Revista Mexicana de Anestesiología

ORIGINAL ARTICLE
Vol. 31. No. 4 October-December 2008
pp 263-270

Conditions for endotracheal intubation and hemodynamic effects in Mexican population at different doses of remifentanyl by infusion

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Received for publication: 07-11-07
Accepted for publication: 21-01-08

SUMMARY

Objective: To demonstrate the optimal dose of remifentanyl between 5, 7 and 10 ng/mL during laryngoscopy in ASA I and ASA II patients. To asses the hemodynamic response that occurs during laryngoscopy and intubation when using a remifentanyl dose of 5 to 10 ng/mL. To determine the optimal conditions for endotracheal intubation with the administration of a remifentanyl dose of 5 to 10 ng/mL by the Helbo Hansen's scale. **Materials and methods:** 51 patients being under general anesthesia for elective ASA I, and ASA II surgeries, ranging between 18 and 65 years old, randomly divided into 3 groups were included in this study; Remifentanyl dosages of 5 ng/mL, 7 ng/mL and 10 ng/mL; the following measurements were performed in preoperative, at surgery admission, 1, 2 and 5 minutes from the intubation of the variables: blood pressure, heart rate, oxygen saturation and bispectral index. The patients were medicated with midazolam, induced with remifentanyl at the established doses according to the group they belonged to (1, 1.4 and 2 µg/kg), cisatracurio (150 µg/kg) and propofol (2, 1.5 and 1 mg/kg) respectively. **Results:** There was a significant difference ($p < 0.05$) in heart rate and blood pressure during the first minute at the laryngoscopy and in the group of remifentanyl at doses of 7 and 10 ng/mL. In addition to this, the conditions for the intubation, measured through the Helbo-Hansen's scale, from the remifentanyl Group at 10 ng/mL were more favorable than in the other groups. **Conclusion:** The study concludes that a remifentanyl dose of 10 ng/mL in the therapeutic window, combined with propofol at a dose of 1 mg/kg, provides excellent intubation conditions and increased hemodynamic stability during laryngoscopy and endotracheal intubation.

Key words: Laryngoscopy, tracheal intubation conditions, remifentanyl, fentanyl, hemodynamic response.

RESUMEN

Objetivo: *Demostrar la dosis óptima de remifentanyl entre 5, 7 y 10 ng/mL durante la laringoscopía en pacientes ASA I y ASA II. Valorar la respuesta hemodinámica que ocurre durante la laringoscopía e intubación cuando se utilizan dosis de remifentanyl de 5, 7 y 10 ng/mL. Determinar las condiciones óptimas de la intubación endotraqueal con administración de remifentanyl en dosis de 5, 7 y 10 ng/mL por medio de la escala de Helbo Hansen.* ***Material y métodos:*** *Se incluyeron 51 pacientes bajo anestesia general para cirugía electiva ASA I, II, entre 18 y 65 años, divididos de manera aleatoria en 3 grupos; Remifentanyl a 5 ng/mL, 7 ng/mL y 10 ng/mL; se realizaron mediciones en*

preoperatorio, ingreso a quirófano, 1, 2 y 5 minutos de la intubación de las variables: tensión arterial, frecuencia cardíaca, saturación de oxígeno e índice biespectral. Fueron medicados con midazolam, inducidos con remifentanyl a las dosis establecidas de acuerdo al grupo que pertenecían (1, 1.4 y 2 µg/kg), cisatracurio (150 µg/kg) y propofol (2, 1.5 y 1 mg/kg) respectivamente al grupo correspondiente. ***Resultados:*** *Se encontró diferencia significativa (p < 0.05) en la frecuencia cardíaca y la tensión arterial durante la laringoscopía y al primer minuto en el grupo de remifentanyl a 7 y 10 ng/mL; así mismo las condiciones de intubación medidas con la escala de Helbo-Hansen del grupo de remifentanyl a 10 ng/mL fueron más favorables que el resto de los grupos.* ***Conclusión:*** *El estudio concluye que el remifentanyl a dosis de 10 ng/mL en la ventana terapéutica, en combinación con propofol a 1 mg/kg, proporciona excelentes condiciones de intubación y una mayor estabilidad hemodinámica durante la laringoscopía e intubación endotraqueal.*

