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Inhalatory Anaesthesia Vs. TIVA in Oral Surgery and Laryngectomy with Lateral Clearing: Our Experience

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Abstract: From the second half of the nineties, Total IntraVenous Anaesthesia (TIVA) has been adopted with more than satisfactory results in oral medicine and otolaryngology surgical interventions of medium duration. The aim of the research was to evaluate the Inhalatory anaesthesia Vs TIVA in oral surgery and laryngectomy. Forty six patients were enrolled and randomly divided in 2 groups, identified with letters A and B. On group A patients, anaesthesia was carried out with TIVA method, while group B patients received a conventional balanced gasoeus anaesthesia. The data collected revealed an undeniable superiority of TIVA compared to gaseous anaesthesia with regard to patient comfort and to a remarkable reduction of surgical and hospitalization times. The key factor to fulfil these conditions, however, was a thorough knowledge of the technique and the possibility of having proper monitoring. TIVA can be adopted with satisfactory results in oral and otolaryngology surgery.

Key words: TIVA, oral, otolaryngology, surgery

INTRODUCTION

From the second half of the nineties, Total IntraVenous Anaesthesia (TIVA) has been adopted with more than satisfactory results in oral medicine and otolaryngology surgical interventions of medium duration. Since 2000, given the quite positive intra- and postoperative experience in ENT and oral surgery of short and medium duration, TIVA was also experimented on operations of wide field laryngectomy with mono- and bilateral laterocervical clearing (Zaba *et al*., 2007; Yamashita *et al*., 2007; Umar *et al*., 2007; Dagtekin *et al*., 2007; Vabishchevich *et al*., 2006).

Apart from maxillofacial interventions, laryngectomies are the most demanding and time-consuming operations in ENT surgery.

On the basis of past experience, the aims of our anaesthetists for these interventions were:

- Maximum reduction of bleeding.
- Reduction of intraoperative oedema.
- Reduction of surgical time.
- Elimination of further recurarization after the initial dose.
- Observation and correction of diuresis contraction due to hypotension effects.
- Fast and almost complete awakening in the immediate postoperative period.
- Elimination of awareness.
- Reduction of rehabilitation time during postoperative period and therefore hospitalization times.

Regarding the first point, that is bleeding reduction, this is obtained by inducing an arterial BP lowering by means of propofol and remifentanyl properties (Wallden *et al*., 2006; Rohm *et al*., 2006). For medium duration surgery, these 2 drugs are infused at such a speed as to obtain systolic BP values from 80-100 mm Hg and diastolic values of 50-60 mm Hg. In such conditions, the patient is properly anaesthetized and no curare booster doses are required (Dagtekin *et al*., 2007).

At higher values, a superficialization of the anaesthetic plane occurs, with the possibility of patient movement and an increase of pulmonary resistance.

On the contrary, lower values might not assure proper tissue blood perfusion. This eventuality is more probable and dangerous when the patient is older or compromised by pathologies like arterial hypertension, ischaemic cardiopathy, or COPD (Ledowski *et al*., 2006).

The candidates for laryngectomy are actually over 50 in almost all case Ledowski and they all show more or less severe concurrent diseases of the respiratory system,

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besides, many of them suffer from cardiovascular diseases and not infrequently also from metabolic disorders, renal and thyroid diseases. Under these clinical conditions and given the duration of the operation, it is advisable to keep the systolic arterial BP between 90 and 110 mm Hg and the diastolic BP between 60 and 70 mm Hg. With these values, at the end of the operation there will be from 0 (in 90% of the cases) to 100cc of blood in the aspirator jar. These results cannot be reached at all with other anaesthetic methods. The second point, that is oedema reduction, occurs because hypotension, by causing a minor loss of blood, determines a reduced tissue inhibition. Besides, this favours a faster cicatrisation of the surgical wound and fewer complications, such as local infections, fistulas, etc. A bloodless operation field naturally permits a faster progress of resections and blunt dissections, with a considerable reduction of aspiration and tamponage times; in this way, also the third point (surgical time reduction) is satisfied (Turan *et al*., 2007; Nonaka *et al*., 2006; Modesti *et al*., 2006). In 1990 andreassen had already stated that the results of this type of surgery do not depend only on the operator's competence, but also on the anaesthetist's skill and cooperation.

