Hypotensive Anesthesia and Recovery of Cognitive Function in Long-term Craniofacial Surgery

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The aim of our study was to compare three different anesthesiological techniques with regard to hemodynamics, recovery, and postoperative morbidity, for craniofacial surgery. One hundred twenty patients with American Society of Anesthesiologists (ASA) classification of I or II patients, 18 to 32 years old, and undergoing maxillary and mandibular osteotomies were randomly assigned to receive anesthesia with propofol-remifentanil (group P), desflurane-remifentanil (group D), or sevoflurane-remifentanil (group S). All patients were given premedication: midazolam 0.03 mg/kg, atropine 0.007 mg/kg, desametasone 0.1 mg/kg, NaCl 0.9% 100 mL + 2 mg/kg ketoprofene + 1.5 mg/kg ranitidine + 1 μg/kg clonidine. Anesthesia was induced by O_2/air (FiO_2 0.5), remifentanil 0.5 μg/kg/min, propofol 2 mg/kg, rocuronium 0.6 mg/kg. Maintenance group P received O_2/air (FiO_2 0.5), remifentanil 0.25 to 1.5 μg/kg/min, propofol 6 to 10 mg/kg/h; groups D and S received O_2/air (FiO_2 0.5), remifentanil 0.25 to 1.5 μg/kg/min, and respectively, sevoflurane or desflurane 0.5 minimum alveolar anesthetic concentration. The dosage of propofol, desflurane, and sevoflurane, obtained with a value of bispectral index (BIS) 40, was kept unchanged throughout the course, and remifentanil was titrated to maintain controlled hypotension: systolic arterial blood pressure 70 to 90 mmHg and mean arterial blood pressure 50 to 65 mmHg. A 24-hour elastomeric infusion system (ketoprofene 320 mg) was started 60 minutes before induction and cloridrat ondansetron 0.1 mg/kg was administered 30 minutes before the end of surgery. Hypotension was successfully obtained in all three groups with a bloodless surgical field, and there was no need for additional use of a potent hypotensive agent. Early and late recovery were faster and more complete in the D group; $P < 0.05$. Postoperative morbidity (nausea, vomiting, shivering, pain, and edema) was slight and did not significantly differ among the groups.

Key Words: Controlled hypotension, craniofacial surgery, recovery

Craniofacial surgery needs a great deal of support from the anesthesiological point of view because controlled hypotension and prompt recovery are necessary in this kind of procedure.

Induced hypotension is required because the surgical district in consideration is highly vascularized, and the bleeding may become a real problem for the technical procedure. A bloodless surgical field is essential for an easy procedure, which requires extreme precision, being responsible for the overall surgical timing.[1] The direct consequence of optimizing the surgical field is a reduction of perioperative complications.

Many drugs have been used to attempt controlled hypotension to minimize intraoperative bleeding and blood loss during craniofacial procedures: sodium nitroprusside,[2] isoflurane,[3] trinitroglycerin,[4] labetalol,[5] and calcium blockers.[6] Investigations conducted about these drugs often resulted in intra-or postoperative complications caused by pharmacological toxicity.[5,7,8] Other anesthesiological techniques achieved good control of hemodynamic stability and blood loss by inducing a profound anesthetic state; however, this usually carried the penalties of slow emergence and delayed recovery.

In this type of surgery, such penalities are very inconvenient because of the need for a prompt and

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complete collaboration during the postoperative period. Actually, an urgent resuscitation may not only be of extreme difficulty because of the altered facial anatomy but also may even compromise the delicate metallic osteosinthesis.

The aim of our study was to compare three different anesthesiological techniques to elaborate a set of guidelines to best cope with this type of surgery and its problems.

Materials and Methods

One hundred twenty patients with American Society of Anesthesiologists' (ASA) physical status of I or II, who were 18 to 32 years old, and were undergoing maxillary and mandibular osteotomies were enrolled in the study after informed, written consent was obtained.

Exclusion criteria included ASA physical status III or IV, history of a significant hepatic, renal, cardiovascular or pulmonary disease, chronic alcohol and drug abuse, disabling neuropsychiatric disorders, hypersensitivity to anesthetics, personal or familial history of malignant hyperthermia, morbid obesity, and pregnancy.