Palabras clave: *Laringoscopía, intubación, remifentanyl, fentanyl, respuesta hemodinámica.*

INTRODUCTION

The peri-intubation period is one of the moments of most stress during general anesthesia[4]. Tracheal intubation induces clinical neurovegetative responses which results in increased response and blood pressure. However, several pharmacological strategies have been proposed for the control of neurovegetative responses to intubation. Opioids, particularly fentanyl, remifentanyl, and sufentanyl alfentanyl, have been used for the control of neurovegetative responses. There is a linear relationship between opioid doses and decreased cardiovascular response[6]. The interaction of fentanyl with propofol has been demonstrated in several clinical studies; however, the pharmacodynamics of remifentanyl in combination with other intravenous agents is poorly described[9].

In our profession it is essential to gain access quickly and safely to the airway; to achieve this situation is vital to use drugs in order to abolish or limit the physiological responses to this maneuver of each patient.

Laryngoscopy and tracheal intubation may be accompanied by hypertension, tachycardia, increased intraocular and intracranial pressure, and may be associated with myocardial ischemia in susceptible individuals.

This response may be exaggerated in patients with or without treatment of essential hypertension; these patients have a higher incidence of cerebrovascular and coronary artery diseases.

It may be reduced or mitigated by using different drugs; in this study we will use opioids as mediators of these manifestations and assess whether the remifentanyl by infusion offers better benefits by the use of propofol for our patients when a general anaesthesia is going to be realized, and when the airway of patient must be secured via a catheter[12].

Currently both remifentanyl and propofol are used for analgesia during laryngoscopy in various procedures to ensure the airway. There is no consensus about what is the dose at which the synergy of drugs has lower hemodynamic changes during this procedure[14].

It is responsibility of our profession to keep the patient in optimal conditions during the anesthetic state, so it is necessary to use different drugs in order to provide analgesia, hypnosis, amnesia, adequate protection neurovegetative and an adequate neuromuscular block, which are components essential for a suitable anesthesia[8].

In 1988 Helbo-Hansen et al. determined a scale that assesses the ease of endotracheal intubation, which describes jaw relaxation, laryngoscopy, vocal cords, coughing, and movement of the patient. A score of 1-2 is considered as an acceptable intubation condition, while a score of 3-4 is considered an unacceptable intubation condition[2] (Table I).

Studies in adults have shown that the combination of propofol and remifentanyl provides acceptable conditions for endotracheal intubation and recommended 4 µg/kg dose of remifentanyl[3].

OBJECTIVE

This study compared different 1, 1.4 and 2 µg/kg doses of remifentanyl by infusion (plasma concentration of 5, 7, and 10 ng/mL) in combination with propofol, and also its hemodynamic response to laryngoscopy, as well as the endotracheal intubation conditions of different groups, with the aim of establishing the best dose to maintain a hemodynamic response stable to changes during this frequently used anesthetic procedure[5].

Table I.

	1	2	3	4
Maxillar relaxation	Complete	With tone	Tense	Rigid
Laryngoscopy	Easy	Good	Dificult	Impossible
Vocal cords	Open	With movement	Close in	Close
Cough	No	Scaty	Moderate	Severe
Movements of extremities	No	Scanties	Moderates	Severe

MATERIAL AND METHODS

Upon approval by the Ethics Committee of the North Central Hospital and Biosafety Committee, 51 patients with physical status ASA I and II, of both sexes between 18-65 years of age were included prior informed consent and preanesthetic assessment in the outpatient department of anesthesiology at the North Central Hospital "PEMEX".

Exclusion criteria were as follows: Patients with previous acute myocardial infarction or heart failure and have data on difficult airway, who usually consume sedatives or related drugs, and patients with a history of bronchial asthma or chronic obstructive pulmonary disease.