The 4th point, that is non-recurarization, has been an important technical achievement. As a general rule, the anaesthetic cover is inadequate if an increase in arterial BP, heart rate and pulmonary resistance, or limb movements are noticed during surgery. Under these conditions, narcosis must be increased and the patient must be recurarized. The experience made on middle ear operations and on oral surgery carried out under TIVA without further recurarization has shown how the above clinical signs do not appear with systolic arterial BP lower than 100 mm Hg; therefore, the anaesthetic cover is complete and no further curare boluses are required (Ledowski *et al*., 2006). These observations are corroborated at the awakening, when the patient complains of none or few painful symptoms at least in 90% of the cases.

Unfortunately, it is not wise to induce an excessive, prolonged hypotensive state within laryngectomy and oral surgery, both for the clinical conditions of the patients and for the length of the operation. Therefore, the alternatives are:

- Use of further curare doses.
- Increase of analgesic cover without inducing excessive hypotension.

On the basis of their experience, our anaesthetists decided to rely on the second hypothesis, since they observed that the absence of recurarization plays an important role in shortening the hospitalization times.

It is useless to repeat that the total analgesic cover could not depend only on remifentanyl, due to its hypotensive effects; therefore, an additional infusion of fentanyl by pump was used. This too is a strong opioid which, at low doses, shows great haemodynamic stability and has a longer pharmacological activity lasting about 30 min. In reality, the combination of remifentanyl-fentanyl causes a longer effective analgesia compared to a single administration, so much so that the patient usually does not complain of painful symptoms in the immediate postoperative period. From the combination of propofol, remifentanyl and fentanyl, an anaesthetic plane deep enough as not to require recurarization can be obtained, provided that BP values are kept at about 90-100 mm Hg (Lo *et al*., 2006; Bappsc *et al*., 2006).

The achievement of the 5th point is derived from our observation made during abdominal surgery carried out under TIVA. In fact, we noticed how, after the initial dose of curare, no further doses were required for a long time. Under these conditions, the patients did not show a total inhibition of intestinal peristalsis during surgery, but only a slowdown, which was almost exclusively ascribable to opioids. In our research group we noticed how, among the patients subjected to TIVA and those subjected to balanced anaesthesia with recurarization, the first had on average intestinal canalization at least 12 h earlier (Wallden *et al*., 2006). This too contributes to a faster recovery, with considerably shorter hospitalization times.

Another important aspect of prolonged hypotension, though moderate, is diuresis contraction. In fact, compared to the 2.3-2.8 L infused intraoperatively, no more than 400 mL were collected in the urine bag. This problem was overcome by infusing, after the first half of the operation, 500 mL of 5% glucosate solution made hypertonic by addition of 5 vials of No. 7 solution and by intravenously administering a 10 mg furosemide bolus during the last suture stitches. The diuresis drive performed with this method is another factor which certainly influences both a prompt regaining of consciousness of the patient and oedema reduction (Umar *et al*., 2006).

In the last decade, some hundreds of operations were carried out with TIVA method. This was adopted first mainly in oral and middle ear surgery, for the possibility to have a bloodless operation field and to monitor facial nerve integrity. At the beginning of 2000, TIVA was also extended to oral surgery and to laryngectomy with mono- and bilateral laterocervical clearing. The aim of the research was to evaluate the Inhalatory anaesthesia Vs. TIVA in oral surgery (operator GAS) and laryngectomy.

