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ORIGINAL ARTICLE

A Comparative Study of Different Induction Techniques (Propofol-Placebo, Propofol-Ephedrine and Propofol-Placebo-Crystalloid) on Intubating Conditions after Rocuronium Administration

Muhd Helmi Azmi[1], Karis Misiran[1]

[1] *Department of Anaesthesiology and Intensive Care, Faculty of Medicine, Universiti Kebangsaan Malaysia, Kuala Lumpur.*

ABSTRAK

Ini adalah kajian terkawal rawak rabun berganda prospektif, untuk membandingkan keadaan intubasi pada 60 saat dengan rocuronium sebanyak 0.6 mg/kg menggunakan tiga teknik induksi: propofol-placebo(PP), propofol-ephedrine(PE) dan propofol-placebo crystalloid(PC). Sembilan puluh pesakit telah dipilih, dan menerima secara rawak salah satu daripada teknik di atas. Induksi dilakukan dengan memberikan fentanyl 2 µg/kg, diikuti dengan sama ada propofol 2.5 mg/kg dan normal saline plasebo (kumpulan PP dan PC) atau propofol 2.5 mg/kg dan ephedrine 70 µg/kg (kumpulan PE) dalam masa 30 saat. Selepas itu rocuronium 0.6 mg/kg diberikan dan intubasi trakea dilakukan selepas 60 saat. Keadaan intubasi boleh diterima secara klinikal dalam semua pesakit kecuali empat pesakit dari kumpulan propofol-placebo. Kadar intubasi yang terbaik adalah paling tinggi dalam kumpulan PE (94%) diikuti oleh kumpulan PC (81%) dan terendah pada kumpulan PP (50%)**.** Kesimpulannya, induksi dengan menggunakan propofol-ephedrine dan propofol-placebo-crystalloid memberikan keadaan intubasi yang lebih baik daripada propofol-placebo apabila rocuronium 0.6 mg/kg digunakan untuk intubasi pada 60 saat.

Kata kunci: rocuronium, ephedrine, propofol, keadaan intubasi.

ABSTRACT

This was a prospective randomized double blind controlled study to compare intubating conditions at 60 seconds with rocuronium 0.6 mg/kg by using three different induction techniques: propofol-placebo (PP), propofol-ephedrine (PE) and propofol-placebo-crystalloid (PC). Ninety patients were included and randomly allocated to receive one of the three combinations. The patients were induced using fentanyl 2 µg/kg, followed by propofol 2.5 mg/kg with normal saline as placebo (Group PP and Group PC) or ephedrine 70 µg/kg (Group PE) given over 30 seconds. Subsequently, rocuronium 0.6 mg/kg was given over five seconds and endotracheal intubations were performed 60 seconds later. Intubating conditions were clinically acceptable in all patients except in four patients in PP group, who had poor intubating conditions. The proportion of excellent intubating conditions was significantly highest in Group PE (94%) followed by Group PC (81%) and lowest in Group PP (50%). In conclusion, induction with propofol-ephedrine and propofol-

Address for correspondence and reprint requests: Muhd Helmi Azmi, Department of Anaesthesiology and Intensive Care, Faculty of Medicine, Universiti Kebangsaan Malaysia, Jalan Yaacob Latif, Bandar Tun Razak, Cheras, 56000 Kuala Lumpur.Email:mdhelmi2001@yahoo.co.uk

placebo-crystalloid combinations provided significantly better intubating conditions than propofol alone, when rocuronium 0.6 mg/kg was used for intubation at 60 seconds.

Key Words: rocuronium, ephedrine, propofol, intubating conditions

INTRODUCTION

Rocuronium bromide is a non-depolarizing neuromuscular blocking agent that may be used during 'rapid sequence induction' (RSI) should suxamethonium be contra-indicated. However, its dose-dependent onset and duration of action occasionally limits its use. It has been reported that rocuronium is only comparable to suxa-methonium during RSI in 0.9-1.2 mg/kg (3-4x ED95) dosage, but its duration of action may be up to fifty minutes as opposed to thirty minutes when used at 0.6 mg/kg (Cooper et al 1992).