The patients were divided randomly into three groups: Remifentanyl by infusion at 1, 1.4, and 2 μg/kg doses (plasma concentration of 5, 7, and 10 ng/mL).

Upon entering the operating room, all patients were monitored in a non invasive manner for non-invasive blood pressure (NIBP), heart rate (HR), respiratory rate (RR), electrocardiogram (EKG), partial oxygen saturation (SpO_2), and BIS.

Premedication was done in the operating room with intravenous midazolam at a dose no higher than 0.05 μg/kg body weight for the purpose of anxiolysis.

In group 1, induction was initiated with a basal narcosis with remifentanyl by continuous infusion at a dose of 0.20 μg/kg/min to complete a dose of 1 μg/kg body weight for 3 minutes; in group 2, it was initiated with remifentanyl by continuous infusion at a dose of 0.28 μg/kg/min to complete a dose of 1.4 μg/kg body weight for 3 minutes; and In group 3, it was initiated with remifentanyl by continuous infusion at a dose of 0.32 μg/kg/min to complete a dose of 2 μg/kg body weight for 3 minutes. In all three groups cisatracurium was used at a dose of 0.6 mg/kg as neuromuscular blocker to facilitate orotracheal intubation and it was supplemented with propofol at a dose of 2 mg/kg in the first group, 1.5 mg/kg in the second group and 1 mg/kg in the third group for the purpose of hypnosis.

Direct laryngoscopy was performed using a No. 3 curved blade with a maximum of 2 attempts of intubation with Murphy endotracheal tube according to the sex. We evaluated the hemodynamic response to laryngoscopy and intubation conditions of each group through measurements of the systolic, diastolic and mean pressure and heart rate. The intubation conditions were assessed according to the scale established by Helbo-Hansen through jaw relaxation, ease of laryngoscopy, vocal cord movement, presence of cough, and patient movement. A score of 1-2 is considered as an acceptable intubation condition, while a score of 3-4 is considered as an unacceptable intubation condition.

The type of analysis conducted was as follows:

Measurement. Hemodynamic variables were determined with parametric scales by calculating measures of central tendency with standard deviation and average. Differences were calculated using analysis of variance on averages through Student's t-test. p-value less than or equal to 0.05 was considered significant.

Kolmogorov test for homogeneous groups or Shapiro Well test for non-homogeneous groups was used to know the normal distribution of variables. Calculation of measures of central tendency with 25th and 75th percentiles and median was used to measure the variable of "endotracheal intubation conditions". Differences were calculated using an analysis of variance with a classification of ranges such as the Kruskal-Wallis test.

RESULTS

A total of 51 patients were studied, they were divided into three groups, each comprising 17 patients and referred as group 1, 2, and 3, all were underwent a general anesthesia procedure. There were no differences in the demographic variables (Table II).

Association variables of groups such as obtained ASA, concomitant diseases such as diabetes mellitus, hypertension, smoking and body mass index were analyzed, no statistically significant differences for this population were found (Table III).

As for the airway variables, Mallampati, Patil Aldreti, Bellhouse Doré, sternum length were analyzed as predictors of difficult airway, as well as Cormack Lehane and

number of attempts at laryngoscopy were analyzed as determinants of successful intubation. No statistically significant differences were found among the groups in this population (Table IV).

Vital signs were measured including: Blood pressure, mean blood pressure, heart rate, oxygen saturation and Bispectral Index (BIS) in each group from preoperative period to 5 minutes after intubation.

There was a statistically significant difference in the results of blood pressure and heart rate for the three groups, which indicates adrenergic activity during laryngoscopy. In group 1 and 2 there was a statistical difference in the SBP, MBP and HR parameters during laryngoscopy and two minutes after intubation with a $p \leq 0.05$ and in group 3 there was a statistical difference in the SBP, MBP and HR parameters during laryngoscopy, and 2 minutes and 5 minutes after endotracheal intubation with a $p \leq 0.001$ (Table V and Figures 1 and 2).

