnancy.

Diagnosis was made from clinical, radiographic and cephalometric findings. Treatment was planned giving prime importance to patient's concern. Surgeries included single jaw osteotomies and double jaw osteotomies. Patients were randomly allotted to normotensive (group I) or hypotensive

group (group II). Baseline blood pressure was recorded in the wards, before the day of surgery, in the morning prior to surgery and in operation theatre before administering general anesthesia. The mean was then calculated.

Method

Premedication comprised of oral Diazepam and Ranitidine. Anesthesia was induced by Thiopentone/Propofol (mixed to Glycopyrrolate) and Succinylcholine intravenously. Anesthesia was maintained by Halothane and mixture of N₂O and O₂ (60:40 ratios). Long acting muscle relaxant (Pancuronium) was given when indicated.

Head end was kept elevated. 2% Lignocaine hydrochloride (2% Xylocaine ® DENTAL) with 1:80000 Adrenaline was infiltrated before making incision in all cases. Patient on hypotensive anesthesia were given Esmolol (ESOCARD, Samarth Pharma Pvt. Ltd.) 0.5 mg/kg body weight in bolus and 0.1-0.3 mg/kg intermittently to maintain mean arterial pressure in the range of 70-80 mm of Hg till osteotomy fragments were fixed (5) Intermittent administration of Esmolol was stopped after the last screw was fixed. Reversal from anesthesia was achieved by drugs like Neostigmine and Glycopyrrolate. Intravenous infusion of antibiotics and steroid (Inj Dexamethasone 8 mg/ Hydrocortisone 100 mg) were given intra operatively.

Intraoperative monitoring comprised Electrocardiography, blood pressure, pulse oximetry and heart rate. Blood pressure was monitored by non-invasive method. Oxygen saturation and heart rate were continuously monitored using Philips SureSigns VS3 Vital Signs Monitor.

Though invasive blood pressure monitoring is considered the gold standard, we have used non-invasive monitoring. Non-invasive method can be used for mild hypotensive procedures (6).

Duration of anesthesia was calculated from the time of induction to reversal. Duration of surgery was measured from starting of incision to placement of last suture. A provision for single observer for measurement of blood loss after every surgery was strictly followed. It was measured by reducing the amount of saline used from the volume of fluid in suction unit. Weight of the dry gauze was deducted from weight of blood soaked

gauze, 1 gm of weight was considered equivalent to 1ml of blood (7). The need to transfuse blood perioperative was a combined decision of operating surgeon and anesthetist. MAP was gradually raised and adequate hemostasis was achieved.

Statistical analysis was done using student's t-test. Differences were considered statistically significant when $p < 0.05$. All data are presented as mean $\pm$ SD.

$$\text{Blood loss} = A + B$$

A = Volume in suction-Volume of saline used

B = Weight of wet gauze-weight of dry gauze

Results

The study group consisted of 16 healthy individuals undergoing elective orthognathic surgical procedures. They were divided into two groups; each consisting of 8 patients. The female, male ratio was 6:2 in normotensive group and 7:1 in hypotensive group; with an age range of 15 years to 28 years in group I and 18 years to 35 years in group II (Table 1, Fig. 1).

Table 1. Demographic Details of Study Groups

Study Groups	Male	Female	Mean Age (Years)*	Mean Weight (Kg)*
Normotensive	2	6	21.75	49.62
Hypotensive	1	7	23.37	49.12

* $P > 0.05$ NS

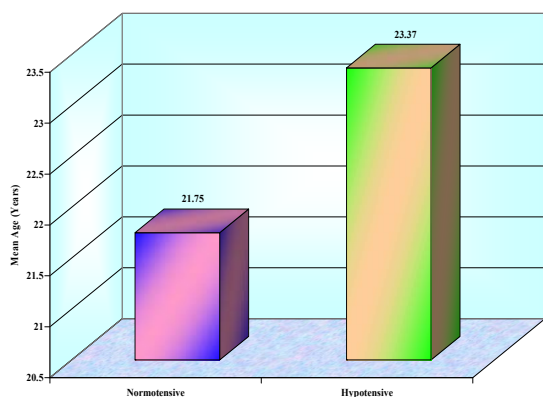


Fig. 1. Age Distribution of Study Groups

The mean age in group I and group II was found to be 21.75 ± 4.46 years and 23.37 ± 5.88 years respectively. There was no statistically significant difference found between the two groups (Table 2, Fig 2).