The long duration of action of rocuronium at 0.9 mg/kg is an obvious disadvantage for short surgical procedures, besides adding to the overall anaesthetic costs. However, if rocuronium at the dosage of 0.6 mg/kg was used, 20-25% of patients had moving vocal cords on direct laryngo-scopy and there was some diaphragmatic response to intubation (Sparr et al 1996). This may be due to a slower onset of rocuronium at the laryngeal muscles and the diaphragm than at other muscles.

The speed of onset of neuromuscular blockade depends in part on physiological factors such as cardiac output, circulation time and muscle perfusion. Studies using induction agents such as etomidate (Fuchs-Buder et al 1998) and ketamine (Hans et al 1999) which maintain cardiac output and blood pressure, have been shown to accelerate the onset of block and to improve intubating conditions when used in association with rocuronium.

A study by Tan et al (2002) showed that when ephedrine 15 mg was added to propofol during intubation, the proportion of patients with excellent intubating conditions increased. However, this technique was associated with significant increase in mean arterial pressure and heart rate after induction. The improvement in excellent intubating conditions observed in this study was possibly due to improvement in cardiac output associated with the use of ephedrine. However, the effect of adding ephedrine at a lower dose of 70 µg/kg on intubating conditions is not known.

The use of fluid loading to treat hypo-tension during anaesthesia has been well established. Fluid preloading does not prevent hypotension associated with propofol, but it has been proposed to affect the cardiovascular response to propofol induction. Turner et al (1998) in their study have proposed that fluid preloading produces an increase in myocardial preload, leading to an increase in stroke volume and therefore, maintaining cardiac output at a lower heart rate without increasing blood pressure. Apart from adding ephedrine to propofol during induction, the crystalloid preloading such as normal saline prior to induction can possibly be used to maintain or improve cardiac output and hence, may influence the intubating conditions during induction with rocuronium.

In order to investigate the effect of ephedrine and crystalloid on intubating conditions when rocuronium was used, this study was carried out. The objective of this study was to compare three different induction techniques which were propofol-placebo, propofol-ephedrine and propofol-crystalloid combinations on intubating conditions at 60 seconds using rocuronium 0.6 mg/kg.

MATERIALS AND METHODS

This study was approved by the hospital

ethics committee. Ninety patients with American Society of Anaesthesiologists (ASA) phy-sical status I or II, aged between 20-55 years and scheduled for elective surgery under general anaesthesia were included in this study. Subjects were excluded if they had a history of allergy to the study medication, hypertension, were on diuretics or vasoactive medication, were at increased risk of pulmonary aspiration and were on drugs known to interact with the neuromuscular junction. They were also excluded if we anticipated airway difficulties and their body mass index (BMI) were more than 30 kg/m^2.

Assignment to each group was concealed using sealed envelopes. On entering the study, patients were allocated randomly into one of three groups.

GROUP	INDUCTION TECHNIQUE
Propofol-placebo (PP)	Propofol (2.5mg/kg) and 1 ml of normal saline without ephedrine (placebo).
Propofol-ephedrine (PE)	Propofol (2.5mg/kg) and 1 ml normal saline with ephedrine (70-µg/kg).
Propofol-placebo-crystalloid (PC)	Ringer's lactate (12 ml/ kg) over the 10-15 min, propofol (2.5mg/kg) and 1 ml of normal saline without ephedrine (placebo).

On arrival in the induction room, an 18-gauge cannula was inserted into a peripheral vein at the dorsum of the hand by the first anaesthetist who was not involved in assessing the intubating conditions score and charting the changes in heart rate and mean arterial pressure. Without the knowledge of the intubating anaesthetist (second anaesthetist), the first anaesthetist prepared combinations of drug to be given according to the group assigned. Group PC was also given Ringer's lactate in the induction room.

A non-invasive arterial pressure monitor, electrocardiogram (ECG) and pulse oximeter (SpO_2) were attached, and baseline measurements were recorded. The sound of the pulse oximeter and ECG was then turned off and the monitoring screen was monitored only by the first anaesthetist. After preoxygenation of three minutes, anaesthesia was induced through an intravenous line with fentanyl 2 µg/kg followed by one of the three combinations mentioned above, given over 30 seconds by a hand-held syringe followed immediately by rocuronium 0.6 mg/kg given over 5 seconds. Placebo or ephedrine, both prepared in 1 ml syringe were given just before propofol was administered to the patient.