Patients were assigned, by single-blinded randomization, to receive one of three anesthetic regimens: propofol-remifentanil (group P), desflurane-remifentanil (group D), or sevoflurane-remifentanil (group S). All patients were given premedication: midazolam 0.03 mg/kg intravenously (IV), atropine 0.007 mg/kg IV, desametasone 0.1 mg/kg IV, 100 mL NaCl 0.9% + 2 mg/kg ketoprofene + 1.5 mg/kg ranitidine + 1 μg/kg clonidine.[9] Anesthesia was induced by O_2/air (FiO_2= 0.5), remifentanil 0.5 μg/kg/min, propofol 2 mg/kg IV, and rocuronium 0.6 mg/kg IV for tracheal intubation.

Anesthesia was maintained in group P withO_2/air (FiO_2 = 0.5), remifentanil 0.25 to 1.5 μg/kg/min, propofol 6 to 10 mg/kg/h. In groups S and D, maintenance of anesthesia was provided with O_2/air (FiO_2 = 0.5), remifentanil 0.25 to 1.5 μg/kg/min and, respectively, sevoflurane and desflurane 0.5 minimum alveolar anesthetic concentration (MAC). The dosage of propofol, desflurane, and sevoflurane, obtained with a value of bispectral index (BIS) 40, was kept unchanged throughout the course, and remifentanil was titrated to maintain controlled hypotension: systolic arterial blood pressure (SAP) of 70 to 90 mmHg, mean arterial blood pressure (MAP) or 50 to 65 mmHg. If this proved inadequate, additional clonidine was administered to maintain the required hemodynamic values.[10] Patients were mechanically ventilated with a fresh gas flow of 3 L/min by using a semiclosed circle system; end-tidal CO_2 concentration was maintained between 30 and 35 mmHg.

Before the beginning of the surgical time, all patients had 1% mepivacaina 20 mL with 1:200,000 adrenaline at each site of the incision and were placed in a 15° head-up position.[11] Fluid replacement with crystalloid solutions, at a rate of 5 mL/kg/h, was used. A 24-hour elastomeric infusion system (ketoprofene 320 mg) was started 60 minutes before induction, and cloridrat ondansetron 0.1 mg/kg was administered 30 minutes before the end of the surgery.

At the end of surgery, all anesthetics (remifentanil, propofol, desflurane, sevoflurane) were turned off simultaneously without previous tapering, and ventilation was controlled with 8 L/min of oxygen until the return of spontaneous ventilation. The trachea was extubated when adequate spontaneous ventilation and patient response to verbal commands were established. Invasive blood pressure, heart rate, ECG, SpO_2%, $EtCO_2$, and urinary output, were continuously measured and recorded. Delay in onset of hypotension from starting maintenance drugs and delay to return to baseline pressure values from discontinuation of anesthesia were calculated. The estimation of blood loss was made by totalling the loss from suction bottles; the quality of the operative field was estimated by the surgeon, unaware of the pharmacological treatments, by a numerical rating scale.[12–15]

Early and late recovery times were recorded. Early recovery times were measured from the discontinuation of anesthesia to: eye opening, hand pressing, spontaneous breathing, tracheal extubation, recalling name and date of birth, and an Aldrete recovery score ≥9.[16] Trieger Dot Test (TDT) and Digit Substitution Test (DSST) were performed at 30, 60, and 90 minutes after discontinuation of anesthesia to evaluate late recovery.[17–19]

The incidences of postoperative nausea and vomiting (PONV), shivering, and additional use of antiemetics and antishivering were analyzed. The postoperative pain intensity was estimated by a visual analog scale (VAS); the postoperative analgesics were recorded. Postoperative edema was estimated by a numerical rating scale, with scores ranging from 1 to 3: 1 = slight, 2 = moderate, 3 = severe.

The data yielded by our study were expressed as mean ± standard deviation (SD) and number and percentage *n* (%), and were analyzed by statistical software SPSS11.1. Intergroup comparisons were evaluated using one-way analysis of variance. Intragroup comparisons were made using Student *t* test. Chi-square analysis with Pearson's correction was used to assess the statistical significance of the difference between

the three groups. The threshold for statistical significance was $P < 0.05$.

Results

There were no significant differences in demographic data, baseline hemodynamic data, and duration of surgery among the three groups, as shown in Table 1.

