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"TIMING OF INTUBATION IN A MODIFIED RAPID SEQUENCE INDUCTION WITH REMIFENTANIL"

Mémoire présenté en vue du diplôme d'études spécialisées
en anesthésie-réanimation

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Abstract

Neuromuscular blocking drugs, particularly succinylcholine, may cause serious side effects but remain in clinical use to facilitate tracheal intubation due to a lack of suitable alternatives. [Perry et al.,2008]

A combination of propofol and remifentanil has been demonstrated to reliably provide good to excellent intubating conditions. [Erhan, E. et al., 2003. Grant, S. et al., 1998. Klemola, U.M et al., 2000. McNeil, I.A.et al., 2000]

Remifentanil is a potent opioid with a short half life due to it's metabolism by non specific esterase. At high dosage it suppresses motor as well as hemodynamic response to tracheal intubation. [O'Hare et al., 1999] It has been used successfully at doses of 4 to 5 μg/kg to replace muscle relaxant for tracheal intubation. [Bouvet, L. et al., 2009. Alexander, R. et al., 1999.]

We hypothesize that excellent intubation conditions could be obtained in 60 seconds using a rapid sequence induction, after induction with a bolus dose of 4μg/kg of remifentanil in conjunction with propofol 2.5 mg/kg.

Sixteen ASA class 1 and 2 non-obese, elective surgical patients, aged between 18 and 65 yr who required tracheal intubation for their surgery where studied..

Intubation was attempted sixty seconds after injection of the induction agents.

The quality of tracheal intubation was assessed using the qualitative scoring system proposed by the consensus conference on good clinical research practice on Pharmacodynamic Studies of Neuromuscular Blocking Agents. [Viby-Mogensen, J. et al., 1996]. Hemodynamic variables where recorded each minute for 5 minutes after induction.

Of the 16 patients included, intubating conditions were rated as excellent in eleven patients, good in three patients and poor in two patients. Mean time to intubation was 72.5 seconds.

No treatment was needed for hypotension or bradycardia.

No adverse events were noted.

In healthy premedicated patients with favorable airway anatomy intubation can be attempted with good or excellent conditions 60 seconds after the administration of a bolus of remifentanil 4μg/kg and propofol 2.5 mg/kg.

Introduction

Rapid sequence induction (RSI) for tracheal intubation is performed when the airway has a potential to be compromised by aspiration of gastric content. Succinycholine is still the muscle relaxant of choice for RSI although high dose rocuronium can be used when succinylcholine is contraindicated [Perry et al].
A combination of propofol 2 to 2.5mg/kg and remifentanil 4µg/kg has been demonstrated to reliably provide good to excellent intubating conditions according to the criteria adopted from Viby-Mogensen et al.(Table 1). In addition remifentanil effectively blunts the cardiovascular response to tracheal intubation which is often marked during RSI. [O'Hare et al. 1999] The short context specific half-life of remifentanil and its possible reversal agent naloxone could potentially make it an ideal candidate to replace succinylcholine for RSI. These induction agents have been studied given as infusions over varying periods for induction of anesthesia but not as bolus doses.
We hypothesize that good to excellent intubating conditions could be obtained 60 seconds after a bolus dose of 4µg/kg of remifentanil in conjunction with propofol 2.5 mg/kg.

Methods

After obtaining approval from the Ethics Committee of the Erasme Hospital and informed written consent from patients, we studied 16 ASA I–II patients, aged 18–60 yr presenting for elective surgery requiring endotracheal intubation.
Exclusion criteria included ASA class higher than 2, history of drug or alcohol abuse, cardiovascular disease, BMI 30 or more, anticipation of a difficult airway using morphological variables or a history of difficult intubation.
Alprazolam 0,5mg was given orally approximately one hour before induction of anesthesia. In the operating room standard ASA monitoring were applied, intravenous access was established in a vein of the hand or forearm. Patients were then instructed to take five breaths at maximal lung capacity through a face mask with an oxygen flow delivery of 12L/min.