A statistical difference was found in group 2 with a $p \leq 0.001$ under the endotracheal intubation conditions. However, group 3 had the best conditions to perform an endotracheal intubation assessed by this scale, because in group 2 the ease of intubation was only of 58% (Table VI and Figure 3).

Among the complications that arose during the study were hypotension, bradycardia and low BIS, noting that in group 3 there was hypotension for 23% of the population, but without statistical significance (Table VII).

Table II. Demographic date expressed in average and standard deviation for three groups; they did not find statistical significant differences for being homogeneous groups.

	Group 1	Group 2	Group 3
Age	54.4 ± 6.3	51 ± 10.1	50.7 ± 8.4
Weight	73.8 ± 10.7	72 ± 13	76 ± 14.4
Height	1.60 ± 7.8	64 ± 9.3	164 ± 11.04
Sex	♂ 17.6%	♂ 41%	♂ 35.5%
	♀ 82.4%	♀ 58%	♀ 64.7%

Table III. Asociation variables expressed in percentage for three groups; they did not find statistical significant differences for being homogeneous groups.

	Group 1	Group 2	Group 3
ASA I	5.9%	17.6%	17.6%
II	94.1%	82.4%	82.4%
Associate diseases			
DM	17.6%	17.6%	5.9%
HAS	35.3%	35.3%	29.4%
Mix	23.5%	23.5%	5.9%
Other	5.8%	5.8%	5.9%
None	17.6%	17.6%	52.9%
Smoking			
Sí	5.9%	17.6%	29.4%
No	94.1%	82.4%	70.6%
BMI			
24	7.6%	23.5%	17.6%
25-27	43.2%	41.2%	41.2%
28 30	43.2%	29.4%	23.5%
> 30	0%	5.9%	17.6%

DISCUSSION

Drugs are used to reduce the hemodynamic response to a painful stimulus such as endotracheal intubation and surgical incision during anesthetic induction.

It has now been shown that anesthesia-based analgesia is obtained with the use of narcotics, which do not significantly reduce the adrenergic discharge in the moments of surgical stress, which it is shown as an increase in blood pressure and heart rate.

Table IV. Information of the airway expressed in percentage, average and standar deviation of LEM's variable for three groups; they did not find statistical significant differences for being homogeneous groups.

	Group 1	Group 2	Group 3
Mallampati			
1	52.9%	47.1%	41.2%
2	47.1%	52.9%	52.9%
3			5.9%
Patil Aldreti			
1	94.1%	100%	94.1%
2	5.9%		5.9%
Bellhouse Doré			
1	94.1%	100%	88.2%
2	5.9%		11.8%
Cormack Lehane			
1	88.2%	100%	76.5%
2	11.8%		23.5%
LEM	14.1 ± 1.05	13 ± .77	14 ± .70
Attempts			
1	82.4%	88.2%	88.2%
2	17.6%	11.8%	11.8%

Table V: Group 1. It shows values of vital signs expressed in average ans standard deviation in which there demonstrates a statistical significant difference in comparison with other two groups in BP, MBP and HR in the laryngoscopy and to two minutes with one $p \leq 0.05$

	BP	MBP	HR	SPO_2	BIS
Preoperatory	129/78 ± 7.7	95 ± 10.7	73 ± 5.7	93 ± 2.3	96 ± 1.8
Admission	135/80 ± 8.15	99 ± 6.3	72.2 ± 6-6	93 ± 2.5	96 ± 1.0
Laryngoscopy	137/83 ± 16.7	102 ± 14.7	76.4 ± 13.5	99 ± 0.24	47 ± 15
2 min	126/72 ± 14.2	90.4 ± 10.3	66 ± 6.8	99 ± 0.60	45 ± 6.5
5 min	112/66 ± 12.5	82 ± 10.3	63 ± 7.7	99 ± 0.66	42 ± 6.0

Table V: Group 2. It shows values of vital signs expressed in average and standard deviation in which there demonstrates a statistical significant difference in comparison with other two groups in BP, MBP and HR during the laryngoscopy, to two minutes and 5 minutes witn one $p \leq 0.05$