Table 2. Comparison between Age of Subjects in study Groups

Study Groups	Age (Years) Mean $\pm$ SD	p* Value	Significance
Normotensive	21.75 $\pm$ 4.46	0.62	NS
Hypotensive	23.37 $\pm$ 5.88		

*Student's t Test

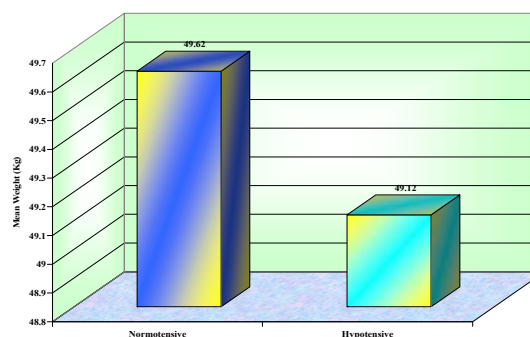


Fig. 2. Mean Weight of Study Groups

Mean blood loss in group I was 490 ± 441.97 ml as compared to 393.75 ± 308.12 ml in group II. The difference in amount of blood loss was not statistically significant. The duration of surgery in group I was 238.12 ± 97.28 min whereas it was 233.12 ± 76.67 min in group II showing no statistical significance (Table 3, Fig 3).

Table 3. Amount of blood loss and duration of surgery

Parameters	Mean $\pm$ SD		% Difference	p* Value	Sig
	Normotensive	Hypotensive			
Blood Loss (ml)	490 $\pm$ 441.97	393.75 $\pm$ 308.12	20	0.62	NS
Duration (Mins)	238.12 $\pm$ 97.28	233.12 $\pm$ 76.67	2	0.91	NS

*Student's t Test

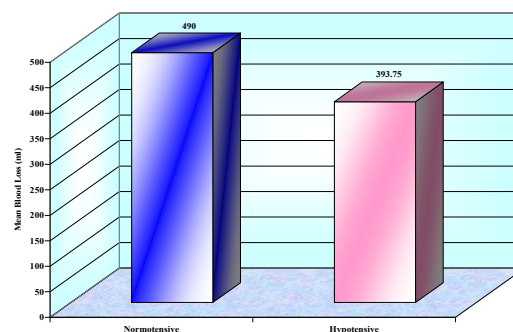


Fig. 3. Mean Blood Loss

The baseline mean arterial blood pressure and intraoperative mean arterial blood pressure in group I was found to be 94.34 ± 4.65 and 93.32 ± 10.33 mm of Hg respectively. The difference between the two values was not significant. Whereas the difference between baselines mean arterial blood pressures and intraoperative mean arterial pressures in group 2 was found to be highly significant (Table 4, Fig 4).

Table 4. Comparison of MAP

Study Groups	Mean $\pm$ SD		% Difference	p* Value	Sig
	Pre OP	Intra Op			
Normotensive	94.34 $\pm$ 4.65	93.32 $\pm$ 10.33	1.15	P=0.75	NS
Hypotensive	94.19 $\pm$ 3.75	75.18 $\pm$ 1.23	20	P<0.001	HS

* Student's Paired t Test

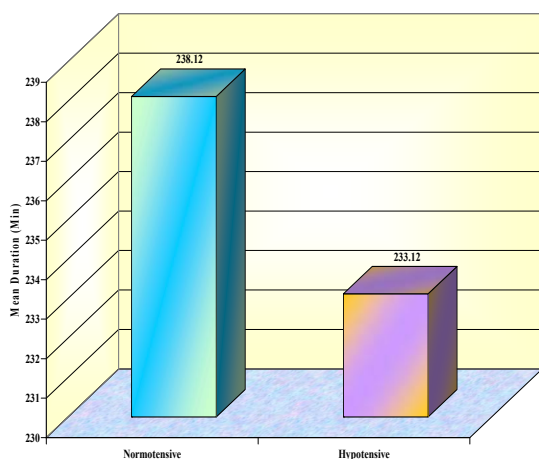


Fig. 4. Mean Duration of surgery (minutes)