Sixty seconds after rocuronium was administered, laryngoscopy was attempted by the second anaesthetist who was blind to the ECG monitor and the drug given. During laryngoscopy and intubation of the trachea, the second anaesthetist performing the intubation assessed each patient for three different variables: jaw relaxation, vocal cords position and response to intubation. Assessment was based on the ease of laryngoscopy manifested by jaw relaxation, the position of the vocal cords and the reaction to tracheal intubation and cuff inflation as described by Cooper et al (1992). (Table 1). A total intubating score of 8-9 was considered excellent, 6-7 good, 3-5 poor and 0-2 bad. Excellent and good conditions were considered clinically acceptable, while poor and bad were considered clinically unacceptable.

After confirming the placement of the endotracheal tube, anaesthesia was maintained with sevoflurane, nitrous oxide and oxygen. Further recording of the heart rate and mean arterial blood pressure at 1, 2, 3, 4 and 5 min after tracheal intubation were done. Assessment of the intubating conditions and haemodynamic parameters were recorded by the second anaesthetist who was blinded to the study drug.

Non-parametric data were analysed using the Kruskal–Wallis test, followed, where significant, by the Mann–Whitney *U*-

test. For normally distributed data, the differences among groups were evaluated by ANOVA. A 'p' value less than 0.05 was considered to be stastistically significant.

RESULTS

The three groups were comparable in terms of age, gender, ASA physical status and BMI (table 2).

Intubating conditions were clinically acceptable in all patients except in four patients from the propofol-placebo group who recorded poor intubating conditions. The percentage of patient with excellent intubating conditions was highest in Group PE (94%) followed by Group PC (81%) and lowest in Group PP (50%) (Fig 1).

Jaw relaxation and vocal cords position scores however, did not differ significantly between the three groups ($p>0.05$).

The baseline value of mean arterial pressure (MAP) and heart rate (HR) did not differ among the three groups. There was no significant difference in the MAP of the three groups at 1, 2, 3, 4 and 5 minutes after intubation. However, there was a significant difference in the HR with the PE group recorded the highest increased in the heart rate at 1, 2, 3, 4 and 5 minutes after intubation ($p<0.01$) (Table 3).

DISCUSSION

In rapid sequence induction, sodium thiopentone is commonly used as an induction agent. However in this study, we used propofol as the induction agent of choice as several studies (Dobson et al 1999, Barclay et al 1997) have shown that this agent is more superior to thiopentone in suppressing the laryngeal reflexes and has frequently been used for tracheal intubation with or without the use of muscle relaxants.

Hypotension after induction of anaesthesia with propofol is well recognized. Mulier et al (1991) in their study, have

Table 1: Scoring of intubating conditions

S	JR	VCP	R
0	Poor (impossible)	Closed	Severe coughing (bucking)
1	Minimal (difficult)	Closing	Mild coughing
2	Moderate (fair)	Moving	Slight diaphragmatic movement
3	Good (easy)	Open	None

S= score, JR = Jaw relaxation, VCP = Vocal cord Position, R = response to intubation.

Table 2: Demographic data and patient's variables. Values are expressed as mean + standard deviation (SD) and number where appropriate.

	Group		
	PP (n=30)	PE (n=30)	PC (n=30)
Age (years)	40.6 $\pm$ 10.2	44.3 $\pm$ 11.1	42.9 $\pm$ 14.3
Gender (M:F)	12:18	14:16	13:17
ASA I/II	28/2	27/3	29/1
BMI (kg/m^2)	25.3 $\pm$ 6.7	26.7 $\pm$ 5.4	27.8 $\pm$ 5.8