	BP	MBP	HR	SPO_2	BIS
Preoperatory	125/75 ± 9.0	92 ± 9.5	74 ± 11.2	94 ± 4.4	97 ± 1.4
Admission	124/79 ± 8.5	93 ± 9.6	70 ± 10.4	94 ± 4.7	97 ± 1.5
Laryngoscopy	111/67 ± 9.1	83 ± 11.6	62 ± 8.8	98 ± 0.95	47 ± 5.8
2 min	105/63 ± 6.3	76 ± 7.1	58 ± 5.1	98 ± 1.1	44 ± 6.2
5 min	103/61 ± 4.6	75 ± 5.0	59 ± 4.8	99 ± 1.1	44 ± 5.2

Table V: Group 3. It shows values of vital signs expressed in average and standard deviation in which there demonstrates a statistical significant difference in comparison with other two groups in BP, MBP and HR during laryngoscopy, to two minutes and 5 minutes witn one $p \leq 0.001$.

	BP	MBP	HR	SPO_2	BIS
Preoperatory	123/78 ± 8.0	93 ± 9.01	71 ± 6.7	93 ± 2.6	97 ± 1.4
Admission	125/78 ± 6.5	93 ± 7.3	70 ± 6.8	94 ± 2.7	97 ± 1.1
Laryngoscopy	99/61 ± 8.4	73 ± 7.7	58 ± 8.0	98 ± 0.65	46 ± 6.8
2 min	98/61 ± 6.0	74 ± 7.0	57 ± 5.5	99 ± 0.43	44 ± 5.6
5 min	96/58 ± 5.1	71 ± 4.8	59 ± 8.6	99 ± 0.65	45 ± 6.5

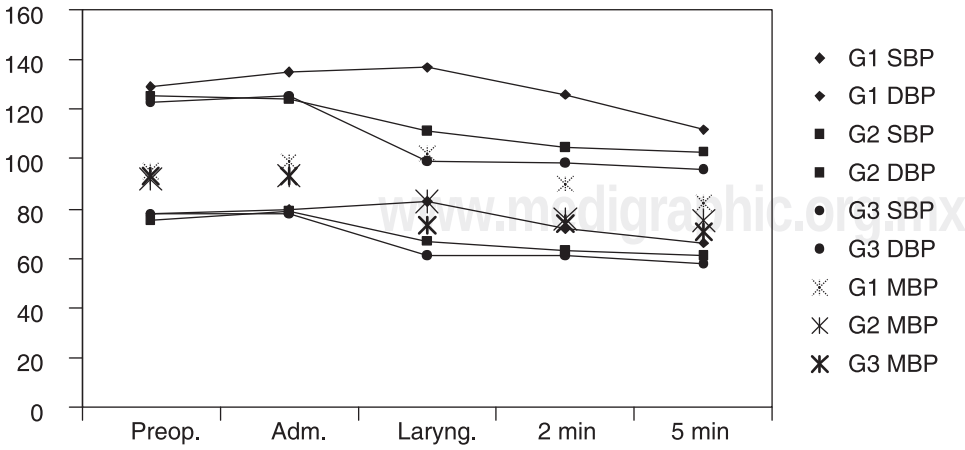

Figure 1. It shows values of blood pressure expressed in average and standard deviation in which there is demonstrated a statistical significant difference in comparison between the three groups in the BP, MBP and HR during the laryngoscopy, to two minutes and to 5 minutes with one $p \leq 0.05$ for the groups 1 and 2 and one $p \leq 0.001$ for the group 3.

