Total intravenous anaesthesia in endoscopic sinus-nasal surgery

Anestesia generale endovenosa nella chirurgia endoscopica naso-sinusale

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Key words

Nasal diseases • Surgical treatment • Endoscopic sinus surgery • Total anaesthesia • Remifentanyl • Propofol

Parole chiave

Patologia nasale • Trattamento chirurgico • Chirurgia endoscopica • Anestesia generale • Remifentanil • Propofol

Summary

Aim of this randomized study (64 patients) was to improve the control of bleeding during functional endoscopic sinusal surgery by means of controlled hypotension achieved through either total intravenous anaesthesia using remifentanyl and propofol (27 patients), or inhaled using isoflurane and fentanyl (37 patients). The following parameters were monitored before administration of anaesthesia (T0), then after 15 (T1), and 30 minutes (T2): systolic, diastolic, and mean arterial pressure; heart rate; concentration of tele-exhaled carbon dioxide ($PetCO_2$) and percentage of peripheral saturation of haemoglobin (SPO_2); bleeding according to the Fromme-Boezaart scale at T2. Mean arterial pressure values were maintained between 60-70 mmHg throughout surgery. At T0, systolic arterial pressure, diastolic arterial pressure and mean arterial pressure values were seen to overlap in the two groups. Both types of anaesthesia were effective in reducing the pressure values of T0-T1 and T1-T2 trends ($p<0.0001$). Systolic arterial pressure at T1 is lower with total intravenous anaesthesia compared to isoflurane and fentanyl ($p=0.02$). $PetCO_2$ and heart rate show a decreasing trend independently of the type of anaesthesia employed. In conclusion, the hypotensive effect of total intravenous anaesthesia and of isoflurane and fentanyl is equivalent, but only total intravenous anaesthesia is effective in reducing bleeding during functional endoscopic sinusal surgery.

Riassunto

L'obiettivo di questo studio randomizzato (64 pazienti) è di ottimizzare il controllo del sanguinamento durante chirurgia funzionale endoscopica naso-sinusale (FESS) mediante la tecnica dell'ipotensione controllata ottenuta con anestesia totalmente endovenosa con remifentanil e propofol (gruppo TIVA 27 pazienti), o inalatoria con isoflurano e fentanil (gruppo INA 37 pazienti). Sono stati monitorati prima dell'induzione anestesiologica (T0), dopo 15 (T1), e 30 minuti (T2) i seguenti parametri: pressione arteriosa sistolica (PAS), diastolica (PAD) e media (PAM); frequenza cardica (FC); concentrazione di anidride carbonica tele-espiratoria ($PetCO_2$) e percentuale di saturazione periferica di emoglobina (SPO_2); il sanguinamento con la scala di Fromme-Boezaart al tempo T2. I valori di PAM sono stati mantenuti nel range di 60-70 mmHg durante tutta la durata della procedura chirurgica. Al tempo T0 i valori di PAS, PAD e PAM sono sovrapponibili nei due gruppi. Entrambe le tecniche anestesiologiche risultano efficaci nel ridurre i valori pressori del trend T0-T1 e T1-T2 ($p<0,0001$). La PAS al tempo T1 risulta più bassa con la TIVA rispetto ad INA ($p=0,02$). $PetCO_2$ e FC diminuiscono nel trend considerato indipendentemente dall'anestesia impiegata. Concludendo l'effetto ipotensivo di TIVA e INA è equivalente, ma solamente TIVA risulta efficace nella riduzione del sanguinamento durante FESS.