MATERIALS AND METHODS

Fourty six patients were enrolled and randomly divided in 2 groups, identified with letters A and B. On group A patients, anaesthesia was carried out with TIVA method, while group B patients received a conventional balanced gasoeus anaesthesia. Group A was composed of 23 patients (20 men and 3 women) aged from 45-85, weighing from 690-100 kg, with ASA II-IV. Group B was composed of 23 patients (4 women and 19 men) aged from 48-87, weighing from 68-98 kg, with ASA II-IV. Group A, whose patients were subjected to TIVA, was further divided in 2 subgroups (1 and 2) according to age, for a proper anaesthetic dosage (Table 1).

The same procedures were followed for both TIVA groups. After peripheral vein incannulation, the patient is premedicated with 0.06 mg kg^{-1} body weight of atropin and 0.05 mg of fentanyl. Actually, the use of fentanyl for premedication in patients for whom the use of remifentanyl is contemplated has been criticized. The reason why the infusion of this opioid was not chosen right from premedication lies in its hypotensive effect, which might be very strong and therefore risky, if added to that of propofol bolus used for induction and in the fact that cases of chest wall stiffness have been observed. These 2 conditions are certainly not desirable in a patient who is still not intubated and in whom intubation may be difficult due to the type of pathology. This protocol contemplated a TIVA administered through 3 drugs infused intravenously by a syringe pump:

- A 2 mg of remifentanyl in 40 mL of water for injections.
- A 2% propofol.
- A 0.2 mg of fentanyl in 40 mL of water for injections.

Anaesthesia was induced by administration of 0.2 mg kg^{-1} body weight of cysatracurium and then 2 mg kg^{-1} body weight of propofol. Immediately after induction, brief, transitory hypotension was observed. Two minutes after pure oxygen mask ventilation, orotracheal intubation was carried out, the patient was connected to the ventilator, supplying an air-oxygen mixture in a 2:3 ratio with half-closed circuit and the 3 infusion pumps were started. In subgroup 1 patients, the initial infusion speed for remifentanyl was 0.375 μg/kg/h; this value was subjecte to variations of ±0.125 μg/kg/h, in order to keep arterial BP values around 100 mm Hg. The initial propofol dose was 7 mg/kg/h for the first 10 min, subsequently reduced to 5-6 mg/kg/h. In subgroup 2 patients, the initial remifentanyl dose was 0.25 μg/kg/h; in this case too, this value was subjected to variations of ±0.125μg/kg/h during the operation. The initial propofol dose was 6 mg/kg/h for the first 10 min, subsequently reduced to 4-5 mg/kg/h. It emerged that propofol dosage can be more easily standardized according to age and body weight, while the variability range is wider for remifentanyl; therefore, it must be adjusted in function of the required target PaO (Table 2).

Table 1: A proper anaesthetic dosage

TIVA	Sub-group 1	Sub-group 2
age	45-65 years	66-87 years
Men	10	9
Women	1	2
Total	11	12

Table 2: TIVA administration through 3 drugs

	Sub-group 1	Sub-group 2
Age	45-65	66-85
Remifentanyl average dosage	0.375 μg/kg/h ±0.125 μg/kg/h (i.e., ±15 mL h^{-1} for a patient of 70 kg at the speed of 31.5 mL h^{-1})	0.25 μg/kg/h ±0.125 μg/kg/h (i.e., ±10.5 mL h^{-1} for a patient of 70 kg at the speed of 21 mL h^{-1})
Propofol dose in the first 10 min	7 mg/kg/h	6 mg/kg/h
Propofol maintenance dose	5-6 mg/kg/h	4-5 mg/kg/h
Fentanyl	15 mL h^{-1} in the 1st h, then 5 mL h^{-1}	idem