Controlled hypotension was promptly achieved in all three groups (P-D-S), respectively, in a mean time of 4 ± 1.8 minutes, 3.6 ± 1.7 minutes, 5 ± 2 minutes, and sustained throughout surgery; $P > 0.05$ (Fig 1). Delay to return to baseline arterial blood pressure was significantly faster in group D (6 ± 2.5 min) as compared with the other two groups (S = 13.5 ± 3 min; P = 14 ± 3 min). Heart rate was stable in all three groups throughout surgery; the mean value of this parameter remained statistically unchanged from baseline only in group D: 70 ± 4 beats/min (D) vs 54 ± 5 beats/min (P) vs 58 ± 5 beats/min (S). Additional use of clonidine to maintain induced hypotension was statistically greater in group P if compared with groups D and S (25% vs 5% vs 10%) (Table 2). The same tendency was detected with regard to the mean remifentanil consumption in each group (Table 1).

Intraoperative blood loss was minimal in all groups with no significant differences among them—160 ± 39 mL (P); 156 ± 42 mL (D), and 166 ± 40 mL (S)—and the operating field was judged to be excellent by the surgeons at all times (Table 2). No complications were recorded at any time during the induced hypotension period or during the postoperative period.

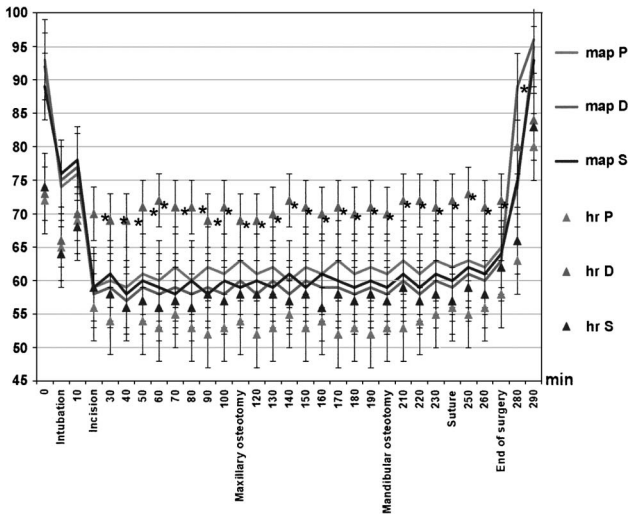

Fig 1 Mean arterial blood pressure and heart rate.

Early recovery times were faster in group D than groups P and S (Table 3). The same was recorded for late recovery: the percentage of correct answers at the TDT and DSST was >50% at 30 minutes in group D, whereas the same percentage was reached in the other two groups at 60 minutes (Fig 2).

Postoperative morbidity (nausea, vomiting, shivering, pain, and edema) was slight and did not differ significantly among the groups (Table 4).

Table 1. Demographic Data, Surgery, and Anesthesia

	Group P (n = 40)	*Group D (n = 40)*	*Group S (n = 40)*
Sex (M/F)	18/22	16/24	14/26
Age (y)*	25 ± 7	26 ± 6	24 ± 6
Weight (kg)*	73 ± 15	70 ± 14	68 ± 15
Height (cm)*	174 ± 12	172 ± 10	169 ± 9
Baseline hemodynamic parameters			
Systolic arterial blood pressure (mmHg)*	122 ± 15	116 ± 14	118 ± 13
Mean arterial blood pressure (mmHg)*	93 ± 9	92 ± 8	89 ± 9
Heart rate (beats/min)*	72 ± 11	73 ± 10	74 ± 12
Duration of surgery (min)*	250 ± 57	245 ± 50	248 ± 56
Duration of anesthesia (min)*	265 ± 45	261 ± 50	262 ± 55
Duration of hypotension (min)*	246 ± 40	241 ± 42	244 ± 45
Maintenance of anesthesia			
Propofol (mg/kg/h)*	6 ± 0.5		
Remifentanyl (μg/kg/min)*	0.9 ± 0.44†	0.6 ± 0.3	0.7 ± 0.3
Consumption of remifentanyl (mg)*	15.3 ± 3.5†	9.5 ± 2	11.7 ± 2
Inhalation anesthesia, MAC		0.6	0.5

*Values are mean ± SD.
*$P < .05$ versus D and S.

Table 2. Blood Loss, Surgical Field Quality, Need for Hypotensive Drugs

	Group P (n = 40)	*Group D (n = 40)*	*Group S (n = 40)*
Additional use of clonidine *n* (%)	10/40 (25%)*	2/40 (5%)	4/40 (10%)
Consumption of clonidine (μg)†	75 ± 30	75 ± 30	75 ± 30
Blood loss (mL)†	160 ± 39	156 ± 42	166 ± 40
Surgical field quality†			
1 = No bleeding			
2 = Mild bleeding			
3 = Moderate bleeding	1.7 ± 0.3	1.6 ± 0.32	1.8 ± 0.28
4 = Heavy but controllable bleeding			
5 = Massive uncontrollable bleeding			
Complications due to hypotension *n* (%)	0	0	0

*$P < .05$ versus D and S.
†Values are mean ± SD.