Introduction

The aim of functional endoscopic sinusal surgery (FESS) is to restore the drainage and aeration of the paranasal sinuses, while maintaining the natural mucociliary clearance mechanism, and seeking to preserve the normal anatomical structures [1 2]. The excellent results achieved have led to FESS becoming a widely used endoscopic surgical technique. However, this surgery can lead to serious complications such as orbit cellulitis, rhino-liquoral fistulas, lesions to the optic nerve of the dura mater, meningitis [2-4]. These complications are often the result of excessive bleeding which may occur during surgery [5]. Hence, to improve the surgical technique by reducing the incidence of complications, it is important to have a surgical field as free of blood as possible to improve visibility. This can be achieved with the use of local anaesthesia, with topically applied vasoconstrictors or general anaesthesia, associated with controlled hypotension. Total intravenous general anaesthesia (TIVA), with remifentanyl and propofol (REM/PRO), should be the most effective technique to obtain reduced bleeding. Remifentanyl, as all morphine-like molecules, acts on specific receptors located in the neuraxis producing a state of analgesia, sedation and

drowsiness. In the cardiovascular system, this molecule causes sinusal bradycardia by vagal hyperstimulation [6] and dose-dependent hypotension [7 8]. Propofol is an intravenous (i.v.) hypnotic with no analgesic properties and is used to induce and maintain narcosis. Also this drug causes a lowering of mean arterial pressure (MAP) by reducing peripheral vascular resistance and slightly decreasing cardiac output (CO), with no significant variations in heart rate (HR) [9].
Aim of the present study was to improve the control of bleeding in the surgical field during FESS by employing TIVA and to compare the effect, at the same MAP, with the gaseous anaesthesia previously used.

Materials and methods

Prior to the study, informed consent was obtained to perform surgery, from those patients candidates for this treatment, as well as consent for randomised administration of one of the two types of anaesthesia (INA or TIVA). Included in this study were 64 patients (41 male, 23 female) submitted to endoscopic sinusal surgery for simple chronic sinusitis or chronic sinusitis with polyposis. Patients were divided into 3 groups as follows: a) anterior ethmoidectomy (resection of the uncinate process end opening of the bulla) and/or middle hiatal anthrostomy; b) A + posterior ethmoidectomy with opening of the middle lamina of the turbinate and/or sphenoidotomy; c) A + B + anterior ethmoidectomy opening of the middle lamina of the turbinate and/or opening of the frontal recess (Table I).
In the "INA" group, 10 were in class ASA (American Society of Anesthesiologists) 1, and 27 ASA 2, while in the "TIVA" group, 7 were in class ASA 1, 20 in ASA 2 (Table II). The 27 patients in the TIVA group received remifentanyl and propofol (REM/PRO) in continuous i.v. infusion by means of a specific infusion pump, while the other 37 (INA group) were given an inhaled, balanced, anaesthesia using fentanyl as an analgesic and isoflurane (ISO) as a hypnotic. All patients were pre-medicated with atropine (0.007 mg/kg), midazolan (0.05 mg/kg). Approximately two minutes after pre-medication, general anaesthesia was induced by administration of propofol (1-2 mg/kg) and fentanyl (2 µg/kg) in the INA group. In the TIVA group, anaesthesia was induced by a bolus of remifentanyl (1 µg/kg) followed by propofol (1-2 mg/kg). For easier intubation, succinylcholine (1 mg/kg) was administered in both groups. Once intubation was complete, ventilation was guaranteed by an automatic respirator providing a mixture of air and oxygen at 40% and muscular paralysis was maintained with a bolus of vecuronium (1 mg/kg) followed by maintenance doses of 10-20 mg. Anaesthesia was maintained by slow infusion of remifentanyl and propofol using a specific infusion pump previously prepared with two syringes containing 2 mg of remifentanyl in 40 cc of physiological solution and 50 cc of propofol. The rate of infusion was 38-155 ml/hour for remifentanyl and 35-45 ml/hour for propofol in patients in the TIVA group (ASA I) and 35-44 ml/hour of remifentanyl and 32-40 ml/hour of propofol in patients in the TIVA group (ASA II). This rate was adapted according to haemodynamic responses, in order to maintain MAP values in the 60-70 mmHg range. Fluid therapy of 4 ml/kg/h was maintained in both groups with a physiological 0.9% solution alternated with ringer acetate. In the INA group, anaesthesia was maintained with ISO 1-2% in an inhaled air and oxygen mixture of 40%. The minimum alveolar concentration (MAC) of halogenated anaesthetics was successively adapted until reaching the mean target pressure values of 60-70 mmHg. Cardiovascular monitoring was carried out by continuous electrocardiogram (ECG), recording of arterial pressure, recording of the capnographic signal ($PetCO_2$) and measuring via photo-plethysmography of peripheral saturation in oxygen (SPO_2). The two groups were monitored before induction of anaesthesia (T0), after removal of the nasal pledgets, i.e., 15 minutes after induction of anaesthesia (T1), and, finally, 30 minutes after induction of anaesthesia i.e., when MAP values were steady, within the range 60-70 mmHg (T2), for the following parameters: systolic (SAP), diastolic (DAP), and mean (MAP) arterial pressure; heart rate (HR); $PetCO_2$ and SPO_2. For easier venous drainage, the patient was placed supine or inclined (anti Trendelemburg) by approximately