Table 3: Relevant clinical parameters

	S PAO	HR
TIVA group A, subgroup 1		
Basal	150.2±30.3	80±6.3
2 min (after atropin and fentanest)	145±28.4	89.2±6.3
4 min	150±29.6	92±5.9
5 min (after intubation and propofol and remifentanyl pump start)	105.7±6.4	80.3±4.6
10 min (fentanyl pump start)	110±8.4	75.9±4.2
30 min	95.9±4.5	60.2±5.6
90 min	98±6.1	58.9±4
180 min	96±4.2	57.3±5.1
240 min	102±5.1	57.4±4.6
TIVA group A, subgroup 2		
Basal	155.4±25	76.7±6.1
2 min (after atropin and fentanest)	150±7.3	92±5.6
4 min	152±10.4	89.3
5 min (after intubation and propofol and remifentanyl pump start)	110.3±8,2	80.3±5.4
10 min (fentanyl pump start)	100±4.3	70.3±5.5
30 min	100.7±8.5	61±4.3
90 min	94.9±5.4	60.3±3
180 min	97.3±4.3	54±4.1
240 min	99.3±5.7	58±5.8
Group B (balanced gaseous anaesthesia)		
Basal	150±37.2	83.3±5.7
2 min (after atropin and fentanest)	150±34.6	93.6±7.5
4 min	145.2±35.1	89.5±4.2
5 min (after intubation and 2% sevofluorane and 0.1 mg fentanyl intravenously)	139.1±8.9	82.6±6.3
10 min	135.8±3.5	79.7±5.7
30 min	120.4±5.4	76.9±6.8
90 min	129.6±5.7	78.9±7.8
180 min	124.2±3.4	74.7±8.6
240 min	122±4.4	73.7±6.7

As shown by previous experience, these dosages do not permit the attainment of a sufficiently deep anaesthetic plane, such as to avoid curare booster doses. Therefore, total analgesic cover depended on fentanyl. Its infusion started about 10 min after the beginning of the operation, at a speed of 15 mL h^{-1} for the 1st h, subsequently reduced to 5 mL h^{-1}. The infusion was suspended about 40 min before the end of the operation. No differences in modus operandi were needed between the 2 age groups (Table 3). The same procedure was applied to the group of patients subjected to gaseous anaesthesia, except for the fact that the anaesthetic agent was 2.5±0.5% sevofluorane and that further 0.02 mg kg^{-1} cysatracurium boluses were administered every 20 min. Analgesia depended on 0.03 mg kg^{-1} fentanyl boluses every 30 min. In this way, the relevant clinical parameters

RESULTS AND DISCUSSION

As described in TIVA method, the initial and maintenance doses of remifentanyl and propofol in order to reach and maintain an optimal hypotensive level were different in the 2 subgroups. For balanced gaseous anaesthesia, instead, it was not necessary to divide the patients into groups; only the parameters concerning age and ASA risk were taken into account. A continuous PaO and HR monitoring is absolutely necessary, especially for TIVA, since the variability and rate of pharmacological response can rapidly lead to very marked hypotensive and bradycardizing pressure values, which are neither advisable, nor necessary. To avoid this, it is necessary to act in time both as regards the adjustment of the TIVA drug infusion speed and the percentage of vapour delivered in the group of patients subjected to gaseous anaesthesia. In extreme cases, it is advisable to suspend anaesthetic agent delivery for a few minutes, so that the arterial BP can rise again naturally and quickly and so resume drug administration at lower doses. It seems clear that both methods must induce an arterial BP reduction which satisfies surgical requirements. While, TIVA easily assures reduced bleeding and absence of contamination in the operating theatre, the latter condition is not possible with balanced gaseous anaesthesia. Another problem of this method is the impossibility of attaining an optimal hypotension depending on the doses of anaesthetic vapour, since a high gas concentration would determine an undesirable narcosis depth.

The first result shows that the haemodynamic response under TIVA is very variable and that the most correct way to proceed is still to start with standard doses, while being ready to vary them promptly according to PaO and HR values. This makes close control necessary and IBP monitoring essential. Of course, anaesthesia carried out with halogenated vapours, opioid and recurarization is easier to manage and haemodynamically safer, as the comparison between the average pressure values shows. The comparison between the other arranged substitute endpoints (Table 4).