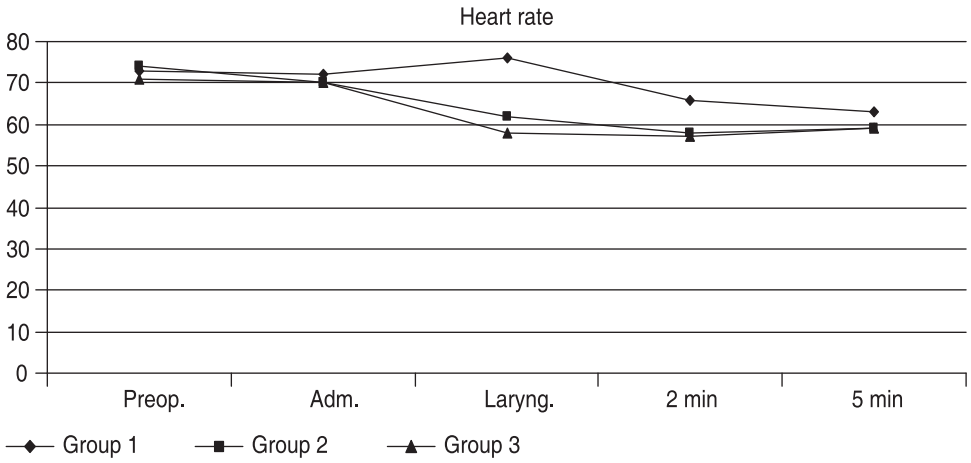

Figura 2. It shows values of heart rate expressed in average and standard deviation in which there is demonstrated a statistical significant difference in comparison between the hree groups in HR during laryngoscopy, to 2 minutes and to 5 minutes with for the 1 and 2, and $p \leq 0.001$ for the group 3.

Table VI. It shows values of the scale of intubation expressed in average, in which there demonstrates a statistical significant difference for the group 2 with $p \leq 0.001$

	Group 1	Group 2	Group 3
Maxilar relaxation			
Complete	88%	100%	100%
With tone	11%		
Laryngoscopy			
Easy	5.9%	64%	100%
Good	94%	35.3%	
Vocal chords			
Open	5.9%	88.2%	100%
In movement	94%	11.8%	
Cough			
No	83%	82.4%	100%
Scanty	17%	17.6%	
Movements			
Without	41.2%	82.4%	100%
Scanty	47.1%	11.8%	
Moderates	11.8%	5.9%	
Assessment scale			
Easy		58.8%	100%
Acceptable	100%	41.2%	

With the entry of new drugs such as remifentanyl not only a satisfactory analgesia is ensured throughout the anesthetic procedure, but also a fast and secure arousal for the patient.

Thanks to the combination of inducing drugs such as propofol, also important synergism has been demonstrated with reduced consumption of drugs and accordingly reduced adverse effects with a pharmacological safety.

Regarding our study groups, no significant differences were found in regard to demographic variables such as age, sex, weight and height, thus avoiding that adrenergic discharge had negative or positive impact on laryngoscopy and intubation conditions of any the patients studied in this population.

As regards the association variables, differences among our study groups were not significant and literature do not report that some variation in these variables influences directly on the hemodynamic response to laryngoscopy and intubation conditions.

In 2000 Klemola conducted in Finland a study in adult population and defined a 4 μg/kg dose of remifentanyl administered by bolus no less than 90 seconds, followed by 2.5 mg propofol, obtaining very satisfactory results for the intubation conditions and without altered hemodynamic response during laryngoscopy, thus demonstrating that the remifentanyl is 20 to 30 times more potent than the alfentanyl. In his study, on the other hand, he administered different 3 and 4 μg doses per group of 20 patients, each dose in combination with propofol, then he compared it with alfentanyl at 30 μg dose[3].

It has now been observed that drug administration can be performed in various forms, the drug can be administrated by bolus or perfusion. As there is presence of peaks and valleys when administration is performed by bolus as opposed to a linear and sustained plasma concentration when it is administered by infusion.

Troy used the TCI system to administer propofol plus remifentanyl, but without neuromuscular blocker, in 60 patients at concentrations of 11, 15, and 19 ng/mL (2, 3, and 4 μg/kg) by reducing the dose after 1 minute of the onset of the drug at 6, 8 and 10 ng/mL doses. His results show that with higher plasma concentrations of remifentanyl by infusion, best intubation conditions are obtained without a high hemodynamic response[4].