Table I. Patients classified according to surgical procedure and type of anaesthesia.

Surgical procedure	Type of anaesthesia	
	TIVA (27 patients)	INA (37 patients)
A	10	13
B	10	14
C	7	10

Table II. Demographic data: age and ASA class ± standard deviation.

Group	Patients	Age (years)	p	ASA	p
INA	37	45.35 ± 10.91	ns	1.73 ± 0.45	ns
TIVA	27	48.07 ± 9.40	ns	1.74 ± 0.44	ns

ns = not significant

Table III. Evaluation scale for bleeding of surgical field.

0 No bleeding
1 Slight bleeding – no suctioning of blood 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 suctioning required. Bleeding appears faster than can be removed by suction. Surgical field severely threatened and surgery impossible

25°. Immediately after naso-tracheal intubation, patients, in both groups, underwent packing of the nasal cavity with adrenaline soaked pledgets (1:1000) in order to obtain maximum contraction of the mucosa and thus better visualize the main features of the nasal cavity [10]. Prior to insertion in the nasal cavity, liquid is removed from the pledgets and then, under endoscopic guidance, carefully applied on the nasal mucosa. The middle meatus is packed with cotton pads which are introduced using small auricular forceps. The hiatus semilunaris and the spheno-ethmoidal recess are packed in the same way. After 5 minutes, the pledgets are removed. Additional local anaesthesia is then commenced, usually by injection below the mucosa of the uncinate process, at the level of the head of the middle turbinate and the inferior part of the bulla. It is important to give the injection at the point of insertion of the middle turbinate, since, in this way, it is possible to block the vessels and the nerve fibres which come from the artery and the anterior ethmoidal nerve. In most cases, 1-1.5 ml of this submucosa infiltration is sufficient, for which carbocaine with adrenaline 1:1000 was used. After 15 minutes, having removed the pledgets, the above-mentioned parameters were assessed (T1). Then 30 minutes after induction of anaesthesia, i.e., when MAP values were reached and stable, within the range 60-70 mmHg (T2), the surgeon, unaware of the drugs used, evaluated the quality of the surgical field using the Fromme et al. [11] scale adapted by Boezaart et al. (Table III) [5].

Results

The parameters taken into consideration, in the present study, were mean values of SAP, DAP, MAP, HR and $PetCO_2$, at times T0, T1,T2, in the two groups, namely, INA and TIVA. Statistical analyses with Student test for unpaired data (Table IV) show that the difference at T0 is not statistically significant thus indicating that the two groups commenced with comparable mean values of the variables under consideration. To evaluate the significance of the differences between the mean scores of the parameters, in the TIVA and INA groups, one-way ANOVA was used, while to evaluate the significance of the differences in the parameters considered between the two groups, in function of time (Within) or in function

Table IV. Haemodynamic values in TIVA and INA groups at T0.