In LeFort I/LeFort I combined with anterior maxillary segmental osteotomy, there was 60% reduction in blood loss i.e. from 690 ml to 276.7 ± 128.6 ml. In BSSO the difference in amount of blood loss between both groups was statistically significant. There was 40% reduction in amount of blood loss in group II as compared to group I in patients undergoing bijaw surgery. The lone case that underwent anterior maxillary segmental combined with mandibular subapical osteotomy in group I and group II had blood loss of 380 ml and 850 ml respectively (Table 5, Fig 5).

Table 5. Comparison of Study Groups with respect to Surgical Procedure

Procedure	Mean $\pm$ SD		% Difference	p* Value	Sig
	Normotensive	Hypotensive			
Le Fort I/Le Fort+AMS	690	276.7 ± 128.6	60	-	-
BSSO	353.3 ± 23.09	190 ± 26.46	46	0.001	HS
Bijaw	1500	900	40	-	-
AMS+MSA	380	850	-123	-	-

* Student's t Test

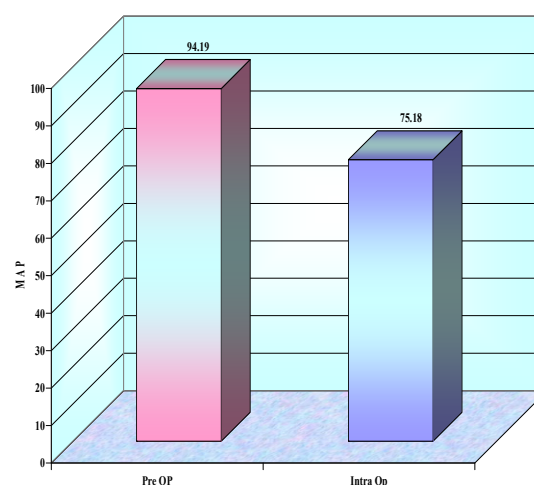


Fig. 5. MAP in Case of Hypotensive group

In LeFort I / LeFort I combined with anterior maxillary segmental osteotomy the mean time taken was 270 min in group I as compared to 213.3 ± 59.65 min in group II. In cases of BSSO the mean time taken was 210 ± 15 min and 193.3 ± 38.84 min for group I and group II respectively. However the difference in duration of surgery between both groups was not found to be statistically significant. Similarly the lone case that underwent anterior maxillary segmental combined with mandibular subapical osteotomy in group I and group II had duration of surgery for 225 min and 255 min respectively (Table 6, Fig 6). Table 7 and figure 7 describes correlation between blood loss and reduction in MAP in the two groups and it was not statistically significant. In group II p value was 0.06 which was not statistically significant.

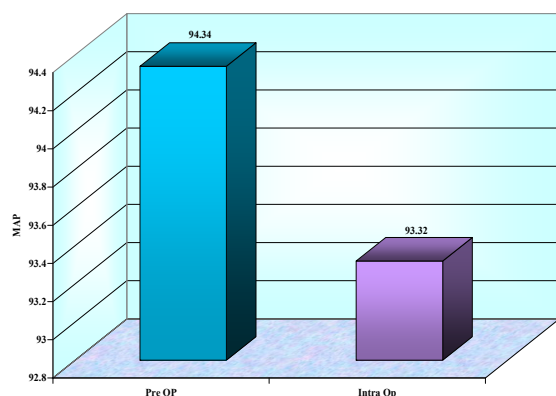
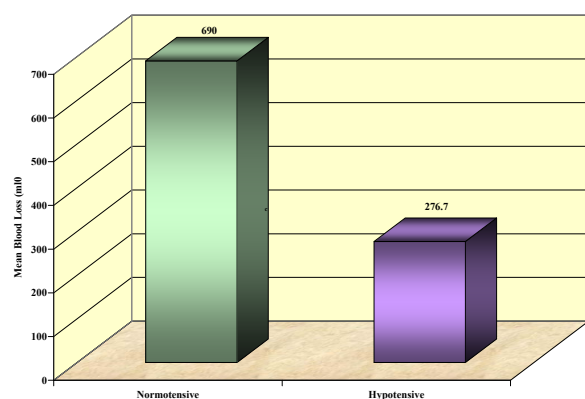
Table 6. Duration (Minutes) of Surgery