Table 3. Early Recovery

	Group P (n = 40)	*Group D (n = 40)*	*Group S (n = 40)*
Eye opening (min)*	14.5 ± 3.4	7.3 ± 2†	13.8 ± 3.2
Squeeze fingers (min)*	15.2 ± 4	8 ± 3†	14.6 ± 3.8
Spontaneous breathing (min)*	11.2 ± 3.2	5 ± 2†	11 ± 3
Extubation (min)*	16 ± 3.3	8.3 ± 2†	15.2 ± 3.2
State Name, birth date, age (min)*	17.8 ± 3.2	10 ± 2†	17 ± 3
Aldrete recovery score ≥9 (min)*	18.8 ± 3.2	10.8 ± 2†	18 ± 3.1

*Values are mean ± SD.
†$P < .05$ versus P and S.

Table 4. Postoperative morbidity

	Group P (n = 40)	*Group D (n = 40)*	*Group S (n = 40)*
Edema to 24 h (%)			
Slight	60%	62%	58%
Moderate	37%	36%	39%
Severe	3%	2%	3%
Shivering (%)	12.5%	11%	12.5%
PONV (%)	6%	7%	12%
Postoperative antiemetics and antishivering (%)	12.5%	10%	12.5%
Pain (%)			
VAS >5 at awakening	5%	2%	3%
VAS >5 to 2 h	1%	0	0
VAS >5 to 24 h	0	0	0
Postoperative analgesics (%)	3%	2%	2%

PONV = postoperative nausea and vomiting; VAS = visual analog scale.
$P > .05$.

DISCUSSION

We believe that controlled hypotension is essential in the surgical procedures considered in our study. It is also essential that such technical procedures are followed by a prompt, predictable, and complete emergence from anesthesia.

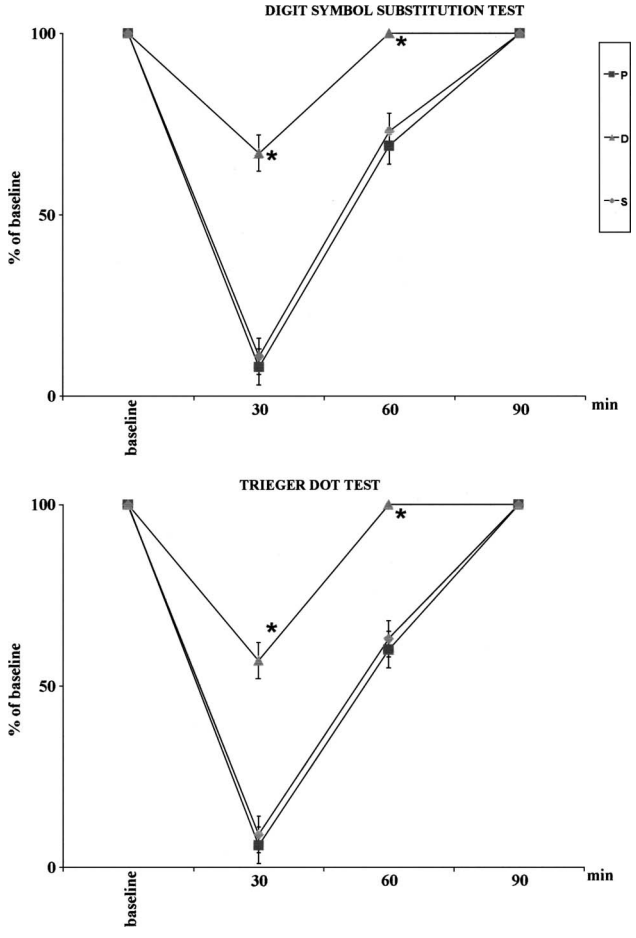

Fig 2 Late recovery.

The constant overuse of new, short-acting anesthetics obliges us to investigate whether their use may be more appropriate in this type of surgery, with better outcomes and higher quality for both the surgical procedure and the patient.