	Group	T0	p
SAP	TIVA	138.14 ± 16.47	0.19
	INA	142.97 ± 17.01	
DAP	TIVA	82.85 ± 9.02	0.26
	INA	86.29 ± 11.30	
MAP	TIVA	99.19 ± 10.06	0.09
	INA	104.29 ± 12.64	
HR	TIVA	74.44 ± 11.03	0.09
	INA	79.86 ± 13.38	
$PetCO_2$	TIVA	31.23 ± 4.30	0.37
	INA	33.58 ± 12.68	

Table V. Effects on haemodynamic values, $PetCO_2$ (mmHg), SPO_2 (%), of anaesthetics at times T0, T1, T2, in INA and TIVA groups.

Variables	Group	T0	T1	T2	One-way F (p)	Two-ways T0-T1 Within F (p)	Two-ways T0-T1 Interact F (p)
P syst	INA	142.97 ± 17.01	129.73 ± 13.99	93.21 ± 6.96	205.22 (< 0.0001)	285.93 (< 0.0001)	4.49 (0.013)
	TIVA	138.14 ± 16.47	117.96 ± 17.55	93.40 ± 4.08	101.82 (< 0.0001)		
P diast	INA	86.29 ± 11.30	78.92 ± 10.48	56.54 ± 3.65	169.22 (< 0.0001)	262.99 (< 0.0001)	4.13 (0.018)
	TIVA	82.85 ± 9.02	72.59 ± 9.84	57.26 ± 2.86	110.70 (< 0.0001)		
P mean	INA	104.29 ± 12.74	95.18 ± 9.99	68.32 ± 2.73	217.30 (< 0.0001)	269.71 (< 0.0001)	4.51 (0.012)
	TIVA	99.19 ± 10.06	87.65 ± 12.07	68.92 ± 1.44	26.92 (< 0.0001)		
$PetCO_2$ (mmHg)	INA	31.50 ± 2.96	29.35 ± 2.60	27.80 ± 2.42	25.09 (< 0,0001)	30.56 (< 0.0001)	1.84 (0.167)
	TIVA	31.00 ± 3.81	30.16 ± 2.97	28.58 ± 3.28	11.95 (0.0003)		
HR	INA	79.54 ± 13.88	75.60 ± 11.16	67.72 ± 9.021	13.88 (< 0.0001)	19.82 (< 0.0001)	0.569 (0.567)
	TIVA	74.54 ± 11.22	73.18 ± 15.08	66.13 ± 12.53	8.35 (0.0009)		
SPO_2 (%)	INA	96.59 ± 1.75	97.87 ± 5.76	98.68 ± 0.96	2.87 (0.006)	3.88 (0.023)	0.27 (0.76)
	TIVA	98.10 ± 2.33	98.94 ± 1.02	99.31 ± 0.75	3.46 (0.042)		