Proce- dure	Mean $\pm$ SD		% Diffe- rence	p* Value	Si g
	Normo- tensive	Hypo- tensive			
Le Fort I/ Le Fort+AM S	270	213.3 $\pm$ 9.65	21	-	-
BSSO	210 $\pm$ 15	193.3 $\pm$ 38.84	8	0.69	N S
Bijaw	460	390	15	-	-
AMS+ MSA	225	255	-13	-	-

* Student's t Test

Table 7. Correlation between Blood Loss and Reduction in MAP

Study Groups	Correlation Coefficient	Sig
Normotensive	0.29	P=0.44 NS
Hypotensive	0.6	P=0.06 NS

**Fig. 6.** MAP in Case of Normotensive group**Fig. 7.** Blood Loss in Case of LeFort I/LeFort + AMS

Discussion

Progress in the fields of orthodontics, anesthesia and maxillofacial surgery has ensured that Orthognathic surgery can be carried out in a safe fashion leading to predictably stable results. A significant and most frequently complication encountered intraoperatively is blood loss(8),(9). It has been assessed that 50% of a surgeon's time and a great deal of nervous energy is spent in controlling bleeding (10). Bleeding is the quantity of blood that appears in the operative field in a given time period and it can be expressed in flow 'D' (volume/unit of time) and is mathematically related to the pressure by the relationship, $D = P/R$, where 'P' is pressure and 'R' represents vascular resistance. When P decreases and R remains constant or increases (vasoconstriction) the flow D decreases. On the other hand when P and R (vasodilatation) both decrease, the flow D remains constant or varies little (4).

P' and 'R' are local pressure and local vascular resistance at the level of the surgical field and they depend on (1) the central blood pressure and its regulation. (2) The regulation of the local arteriolar vasomotor tone by the sympathetic nervous system. (3) The microcirculatory auto regulation of the organ (when it exists).

In certain controlled hypotension techniques, the decrease in cardiac output is the determining factor in the reduction of blood loss whereas in other techniques it is the fall in MAP that determines the levels of blood loss. The mechanisms responsible for the reduction of intraoperative bleeding depends on (1) The technique used (that is the effect of the agents used on the heart and the vascular network) (2) The mechanisms of regulation that these agents antagonize and (3) The counter-regulatory mechanisms that they cause, which are intricate (4)(11).

It is unsafe to assume that the response of all vascular beds to hypotension and surgical trauma is identical because it is well known that blood flow to each tissue is governed by neural, hormonal and local factors. The few studies reported in the field of orthognathic surgery have been poorly done and inconclusive (12).

Potential benefits attributable to hypotensive anesthesia in orthognathic surgeries are:

- 1) Reduced blood loss with a consequent reduction in risks associated with blood transfusion.
- 2) Improved quality (dryness) of the operative field, potentially allowing more accurate dissection and improved surgical results
- 3) Reduced operative time.
- 4) Reduced postoperative swelling due to decreased hematoma formation.

The risk of tissue hypoxia and the difficulty in evaluating this risk are very real, although there were no specific complications seen in a large series of patients subjected to severe controlled hypotension (MAP<50mm of Hg) over a prolonged duration (11) The current goal of controlled hypotension is to maintain a pressure sufficiently low to allow a reduction in bleeding without suppressing the microcirculatory auto regulation of the vital organs (i.e. brain, heart or kidney). Another potential complication in hypotensive anesthesia is anuria (13).

None of the current data indicate that controlled hypotension with a MAP between 50 and 65 mm of Hg is a risk in young healthy patients (4).