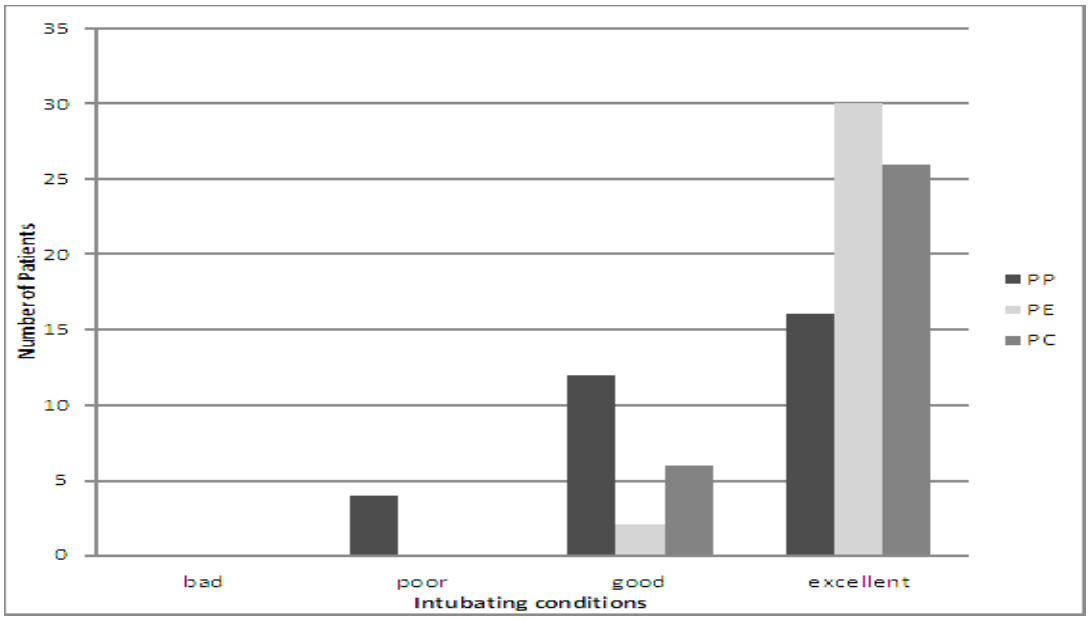

Figure 1: Intubating conditions one minute after induction of anaesthesia. There was a significant difference in the intubating conditions among the three groups ($p<0.01$). The difference in the intubating conditions score between Group PP versus Group PC and Group PP versus Group PE were also statistically significant ($p<0.01$ and $p<0.001$ respectively). There was also a significant difference between Group PE and Group PC ($p<0.05$).

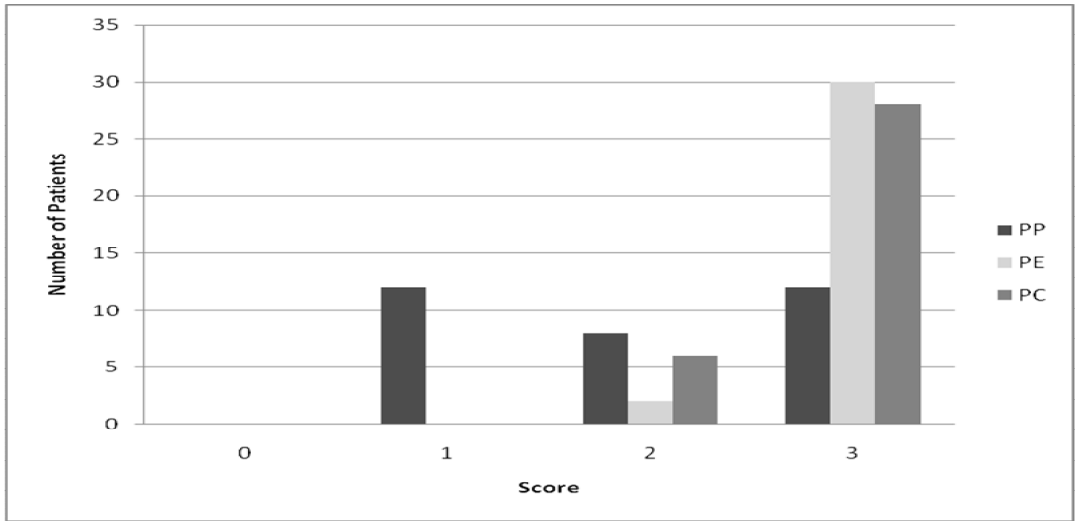

Figure 2: Response to intubation score: 0 = severe coughing or bucking, 1 = mild coughing, 2 = slight diaphragmatic movement, 3 = none. There was a significant difference in response to intubation score between the three groups ($p<0.001$). Difference between Group PP versus Group PC and Group PP versus Group PE were also statistically significant ($p<0.001$ and $p<0.003$ respectively). There was also a significant difference between Group PE and Group PC ($p<0.05$).