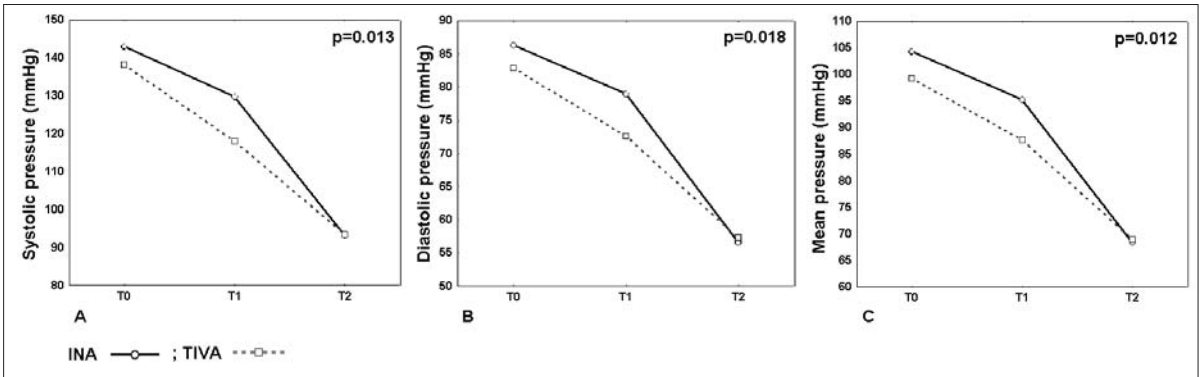

Fig. 1. Two-way ANOVA for repeated measurements (times T0, T1, T2): interaction between types of anaesthesia and variations in time (trend) for variables considered, (A) systolic (SAP), (B) diastolic (DAP), (C) mean arterial pressure (MAP), in INA and TIVA groups.

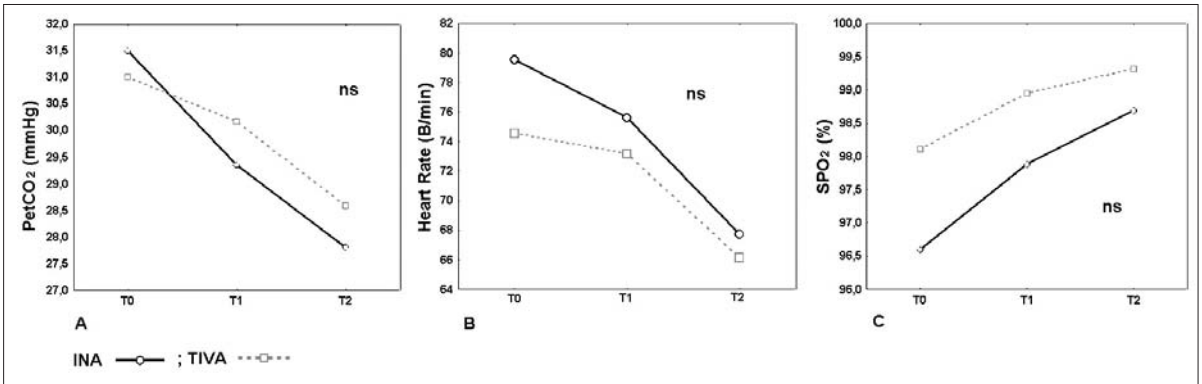

Fig. 2. Two-way ANOVA for repeated measurements (times T0, T1, T2): interaction between types of anaesthesia and variations in time (trend) for variables considered, (A) $PetCO_2$, (B) heart rate, (C) SPO_2, at T0, T1, T2, in INA and TIVA groups.

both of time and of type of anaesthesia used (Interact), two-way ANOVA for repeated measurements was employed (Table V). Clearly, MAP, DAP and SAP, despite starting with comparable values, show a different trend in time, with a more marked decrease in values at T1 in the TIVA group (as a result of the calcium antagonist effect of propofol) compared to the INA group, but then return to similar pressure values at T2 (Fig. 1). This indicates that the two types of anaesthesia influence the variation in time of the pressure parameters considered, but do not influence HR, $PetCO_2$, and SPO_2, the trends of which are independent of the type of anaesthesia used (Fig. 2). The levels of bleeding, evaluated by the scale of Fromme et al. adapted by Boezaart et al., were, overall, 3.05 ± 0.57 for the patients in the INA group and 2.48 ± 0.51 for the patients in the TIVA group. At the same MAP, the score for bleeding, at T2, is higher for INA patients (Table VI). The results, in terms of bleeding, are significantly different in the sample studied, even if the number of patients in the TIVA and INA groups differed (Table VII). There were no severe complications in the present cases. As far as concerns the parameters evaluated in this study, no statistical differences were found between groups A, B and C, at time T0 and T2, for TIVA and INA anaesthesia ($p > 0.05$).