A bolus of remifentanil at the dose of 4µg/kg was given followed immediately by propofol 2.5mg/kg. An independent operator started the time clock at the beginning of induction. Intubation with an endotracheal tube 7 or 7.5mm internal diameter was attempted 60 seconds after the administration of the study drugs by the same physician using a Macintosh 3 laryngoscope blade.
The time clock was stopped after inflation of the tracheal tube's cuff.
The quality of tracheal intubation was assessed using the qualitative scoring system proposed by the consensus conference on good clinical research practice on Pharmacodynamic Studies of Neuromuscular Blocking Agents. [Viby-Mogensen et al., 1996].
The intubating anesthesiologist assessed jaw relaxation, resistance to laryngoscopy, vocal cord position and movement, reaction to tube insertion (cough or movement). Each criterion was graded as excellent, good, or poor (Table 1). Further, a composite intubation score was defined as “EXCELLENT” if all criteria were graded excellent, “GOOD” if any criteria were good and “POOR if any criteria were graded as “POOR”.
Hemodynamic variables were recorded each minute for 5 minutes after induction.
Mask ventilation was not attempted.
If quality of glottic exposure or vocal cord opening was judged insufficient a standard dose of rocuronium 0.5mg/kg could be given.

Results

There was an imbalance in patient gender: 13 females for 3 males. Intubating conditions were rated as excellent in 11 patients good in 3 patients and poor in 2 patients. Of note intubation was attempted too early in the patient with poor intubating condition resulting in sustained cough: time to intubation in this case was 64 seconds. Excluding this patient good or excellent conditions were obtained in 93% of patients.
Mean time to intubation was 72.5 seconds ±4.65s. Mean arterial pressure (MAP) reduction was 32% ±13% heart rate (HR) reduction was 28% ± 13%. Hemodynamic response to laryngoscopy and intubation was completely blocked. No patient experienced arterial desaturation. No treatment was required for protracted hypotension or bradycardia.

No patient required rocuronium to facilitate intubation.
No other adverse events were noted.

Discussion

Our data demonstrates that tracheal intubation is possible in premedicated adult patients, with favorable airway anatomy, 60 seconds after an i.v. bolus induction with propofol 2.5mg/kg and remifentanil 4µg/kg with good to excellent conditions. This is similar to results obtained from a traditional RSI with succinylcholine 1mg/kg. [Naguib et al., 2003]. In addition this regimen abolished the stress response associated with direct laryngoscopy. Previous studies with different drug delivery times have shown similar results. [Bouvet et al. 2009, Hanna et al. 2010]

This induction regimen resulted in a reduction in MAP and HR values of 32% and 28% respectively consistent with previous reports. The decreases in MAP and HR were well tolerated in the healthy patients enrolled in the study.

In fact, in ASA1 and 2 patients, it has been reported that administration of increasing amounts of remifentanil from 2 to 30µg/kg did not increase the fall in arterial pressure and HR in comparison with lower dosages, while it blunted the potentially noxious circulatory response to laryngoscopy. [Sebel et al., 1995]

This technique cannot however be recommended for hypovolemic or debilitated patients, the elderly or those with clinically significant cardiovascular decease.

An important goal in a RSI is to minimize the duration of apnea so as to avoid hypoxic brain injury in the case that ventilation and intubation prove to be difficult. Stevens et Wheatley recorded a duration of apnea of 4 minutes on average in the group treated with remifentanil 4µg/kg and propofol 2mg/kg. On the other hand, McNeil et al. with a similar induction regimen recorded a mean apnea time of 12.8min double that of the succinylcholine 1mg/kg group. Finally Hanna et al. showed mean apnea time was significantly prolonged in patients receiving remifentanil 8.0 ± 4.9 min versus 4.0 ± 3.3 min ($P < 0.005$) for the succinylcholine 1.5mg/kg group.

The theoretical advantage of using remifentanil is the possibility of antagonizing its effect with the µ receptor antagonist naloxone, which could shorten apnea time in case a rapid reversal is needed. [Amin et al., 1995].

