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The administration sequence of propofol and remifentanil does not affect the ED_{50} and ED_{95} of rocuronium in rapid sequence induction of anesthesia: a double-blind randomized controlled trial

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Abstract. – OBJECTIVE: The topic of drug administration sequence in rapid sequence induction (RSI) is still an object of interest in terms of rocuronium effectiveness. The aim of this prospective, randomized trial was to evaluate the effect of administration sequence of propofol and remifentanil on ED_{50} and ED_{95} of rocuronium in a RSI model.

PATIENTS AND METHODS: Eighty-four patients were randomized into Group Remifentanil (Group R, n = 43), where induction of general anesthesia started with remifentanil (2 μg/kg) and followed by propofol (2 mg/kg) and rocuronium administrations; and Group Propofol (Group P, n = 41), where induction of general anesthesia started with propofol and followed by remifentanil and rocuronium. First patients in each group were paralyzed by 0.8 mg/kg rocuronium. In case of acceptable intubation as evaluated according to the criteria described by Viby-Mogensen et al, rocuronium dose was decreased by 0.1 mg/kg for the next patient; otherwise, rocuronium dose was increased by 0.1 mg/kg. After three crossover points, increments or decrements in rocuronium dosage were set to 0.05 mg/kg. The process was repeated until a total of ten crossover points were obtained.

RESULTS: The ED_{50} and ED_{95} doses of rocuronium were similar in Group R (0.182 mg/kg, and 0.244 mg/kg, respectively) and Group P (0.121 mg/kg, and 0.243 mg/kg, respectively) according to 95% CI of the estimates. There was no statistically significant difference in terms of clinically acceptable intubation conditions between the two groups (56.1% in Group R *vs*. 59% in Group P, $p = 0.795$).

CONCLUSIONS: The choice of administration sequence of propofol and remifentanil does not have an impact on estimated ED50 and ED95 of rocuronium in providing acceptable intubation conditions in the RSI technique.

Key Words:
Propofol, Remifentanil hydrochloride, Rocuronium, Anesthesia, Anesthetics, Intravenous, Intubation, Intratracheal.

Introduction

Rapid sequence induction (RSI) is a well-known technique of anesthesia induction since the 1970s, with the aim of achieving a safe and rapid airway control in patients at a risk of pulmonary aspiration[1-3]. The classical approach to RSI as described by Stept and Safar[4] has been evolved over the years with the change in drugs available for anesthesia induction and a better understanding of the process. Propofol as an induction agent, and opioids as an adjuvant, especially remifentanil, are among the widely used agents for RSI[2,5]. Neuromuscular blocking agents (NMBAs) are also recommended as another major component of drug administration to achieve better intubation conditions[3].

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Rocuronium is a widely used non-depolarizing NMBA in RSI[5,6]; but has the main disadvantage of low potency necessitating the higher administration doses for rapid onset[3,7,8]. The usual doses of rocuronium for RSI varies between 0.6 to 1.2 mg/kg, whereas Oh et al[8] determined that the ED_{50} of rocuronium was 0.2 mg/kg for acceptable intubation conditions after induction of anesthesia with conventional doses of propofol and remifentanil for RSI. Recently Siddik-Sayid et al[9] showed the effectiveness of 0.3 mg/kg administration of rocuronium before lidocaine-remifentanil-propofol induction sequence in providing excellent intubating conditions (90% in 92 patients) with a total induction time of 100 s. We experienced that most of the anesthesiologists predispose to reflect their habits related to administration sequence of propofol and remifentanil in a standard anesthesia induction, to their RSI practice. Na et al[10] demonstrated that the prior administration of remifentanil with propofol produced a longer onset time of rocuronium due to decreased cardiac output (CO) in a standard anesthesia induction process. However, up to our knowledge, there is no study evaluating the effect of administration sequence of propofol and remifentanil on rocuronium effectiveness, thereby on intubation conditions in RSI model.