Discussion

Over the last few years, the endoscopic techniques used for diagnostic purposes, combined with the current visualization procedures, particularly computerized tomography, have proven to offer an ideal tool and now constitute, almost worldwide, the diagnostic standard, in the presence of infections of the paranasal sinuses. By means of this diagnostic approach, an endoscopic-surgical procedure has been developed specifically for the areas located in the key points of the lateral nasal wall. After relatively circumscribed surgery, which may comprise resection of the uncinate process, middle hiatal antrostomy,

Table VI. Evaluation scale of bleeding of surgical field.

Boezaart score	Group	N. patients	Mean p (mm Hg) time T2	p
2	TIVA	20	68.30 ± 1.66	ns
	INA	5	66.08 ± 3.44	
3	TIVA	7	69.58 ± 0.79	ns
	INA	25	69.02 ± 2.06	
4	TIVA	0	–	
	INA	7	67.42 ± 3.57	
Boezaart score total				
2.48 ± 0.51	TIVA	27		0.001
3.05 ± 0.57	INA	37		

Table VII. Test of χ^2 to evaluate significance of results obtained, in terms of bleeding, in sample studied.

Boezaart score	TIVA	INA	p
2	20 (74.07%)	5 (13.51%)	0.0013
3	7 (25.93%)	25 (67.57%)	0.049
4	0	7 (18.92%)	0.029
Total	27 (100%)	37 (100%)	

opening of the bulla, of the middle lamina of the turbinate, of the posterior ethmoid, sphenoidectomy and/or opening of the frontal recess, even massive alterations of the mucosa in the larger paranasal sinuses regress without substantially operating upon them, thus recovery is achieved following a surgical technique with reduced traumatism and preservation of the mucosa [2]. As far as concerns the disadvantages of this type of surgery, it is worthwhile mentioning: orbitary cellulitis, rhino-liquoral fistulas, lesions of the optic nerve, of the dura mater, meningitis [2-4]. Complications often arise on account of excessive bleeding during surgery [5]. To reduce complications it is, therefore, important that the surgical field be as free from blood as possible to improve visibility. For this reason, the present study aimed to evaluate the quality of the surgical field during FESS using TIVA compared to INA anaesthesia. To this end, we exploited the pharmacological properties of remifentanyl and propofol (REM/PRO) administered in continuous i.v. infusion via a specific infusion pump. Propofol (12-6 diiso-profilfenolo) is an i.v. anaesthetic in 1% emulsion in soya oil which is highly soluble in lipids, passes rapidly from blood to tissues, with a half-life of distribution between 2-4' ($T_{1/2}$ = 1.8-8.3 min); a rapid drop in blood levels means rapid reawakening, since the half-life of elimination lies between 36 and 60 minutes ($T_{1/2}$ B). It has been reported [9] that, on induction, propofol leads to a lowering of mean MAP by reducing peripheral vascular resistances and a slight decrease in output (CO), without significant variations in HR. A study on the effect of propofol in bovine aortic endothelium cells showed that the associated clinical manifestations, hypotension and/or bradycardia, could be due to inhibition of the release of intracellular calcium (calcium antagonist effect) [12]. The kinetics of propofol remain unchanged in patients with severe liver disease or kidney failure and may be used also in patients undergoing treatment with beta-blockers or with valve defects [9]. As propofol is a hypnotic agent, it has no analgesic effect and must, therefore, be used with a strong analgesic, such as remifentanyl, a new ultra-short-acting opioid agonist of the μ-receptors. Compared to other similiar opioids such as fentanyl [13] or alfentanyl [14-16], remifentanyl appears to offer greater haemodynamic stability during surgery and maintains cerebral perfusion unchanged [13-17]. At the same time, it would appear to induce slight hypotension [16 18]. Remifentanyl is an opioid of the anilidopiperidinic class which interacts selectively with μ receptors. Its particular pharmacokinetics distinguish it from the other synthesis opioids (fentanyl, alfentanile, sufentanile): remifentanyl is rapidly metabolised by aspecific plasma and tissue esterases. This type of metabolism means that elimination is very fast and, therefore, the effect disappears very quickly regardless of the duration of the infusion. At onset, remifentanyl is as rapid as alfentanil, but the patient recovers more rapidly and with no untoward effects. Moreover, since the response can be foreseen, dosage can easily be graduated. Since the effect disappears rapidly after surgery this is felt soon after the infusion is suspended; it is, therefore, necessary to commence adequate post-surgery analgesic treatment before surgery is actually terminated. The side-effects of remifentanyl are similar to those of other opiates, but, since the drug is rapidly eliminated from the body, the effects also dis-