Controlled hypotension and a bloodless surgical field were successfully obtained in all three anesthesiological techniques taken into consideration in the study. Therefore, the surgical technical procedure was easy and optimized in terms of precision and timing. As stated by Sivarajan et al,[13] it is essential to maintain a low mean arterial pressure to reduce intraoperatory blood loss.

The pharmacokinetics of remifentanil allowed easy titration for changing intraoperative conditions, obtaining a more pronounced hypotension during the first phase of the operation, which is characterized for considerable bleeding from mucosal and muscle tissues.[14]

Data recorded from this study encourage us in that a great degree of improvement has been obtained on both sides, from the surgical and anesthesiological point of view, for which blood losses are minimal and transfusions are not taken into consideration. It is not to be forgotten that during the 1980s, patients who were undergoing this type of procedure had important blood loss (mean 900 mL), and the mean surgical time was 7.5 hours.[15]

There was a significant difference between group P and the other two groups in terms of opioids and clonidine intraoperative consumption; nevertheless,

no additional potent hypotensive agent has been used. This is probably because of the lack of analgesic effect within the pharmacological properties of the propofol as compared with that of the inhalator agents.

Heart rate remained stable and unchanged from baseline only in group D, which can be attributed to the intrinsic property of the desflurane to abolish baroceptor responses to hypotension; in the other two groups, we recorded a relative bradycardia. Controlled hypotension has been sustained throughout the procedure in all groups. We have observed that the return to baseline arterial blood pressure was significantly faster in group D. Statistically significant differences also were observed with regard to early and late recovery; group D had a shorter recovery time.

The anesthesiological drugs taken into consideration in this study have a well-known property in terms of hemodynamic stability[18,20]; this characteristic is enhanced by the use of the remifentanyl, which allows predictable intraoperative titration without any increase in significant adverse events.

Remifentanil is a short-acting opioid with a context-sensitive half-time (CSHT) of approximately 3 minutes, influenced by rapid clearance (40 mL/kg/min) and little volume of distribution (100 mL/kg) but independent of duration of infusion. As matter of fact, remifentanil possesses an ester bond, on a side chain from the phenylpiperidine ring, that is readily hydrolyzed by nonspecific plasma and tissue enzymes.

The organ-independent, metabolic breakdown of the remifentanil allows us to use high doses of the drug (effective dose [ED] 90) without having the important side effects that opioid drugs have and giving strong analgesic effects. Normally, opioids are used at their median effective dose,[21] especially to avoid accumulations and prolonged recovery periods, respiratory depression, and side effects.[20,22–24] Combining remifentanil with another short-acting drug such as desflurane, we obtained the shortest time in terms of recovery and cardiovascular parameter modulation.

Desflurane is the inhaled anesthetic with the lowest solubility in blood and tissues and, consequently, with the most rapid increase and decrease of the alveolar concentration, particularly for longer duration of anesthesia.[25] After 90 minutes of anesthesia administration, the 90% decrement time for sevoflurane increases significantly but remains <10 minutes for desflurane.[18,26–28] These observations suggest that desflurane allows a more rapid recovery than does anesthesia with all other potent inhaled anesthetics.

In addition, results from several studies indicate that desflurane produces a more rapid recovery than does propofol; the increasing CSHT for long-term intravenous infusion with propofol[18,26] may be the explanation for the longer and less-prompt recovery from anesthesia in group P than in group D. This hypothesis may be confirmed only by plasmatic dosage of the drug, which was not analyzed in the current study.

Recovery from anesthesia has been free from morbidity factors such as nausea, vomiting, shivering, edema, and pain. The type of surgery examined in our study is proven to have a very high incidence of PONV; for this reason, total intravenous anesthesia (TIVA) was considered more appropriate than inhalation agents because of the antiemetical properties of propofol.[29] However, desflurane has a very low incidence of PONV as compared with the other halogenated agents.[30] In the study by Eriksson and Korttila,[31] administration of ondansetron, before the end of anesthesia, with desflurane decreased the incidence of PONV to that found with a propofol approach to anesthesia. In our study, there is no significant difference among the three groups in terms of PONV. We registered a very low incidence in groups P and D, whereas it is slightly higher in group S.

We may conclude that all groups had very good controlled hypotension with a very low rate of bleeding and excellent operating field. All three techniques are appropriate for this type of surgery; there is only one important advantage, which is backed up by statistical support, for group D, in which the combination of desflurane and remifentanil assures a more prompt and more complete recovery from anesthesia.

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