Patients with treated hypertension did not seem to present risks and for this reason it was not considered an absolute contraindication for controlled hypotension in one study (4)(11). Physical measures are used some time alone or in adjuvant to pharmacological agents for controlled hypotension. In placing the operated area higher than the heart, postural maneuvers (e.g. a head-up tilt position in ear or maxillofacial surgery) have reduced blood pressure in this area and decreased venous pressure (13). However, there is a risk of air embolism with this technique. The hemodynamic effects of artificial ventilation have also been used: hyperventilation (by means of hypocapnia) involves vasoconstriction and a fall in blood flow; and hypoventilation (by means of hypercapnia) induces vasodilatation and an increase in blood flow(4). The ideal agent to induce controlled hypotension does not exist. An ideal one must be easy to administer, have short onset time, an effect that disappears quickly when administration ceases, a fast elimination without toxic metabolites,

negligible effects on vital organs, and a predictable and dose-dependent effect(4).

Drugs used in controlled hypotension include:

1. Primary agents successfully used alone, for example, inhalation anaesthetics, Sodium nitroprusside, Nitroglycerin, Trimethaphan, Alprostadil, Adenosine, Remifentanil and agents for spinal anaesthesia.
2. Agents that can be used alone or as adjuncts to decrease the adverse effects of other agents, for example, calcium channel antagonists (e.g. Nicardipine), β adrenoceptor antagonists (β -blockers) [e.g. Propranolol, Esmolol] and Fenoldopam.
3. Secondary agents that are used adjunctively with primary agents. For example, ACE inhibitors and Clonidine.

Esmolol lowers arterial blood pressure through decrease in cardiac output secondary to the negative chronotropic and inotropic effects of β_1 -adrenergic antagonism(5). In addition, it may produce direct myocardial depression at very high doses (e.g. >500 $\mu\text{g/kg/min}$). Esmolol provides a more stable course of controlled hypotension than did sodium nitroprusside, with a slightly lower mean arterial pressure and fewer deviations from the target arterial blood pressure range(14). Haemodynamic stability in this case may result from the inhibition of autonomically mediated secretion of renin and the attenuation of other compensatory hormonal responses known to occur during controlled hypotension with Sodium nitroprusside or Isoflurane (14).

β -adrenergic blockade will also prevent reflex autonomic increases in heart rate in response to the vasodilation produced by Isoflurane. Esmolol has a brief duration of action, promotes haemodynamic stability, and produces beneficial effects in the surgical field and in blood conservation. For these reasons, it may be preferred as a primary drug for inducing hypotension in healthy patients undergoing orthognathic surgery. In the present study, no apparent adverse side effects occurred when Esmolol was used. Caution is indicated as profound myocardial depression may result from its use. Preliminary evidence that Esmolol infusion at rates >200 $\mu\text{g/kg/min}$ may be deleterious to

total body oxygen balance, although the same may also be true for therapeutic doses of SNP(14). The following recommendations are suggested for minimizing blood loss and optimizing safety during orthognathic surgery(14) : (a) Esmolol may be used as a primary hypotensive drug in healthy patients; (b) the degree of hypotension should be titrated to observed blood loss (extremes of hypotension may not be required); (c) when using Esmolol alone to produce hypotension as low as 60 mm of Hg, cardiac output should be monitored; and (d) Esmolol should be used in combination with other hypotensive drugs to limit the doses required.

W. Chan, D.E. Smith *et al.* compared the blood loss, quality of operative field and the length of surgery in one type of orthognathic surgery i.e. anterior maxillary osteotomy in normotensive and hypotensive anesthesia. They found that by dropping a patient's operative mean blood pressure by 20% or more, the quality of surgical field can be significantly improved (27%) and loss of blood can be decreased (41%). The difference in length of surgery was insignificant(15) Golia J.K, Woo R. *et al.* used Nitroglycerin for controlled hypotension in orthognathic surgeries. NTG was used to lower mean arterial pressure during periods of potential increased blood loss. Estimated blood loss was 439 ± 1.19 ml. (16). Fromme GA, Mackenzie RA *et al* included 56 ASA class I patients requiring orthognathic surgery. Mean measure blood loss was not statistically significant (17).