Finding an alternative to the use of succinylcholine has several advantages as it is associated with mild to life threatening side effects (myalgias, increase in intraocular pressure, masseter spasm, malignant hyperthermia, anaphylactic shock, hyperkalemia and cardiac rhythm disturbances).

The avoidance of muscle relaxant in cases which do not require paralysis offers the advantage of avoiding residual curarisation as well as reversal agent's side effects. However tracheal intubation without neuromuscular block is not without hazard. If laryngoscopy and intubation are attempted under inadequate conditions (e.g., poor jaw relaxation, closed vocal cords) trauma to the airway can result [Mencke et al., 2003]. In contrast when intubation is attempted under good or excellent conditions no difference in postoperative hoarseness or injury to the vocal cords can be made between groups receiving muscle relaxant or placebo [Bouvet et al., 2008]. In our study good or poor conditions resulted mainly from post intubation reaction (coughing), not from suboptimal glottic exposure. Therefore we did not expect significant injury to take place.

A significant amount of patients experienced a slight cough in the first instants following induction. We attribute this to initial vocal cord closure produced by high dose opioid induction as demonstrated by Bennett 1997 and Abrams et al. 1996. Induction agents such as propofol and thiopentone have also been shown to produce vocal cord closure. [Barker et al. 1992]

The deficiency of this study is the imbalance in male to female ratio which could potentially alter the results for male patients. However, pharmacological studies demonstrated no influence of gender on any pharmacokinetic or pharmacodynamic parameter. [Minto et al., 1997] This was confirmed by Hanna et al. 2010, where male patients outnumbered females 3 to 1 without a difference in outcome.

This induction regimen proved to be acceptable in premedicated patients undergoing planned elective surgery, and could probably be unsuitable for unpremeditated, anxious patients as seen prior to emergency surgery.

In healthy premedicated patients with favorable airway anatomy intubation can be attempted 60 seconds after the administration of a bolus of remifentanil 4μg/kg and propofol 2.5 mg/kg with good or excellent conditions. This combination totally prevented the cardiovascular

intubation response but reduced MAP by 32% and HR by 28%. The technique may be appropriate when rapid return of spontaneous ventilation is aimed at, or if neuromuscular blockade is undesirable or not required for the planned surgery. Further studies should directly compare this technique to a classical RSI with succinylcholine.

Table 1 Scoring conditions for tracheal intubation.
Intubation conditions: excellent, all responses are excellent;
good, all responses are excellent or good; poor, the presence of one or more poor response.
Excellent and good intubation conditions are taken to be clinically acceptable intubation conditions.

	Intubation conditions		
	Clinically acceptable		Clinically not acceptable
Variable	Excellent	Good	Poor
Jaw relaxation	Relaxed	Not fully	Poor
Vocal cords position	Abducted	Intermediate	Closed
Vocal cords movement	None	Moving	Closing
Reaction to tube insertion or cuff inflation			
Mouvement of limbs	None	Slight	Vigourous
Coughing	None	Diaphragm	Sustained

References

1. Abrams JT, Horrow JC, Bennett JA, Van Riper DF, Storella RJ. Upper airway closure: a primary source of difficult ventilation with sufentanil induction of anesthesia. *Anesth. Analg*. 1996;83(3):629-632.

2. Alexander R, Olufolabi AJ, Booth J, El-Moalem HE, Glass PS. Dosing study of remifentanil and propofol for tracheal intubation without the use of muscle relaxants. *Anaesthesia*. 1999;54(11):1037-1040.

3. Amin HM, Sopchak AM, Esposito BF, et al. Naloxone-induced and spontaneous reversal of depressed ventilatory responses to hypoxia during and after continuous infusion of remifentanil or alfentanil. *J. Pharmacol. Exp. Ther*. 1995;274(1):34-39.

4. Barker P, Langton JA, Wilson IG, Smith G. Movements of the vocal cords on induction of anaesthesia with thiopentone or propofol. *Br J Anaesth*. 1992;69(1):23-25.