suggested a significant decrease in myocardial contractility and systemic vascular resistance and that would account for the decrease in arterial blood pressure. Ephedrine can possibly be used to counteract the effect of myocardial depression by its action on beta-1 receptor which increases myocardial contractility. The use of this drug during induction has been postulated to increase cardiac output and tissue perfusion **(**Ezri et al 2003). This increase will accelerate the onset time of neuromuscular blockade by means of a faster delivery of neuromuscular-blocking drug to skeletal muscles.

We have also demonstrated that the use of propofol-ephedrine and propofol-placebo-crystalloid combinations can improve intubating condition when rocuronium 0.6 mg/kg was used and the intubations were performed at 60 seconds after induction. Intubating conditions were clinically acceptable (good and excellent) in all patients in the study groups except in four patients in PP group, who have recorded poor intubating conditions. The proportion of excellent intubating conditions was significantly highest in the PE group followed by the PC group and lowest in the PP group.

The improvement in intubating conditions observed in the PE group were most likely due to the effects of ephedrine. Since muscle blood flow was not measured in the present study, we can only speculate as to whether this variable was increased by ephedrine, and whether this was the mechanism for the observed improvement in the intubating conditions. In this study, we postulated that the improvement in intubating conditions were due to a faster delivery of rocuronium to the neuromuscular junction. The finding of the improvement in the intubating conditions using propofol-ephedrine combination is also consistent with the findings by Tan et al **(**2002).

Gamlin et al (1996) have shown that ephedrine reaches its peak effect in two to three minutes and exerts its effect in less than two minutes after its administration. Kim et al (2003) reported that ephedrine 70 µg/ kg given before the induction of anaesthesia improves tracheal intubating conditions at two minutes after vecuronium by increasing cardiac output without significant adverse haemodynamic effects. In this study, we used the same dose of ephedrine but the intubation was done at 60 seconds after administration of ephedrine.

Turner et al (1998) in their study has proposed that fluid preloading produces an increase in myocardial preload, leading to an increase in stroke volume and therefore maintaining cardiac output at a lower heart rate without increasing blood pressure. Despite the drop in blood pressure, probably due to the drop in systemic vascular resistance, the cardiac output is

Table 3: Heart rate (beats/min). Values are expressed as mean + standard deviation (SD)

Minutes after intubation	PP	PE	PC	P value
Baseline	86 ± 8	91 ± 19	88 ± 18	P 0.4
1	85 ± 6	104 ± 26	85 ± 19	p < 0.01
2	84 ± 8	104 ± 24	91 ± 12	p < 0.01
3	86 ± 5	99 ± 20	92 ± 12	p < 0.01
4	85 ± 7	100 ± 24	91 ± 16	p < 0.01
5	85 ± 6	99 ± 24	90 ± 17	p < 0.01

well maintained. The delivery of muscle relaxant to the neuromuscular junction does not slow down and therefore, the fluid preloading has recorded better intubating condition as compared to placebo group observed in this study.

In contrast with the study done by Tan et al (2002), we did not find any significant increase in the mean arterial pressure in the propofol-ephedrine group except from the increase in the heart rate associated with the use of ephedrine. The possible reason behind this observation might be due to a smaller dose of ephedrine used in this study. In this study, we used a dosage of 70 µg/kg whereas in their study a dosage of 15 mg had been used which was about 3 times the dosage that had been used in this study.

As the heart rate was significantly increased in the PE group, caution should be exercised in the use of this combination in patients with ischaemic heart disease. Further studies are needed to identify the ideal dose of ephedrine in this combination, along with quantitative measurement of the onset of neuromuscular blockade among the three combinations of induction agents.

CONCLUSION

We conclude that induction with propofol-ephedrine and propofol-crystalloid provided significantly better intubating conditions than propofol alone, when rocuronium 0.6 mg/kg was used for intubation at 60 seconds.

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