In group B patients, anaesthetic gas delivery was reduced by half at about the last 15 min and suspended 5 min before the end of surgery. In the immediate postoperative period, 15% of the patients complained of painful symptoms. Shivering appeared in 25% of the patients, nausea and vomiting in 2% of them. In group A patients, propofol infusion was suspended about 15 min before the end of surgery, while remifentanyl infusion was continued until the last suture stitch. Fentanyl was suspended about 40 min before the end of surgery. Awakening and estubation occurred calmly. No nausea or vomiting were observed. Postoperative shivering appeared in 10% of the patients; as in the gaseous anaesthesia group, this was rapidly corrected by intravenously administering 15 mg nefopam. In the immediate postoperative period, the patients complained of none or few painful symptoms. In these cases, low dose analgesic therapy was carried out as in the gaseous anaesthesia group. Postoperative analgesic cover is suggested by almost all authors; however, we did not consider this necessary with both methods. Especially in TIVA, this practice was recommended by all the authors who use of remifentanyl. This disagreement can be explained by the use of fentanyl, which has a longer analgesic activity than remifentanyl and by the fact that pharmacological activities are enhanced. No intra- and postoperative complications for anaesthetic reasons were observed in all the groups. The occasional use of equipment for measuring BIS or Narcotrend indexes, which give a neurophysical monitoring derived from EEG processing and which are used for evaluating narcosis depth, confirm both the value of the 2 methods and the effectiveness of TIVA anaesthesia and encourage us to follow this line.

Irrespective of the type of surgery, TIVA, when carried out properly, by virtue of the characteristics of the drugs used, guarantees:

- A deep anaesthetic plan, such as to avoid curare booster doses, except for the cases in which muscular relaxation is required (e.g., during abdominal wall closing).
- A hypotensive state with reduced bleeding in the operating field.
- Absence of operating theatre contamination.

Table 4: The group of patients subjected to gaseous anaesthesia

	Gaseous anaesthesia	TIVA
Surgery duration	3.40 h±30 min	3.20 h±20 min
Awakening time (calculated from estubation with the response to simple commands)	10 min±11 min	7 min.±7 min
Re-canalization	18 h±4 h	10 h±2 h
Hospitalization time	17 d±4 d	15 d±3 d
Surgery duration	5.30 h±40 min	5.10 h±30 min
Awakening time (calculated from estubation with the response to simple commands)	10 min±11 min	7 min.±7 min
Re-canalization	26 h±4 h	10 h±2 h
Hospitalization time	22 d±4 d	20 d±3 d

To attain such results, a pharmacological combination of remifentanyl (opioid) and propofol (hypnotic) has been used.

In the past, the first method of administrating an anaesthetic substance was by injection and goes back to 1656, when Sir Christopher Wren, an architect at Oxford University, injected a dog with opium using a goose quill (Ogawa *et al*., 2006; Liu and Zeng, 2006; Hanss *et al*., 2006; Ozturk *et al*., 2006).

In 1665, Sigmund Elshoz administered opium intravenously.

The first monograph on this subject appeared in 1872 by Pierre Cyprien, who published the results obtained with the experiments carried out on dogs, to which he had injected chloral hydrate (hypnotic) intravenously. Such experiments, repeated on man, were immediately stopped for the high death rate.

The first steps towards modern anaesthesia go back to the second half of the XIX century, when the first inhalation anaesthetics appeared, first ether, then N_2O and chloroform (Rohm *et al*., 2006; Wormald *et al*., 2005; Bein *et al*., 2006; Scott and Perry, 2007).

These three pharmacological substances dominated for about one hundred years. Today, only nitrogen protoxide is still used and to tell the truth, it is the object of great uncertainty.

Another important step forward came towards the end of 1930, with the introduction of sodium thiopentone in clinical practice (Rohm *et al*., 2006; Ledowski *et al*., 2006; Turan *et al*., 2007; Nonaka *et al*., 2006; Modesti *et al*., 2006; Lo *et al*., 2006).