This prospective, randomized, double-blinded study was designed to compare the effect of administration sequence of conventional induction doses of propofol (2 mg/kg) and remifentanil (2 μg/kg) on estimated ED_{50} and ED_{95} of rocuronium in providing acceptable intubation conditions in a RSI model with a sequential study design.

Patients and Methods

Patients and Study Design

This prospective, parallel-group, double-blind, randomized study was approved by the Institutional Review Board of the Harran University Faculty of Medicine (Professor Aksoy, 2016-02-10), and recorded on *www.clinicaltrials.gov* with a registration number of NCT02709473. Nighty-one American Society of Anesthesiologists (ASA) physical status I-II patients, aged between 18-65 years who were scheduled for elective surgery were screened for the study. The exclusion criteria of this study were anticipated or known difficult airway, a significant renal or hepatic dysfunction, a known neuromuscular disease, hypertension, a known allergy to one of the drugs used in general anesthesia, a body mass index lower than 18.5 kg/m^2 or higher than 30 kg/m^2, intake of any medication that might interact with rocuronium or patient refusal. Seven patients were excluded due to patient refusal and anticipated difficult airway. Overall, 84 patients were enrolled (Figure 1).

After written informed consent was obtained from all the study patients, subjects were randomized into two groups as Group Remifentanil (Group R, n = 43), where induction of general anesthesia started with remifentanil and followed by propofol and rocuronium administrations, and Group Propofol (Group P, n = 41), where induction of general anesthesia started with propofol and followed by remifentanil and rocuronium administrations by a blinded physician using sealed envelopes.

Premedication, Induction of General Anesthesia and Monitoring

On arrival at the operating room, standard monitoring (Siemens S5, Munich, Germany) of electrocardiogram, pulse oximetry, non-invasive blood pressure, and temperature was established. Ringer's lactate infusion was started after intravenous (iv) cannulation was performed. All patients were premedicated with 0.05 mg/kg iv midazolam. Baseline mean arterial blood pressure (MAP) was determined in supine position as the average of second and third noninvasive MAP measurements among three consecutive measurements with one-minute intervals. Baseline MAP, heart rate (HR) and peripheral oxygen saturation (SpO_2) were recorded before the induction of anesthesia.

After preoxygenation with 100% oxygen through a facemask for 3 min, 40 mg iv lidocaine were given to all patients in supine position. In Group R (n = 43), general anesthesia was induced with iv remifentanil 2 μg/kg given over 30 s followed by 2 mg/kg propofol given over 15 s. In Group P (n = 41), general anesthesia was induced with iv propofol 2 mg/kg given over 15 s followed by 2 μg/kg remifentanil given over 30 s. Following remifentanil and propofol administration, predetermined dose of rocuronium in a 10 mL syringe was rapidly given in 5 seconds to both groups. Drug administration sequences of both groups were represented in Figure 2. Cricoid pressure was not applied to any of the study subjects, and gentle mask ventilation was used during the apneic period. One minute after