Mc Nultys *et al.* evaluated the effectiveness of Labetalol in producing controlled reduction in mean arterial pressure during orthognathic surgery. They concluded that labetalol is safe and effective alternative for producing controlled hypotension in orthognathic surgery. It offers the advantage of better preservation of arterial oxygen saturation and decreasing myocardial oxygen consumption through its β blocking action. In their 10 patients mean blood loss was 399 ± 142 ml (18).

Blau W.S, Kafer E.R *et al* compared the efficacy of Esmolol and Sodium nitroprusside (SNP) as a primary drug for producing controlled hypotension and limiting blood loss during orthognathic surgery. Both infusions were titrated to obtain a mean arterial blood pressure within target range of 55-65 mm of Hg. They found Esmolol to be more effective than sodium nitroprusside in reducing

blood loss. The MAP was 58.7 ± 0.7 and 61.8 ± 0.4 mm of Hg for Esmolol and SNP respectively. The mean blood loss was 436 ± 65 ml. with Esmolol and 895 ± 101 ml with SNP. The surgical field was judged to be significantly ($p \leq 0.05$) drier with Esmolol than with SNP(14).

Dolman R M did a prospective study to compare quality of surgical field, blood loss and operative time with either hypotensive or normotensive anesthesia during Lefort I osteotomies. It was found that there was a significant correlation between ($p < 0.0001$) surgeon's perception of quality of surgical field and the blood pressure. There was a statistically significant reduction in blood loss ($p < 0.01$) when using hypotensive anesthesia and no significant reduction ($p = 0.44$) in operative time (19).

Yu CNF conducted a prospective study in 32 patients under induced hypotensive anesthesia. It was found that mean estimated blood loss for double jaw surgery was 617.6 ml, mean estimated blood loss during Lefort I was half that of multiple segmentalised osteotomies. For mandibular ramus osteotomies, mean ABL and operating time was 280 ml and 2 hours respectively, for anterior mandibular osteotomies the corresponding values were 171.3 ml and 1 hour 13 min (20)

Praveen *et al.* in a prospective randomized study found out that median blood loss under hypotensive anesthesia was 200 (90-400) ml and under normotensive anesthesia was 350 (130-1575) ml. They justified the use of Hypotensive anesthesia in orthognathic surgeries(21).

Zellin *et al.* studied thirty patients undergoing Lefort I osteotomy. They concluded that blood loss during orthognathic surgery under hypotensive anesthesia could be significantly reduced when a combination of Tranxemic acid and Desmopression is added (22).

Complications following hypotensive anaesthesia are postural hypotension, rebound hypertension, myocardial ischemia, arrhythmia, delayed awakening, impaired cerebral function, neurological deficit, hypoxia, reactionary bleeding, hypothermia, and lactic acidosis. Enderby reported a mortality of $< 0.01\%$ in his series of 9107 patients.(13) Pasch and Huk reported a mortality of 0.06% among 1802 patients(12). Kerr reported 0% mortality in his study (23). However, we did not encounter any

complications intraoperatively or postoperatively. Studies of Lessard *et al.* (1) Precious *et al.* (24) and Fahmy(25) have shown no reduction in duration of surgery when hypotensive anesthesia was used.

The advantages in this study was use of a noninvasive method to monitor blood pressure, use of single drug to induce hypotension, maintaining MAP at an average value of 75.18 mm of Hg without interfering with other organ systems, 0% mortality and morbidity. The added advantage was to have a single operator for performing all the surgical procedures in our study.

1. The sample size was relatively small to yield appreciable results for individual orthognathic surgical procedures.
2. As this study involved a small sample size with dissimilar groups the values could not be averaged leading to marked difference in results.

Conclusion

The following inference can be drawn from this study:

1. Hypotensive anesthesia is a safe method for reducing intra operative blood loss and operative time.
2. Esmolol can be used as a safe and predictable drug to induce hypotension during surgery.
3. Based on Surgeon's and Anesthetist's assessment fast acting agents like Esmolol can be used intraoperative to induce hypotension as and when required such as during osteotomy, down fractures etc.

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