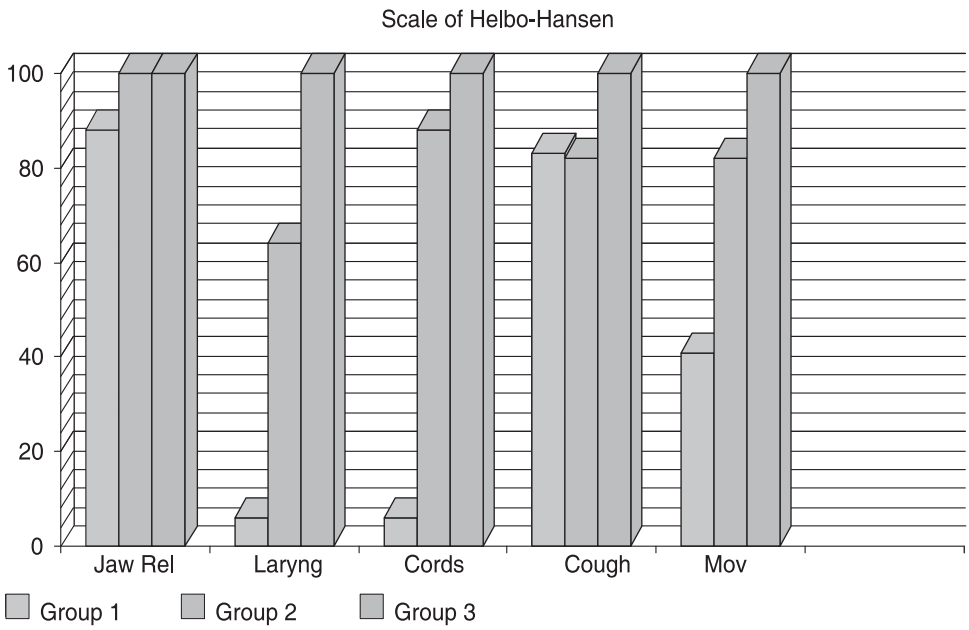

Figura 3. It shows values on a large scale of Helbo-Hansen for the intubation expressed in average, in which there demonstrates a statistical significant difference for the group 2 with $p \leq 0.001$.

Complete jaw relaxation = 100%. Easy laringoscopy = 100%. Open vocal cords = 100%. Without cough = 100%. Without movements = 1.

In our study there are obvious significant differences among the groups with respect to the intubation conditions, while in group 2 a statistical significance was observed, in group 3 the best conditions and the ease of intubation were observed in 100% of patients as contrasted with the other groups.

Our limitations are in the consideration of measurement of cardiac output in order to complete hemodynamic data and correlate them with measurements of catecholamines in the blood

Another important point to be considered is the standardized training of anesthesiology team on pharmacology of remifentanyl and intravenous perfusion systems given by the service in order to improve management in these patients.

Table VII. It shows the complications with managing of different doses of remifentanyl, expressed in percentage, without statistically significant difference for three groups

Complications	%		
Hipotension	5.9	11.8	23.4
Bradicardy	5.9	0.0	5.9
Law level BIS	11.8	0.0	5.9
None	76.5	88.2	64.7

CONCLUSIONS

Gender, age, weight, height and associated disease, as well as proper control thereof, do not influence the hemodynamic response and intubation conditions in these patient groups.

This population included patients with favorable anatomy of airway, this situation would indicate us that the intubation conditions of the three groups should be the same. However, the results of this study suggest that remifentanyl at 10 ng/mL dose in the therapeutic window, in combination with 1 mg/kg propofol, provides excellent intubation conditions.

Group 1 at 5 ng/mL plasma concentrations of remifentanyl in the therapeutic window, being the recommended dose in the literature, showed significant differences in regard to hemodynamic response in patients undergoing laryngoscopy, and it was the group where less favorable intubation conditions were observed.

The combination of these drugs, administrated by infusion at plasma concentrations of 10 ng/mL remifentanyl, prevents a hemodynamic response to laryngoscopy with few cardiovascular depression effects.

Complications observed in group 3 were not statistically significant, so that the administration at this dose of remifentanyl by infusion is safe.

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