appear rapidly. The following side-effects were reported: muscle stiffness, nausea and post-operative vomit, respiratory depression, itching, headaches, vertigo, hypotension [7], sinus bradycardia due to vagal hyperstimulation [6]. Furthermore, the hypotensive action of remifentanyl is dose dependent [8]. As far as concerns balanced, inhaled anaesthesia, this was performed using fentanyl as an analgesic and isoflurane (ISO) as a hypnotic on account of its profile and haemodynamics similar to those of propofol [19]. Indeed, it has been demonstrated that ISO and propofol induce a reduction in total arterial resistance, and have a direct significant negative inotropic effect [20]. In the present study, ISO was chosen also because, of the various types of halogenates available, ISO is that which less often causes problems in rhythm when associated with local vasoconstrictors (10). Despite using adrenaline as a topical anaesthesia, which offers the advantage of a blood-free surgical field, it has been demonstrated that, although there is systemic absorption of adrenaline, side-effects (alpha-sympathomimetic) are extremely rare since, with the sole exception of cocaine, the action of local anaesthetics, which produce vasodilation by directly acting on the vessel muscles, alongside a slight drop in cardiac output (CO) and the peripheral vascular resistances caused by propofol, they contrast the sympathomimetic effect of adrenaline [21]. ISO also has a vasodilatory effect, as demonstrated in a study by Testa et al. which evaluated variations in microcirculation using photopletismography at skin and muscle level [22]. The haemodynamic data in Table V and illustrated in Figure 1 show a significantly greater drop in DAP, SAP and MAP in the TIVA group compared to the INA group at T1. This is in keeping with results obtained in other studies aimed at establishing the efficacy of total iv anaesthesia (TIVA) using remifentanyl and propofol [6 23] and with their pharmacological characteristics [7-9 12-18]. Albeit, at T2, SAP, DAP and MAP values in the INA and TIVA groups are substantially the same. Only in the TIVA group, however, are there good surgical conditions, in terms of quality of the surgical field (Tables VI, VII). This could be due to the characteristics of ISO which leads to a drop in sistemic arterial pressure, by lowering vascular resistances [24] particularly in the skin and muscle [25], which might account for the more severe bleeding in the surgical field observed, by the surgeon, in patients in the INA group who underwent endoscopic nasal surgery. With regard to mean heart rate, $PetCO_2$, and SPO_2, the differences between the mean values in the two groups are not significant since these variables are not influenced, in an identical fashion, by the two types of anaesthesia used (Fig. 2).

Conclusions

This study shows that both TIVA and INA can be safely used to control hypotension. However, with regard to FESS, only TIVA is effective in creating good surgical conditions, in terms of the quality of the surgical field, since the calcium antagonist properties of propofol allow selective vasodilation of the arterial area. This type of anaesthesia has proven to be a valid tool, for the surgeon, since enhanced visualisation of the nose-sinus structures, mainly due to less bleeding in the surgical field, reduces risks in endoscopic nasal surgery. Moreover, it will be important to evaluate not only the quality of the surgical field but also the time of reawakening, nausea and post-operative vomiting before introducing TIVA, for routine use, despite the higher cost involved.

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