5. Bennett JA, Abrams JT, Van Riper DF, Horrow JC. Difficult or impossible ventilation after sufentanil-induced anesthesia is caused primarily by vocal cord closure. *Anesthesiology*. 1997;87(5):1070-1074.

6. Bouvet L, Stoian A, Rimmelé T, et al. Optimal remifentanil dosage for providing excellent intubating conditions when co-administered with a single standard dose of propofol. *Anaesthesia*. 2009;64(7):719-726.

7. Bouvet L, Stoian A, Jacquot-Laperrière S, et al. Laryngeal injuries and intubating conditions with or without muscular relaxation: an equivalence study. *Can J Anaesth*. 2008;55(10):674-684.

8. Erhan E, Ugur G, Alper I, Gunusen I, Ozyar B. Tracheal intubation without muscle relaxants: remifentanil or alfentanil in combination with propofol. *Eur J Anaesthesiol*. 2003;20(1):37-43.

9. Grant S, Noble S, Woods A, Murdoch J, Davidson A. Assessment of intubating conditions in adults after induction with propofol and varying doses of remifentanil. *Br J Anaesth*. 1998;81(4):540-543.

10. Hanna SF, Ahmad F, Pappas ALS, et al. The effect of propofol/remifentanil rapid-induction technique without muscle relaxants on intraocular pressure. *J Clin Anesth*. 2010;22(6):437-442.

11. Klemola UM, Mennander S, Saarnivaara L. Tracheal intubation without the use of muscle relaxants: remifentanil or alfentanil in combination with propofol. *Acta Anaesthesiol Scand*. 2000;44(4):465-469.
12. McNeil IA, Culbert B, Russell I. Comparison of intubating conditions following propofol and succinylcholine with propofol and remifentanil 2 micrograms kg-1 or 4 micrograms kg-1. *Br J Anaesth*. 2000;85(4):623-625.
13. Mencke T, Echternach M, Kleinschmidt S, et al. Laryngeal morbidity and quality of tracheal intubation: a randomized controlled trial. *Anesthesiology*. 2003;98(5):1049-1056.
14. Minto CF, Schnider TW, Egan TD, et al. Influence of age and gender on the pharmacokinetics and pharmacodynamics of remifentanil. I. Model development. *Anesthesiology*. 1997;86(1):10-23.
15. Naguib M, Samarkandi A, Riad W, Alharby SW. Optimal dose of succinylcholine revisited. *Anesthesiology*. 2003;99(5):1045-1049.
16. O'Hare R, McAtamney D, Mirakhur RK, Hughes D, Carabine U. Bolus dose remifentanil for control of haemodynamic response to tracheal intubation during rapid sequence induction of anaesthesia. *Br J Anaesth*. 1999;82(2):283-285.
17. Perry JJ, Lee JS, Sillberg VAH, Wells GA. Rocuronium versus succinylcholine for rapid sequence induction intubation. *Cochrane Database Syst Rev*. 2008;(2):CD002788.
18. Sebel PS, Hoke JF, Westmoreland C, et al. Histamine concentrations and hemodynamic responses after remifentanil. *Anesth. Analg*. 1995;80(5):990-993.
19. Sluga M, Ummenhofer W, Studer W, Siegemund M, Marsch SC. Rocuronium versus succinylcholine for rapid sequence induction of anesthesia and endotracheal intubation: a prospective, randomized trial in emergent cases. *Anesth. Analg*. 2005;101(5):1356-1361.
20. Stevens JB, Wheatley L. Tracheal intubation in ambulatory surgery patients: using remifentanil and propofol without muscle relaxants. *Anesth. Analg*. 1998;86(1):45-49.
21. Viby-Mogensen J, Engbaek J, Eriksson LI, et al. Good clinical research practice (GCRP) in pharmacodynamic studies of neuromuscular blocking agents. *Acta Anaesthesiol Scand*. 1996;40(1):59-74.