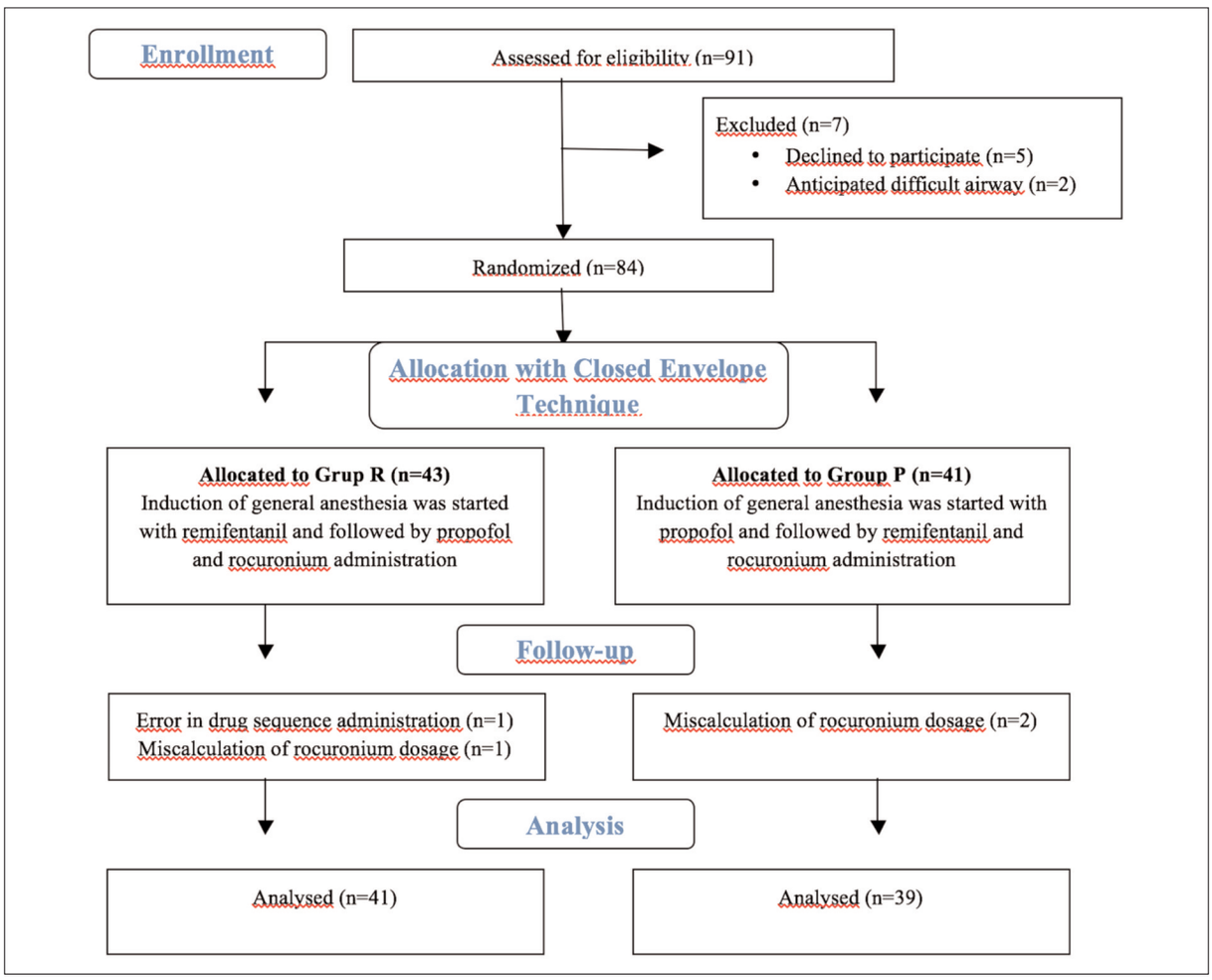

Figure 1. Overview of the study groups.