This molecule was tested during World War II, when it was used for surgical operations on seriously injured patients with haemorrhagic shock; the results were catastrophic, due to inexperience (Ledowski *et al*., 2006).

The ultimate turning point towards modern anaesthesia in its current meaning occurred in 1942, when Griffith and Johnnestone introduced curare.

The first attempts to get rid of gaseous anaesthesia go back to the '60s, with the introduction of neuroleptoanaesthesia. This uses the pharmacological combination of fentanyl (opioid) and droperidol (neuroleptic), but the high doses required often result in a state of deep respiratory depression, which prevents its use in a standard way.

Until some years ago, that is, before the availability of molecules with pharmacokinetic characteristics such as to permit a TIVA, the only way to proceed in carrying out a general anaesthesia was to use a combination of halogenated anaesthetic vapours, analgesics and curares; this method is still the most common (Turan *et al*., 2007; Nonaka *et al*., 2006; Modesti *et al*., 2006; Lo *et al*., 2006; Bappsc *et al*., 2006; Umar *et al*., 2006; Ogawa *et al*., 2006; Liu and Zeng, 2006; Hanss *et al*., 2006; Ozturk *et al*., 2006; Rohm *et al*., 2006; Wormald *et al*., 2005; Bein *et al*., 2006; Scott and Perry, 2007).

In fact, the halogenated anaesthetic vapours are quite easy to handle, they show great haemodynamic stability and act as resistance vessel dilators, causing a certain hypotensive state. However, these vapours have a more or less important toxic action on the liver and the kidneys; the effects are definitely less detectable with the products of the latest generation. Yet, from a personal statistic observation, it seems that in recent years, the number of people working in the operating theatre who show thyroid diseases, especially women, is rather high (Lo *et al*., 2006).

In consideration of these presumably unfavourable effects, for at least a couple of decades some anaesthetists have been trying to reduce the use of anaesthetic vapours as much as possible, up to their almost total elimination from the second half of the '90s, with the introduction of remifentanyl and propofol by pump (Liu and Zeng, 2006; Hanss *et al*., 2006; Ozturk *et al*., 2006; Rohm *et al*., 2006).

Remifentanyl is a very strong synthetic opioid of the new generation, which acts on μ-receptors. It induces a state of analgesia, sedation, bradycardia, hypotension, bradypnoea and may determine muscular stiffness in the ribcage. Since, some of these effects are dangerous, in our experience we prefer not to use remifentanyl for premedication; besides, its use for whatever purpose in non-intubated patients must be supported by close monitoring. This drug is characterized by a fast onset time and by an equally fast offset time, ascribable to metabolization by non-specific esterases present in blood and tissues. This property permits total analgesia without the risk of build-up and therefore of postoperative respiratory depression and delayed awakening (Umar *et al*., 2007; Dagtekin *et al*., 2007;

Vabish-chevich *et al*., 2006; Wallden *et al*., 2006; Turan *et al*., 2007; Nonaka *et al*., 2006; Modesti *et al*., 2006; Lo *et al*., 2006).

Propofol is a hypnotic with no analgesic power used for anaesthesia induction and maintenance and also to sedate ICU patients. Its administration causes transitory hypotension and bradycardia. It has both hepatic and extra-hepatic metabolic clearance and despite its long half-life, the regaining of consciousness is fast, thanks to the high volume of distribution. After administration, the hypotensive response to these 2 drugs is very variable; it mainly depends on the age, on the general conditions and on the individual response (Wormald *et al*., 2005).

So, it must be stressed that their use implies a good knowledge of the individual reactions and of the kinetic-dynamic interaction of the 2 drugs and that the responses obtained require very close and steady control and monitoring, with continuous adjustments of infusion speed (Hanss *et al*., 2006).

The data collected reveal an undeniable superiority of TIVA compared to gaseous anaesthesia with regard to patient comfort and to a remarkable reduction of surgical and hospitalization times. The key factor to fulfil these conditions, however, is a thorough knowledge of the technique and the possibility of having proper monitoring.

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