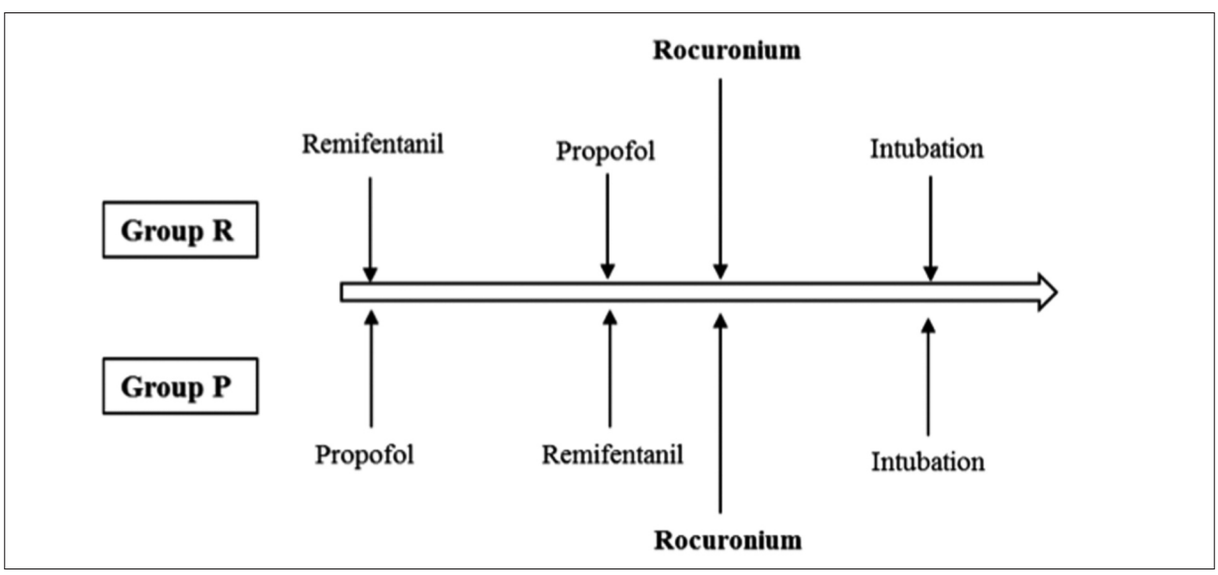

Figure 2. Drug sequence used in the study protocol.

the end of the rocuronium injection, an experienced anesthesiologist who was blinded to the administration sequence of propofol and remifentanil and the administered dose of rocuronium performed endotracheal intubation. The same anesthesiologist also evaluated intubating conditions using six variables: ease of laryngoscopy, jaw relaxation degree, resistance to blade, vocal cord position and movement, reaction to insertion of tracheal tube and/or cuff inflation. The criteria for assessing values to each variable were shown in Table I[11]. Intubation was considered excellent if all the variables were excellent, good when all the variables were excellent or good, and poor in the presence of a single poor variable. The intubation was considered successful in excellent or good intubating conditions, and failure in poor intubating conditions. Additionally, intubation success score was calculated as the sum of the points derived from Table I for each variable with 3 points for excellent, 2 points for good and 1 point for poor variables. The time interval between the initiation of the intubation procedure and the first recognizable end-tidal CO_2 on the patient monitor was also recorded.

An up-and-down method for a sequential study design was used for the determination of the dose of rocuronium to be administered to the next patient in each group[12]. The first patient received 0.8 mg/kg rocuronium in both groups. If the intubation was successful, the dose of rocuronium was decreased by 0.1 mg/kg for the next patient. On the contrary, the rocuronium dosage was increased by 0.1 mg/kg for the next patient when the intubation was a failure (Table I). After three crossover points, where the failure of intubation occurs, increments or decrements in rocuronium dosage were set to 0.05 mg/kg. The process was repeated until a total of ten crossover points were obtained (Figure 3 and 4).

MAP, HR and SpO_2 were recorded immediately after achievement of induction with rocuronium (end of induction), 1 min after induction of general anesthesia (before intubation), immediately after endotracheal intubation (after intubation), and 1 (1st minute), 2 (2nd minute), 3 (3rd minute), 4 (4th minute), 5 (5th minute) and 10 (10th minute) minutes after intubation.

Hypotension was defined as 20% and severe hypotension as 30% decrease in baseline MAP. A 200 mL bolus of crystalloid was administered to the patient in case of hypotension. If severe hypotension occurred, a 5 mg bolus of ephedrine was administered intravenously to the patient, followed by a 10 mg bolus of ephedrine when severe hypotension was not normalized in the next 3 min. Hypertension was defined as 20% in baseline MAP and a 100 mg bolus of nitroglycerin was intravenously administered to the patient in case of hypertension. In the case of bradycardia, which is defined as a decrease of heart rate below 60 beats/min, 0.5 mg atropine was administered intravenously.

For evaluation of memory recall and sore throat, patients were interviewed just before discharge from the postoperative anesthetic care.

Statistical Analysis

Statistical analysis was performed using the R software version 3.2.3. Patients' characteristics were compared between two groups with inde-

Table I. Assessment of intubating conditions according to Viby-Mogensen et al[11].

Variables	Clinically acceptabl		Clinically not acceptable
	Excellent	Good	Poor
Laryngoscopy	Easy	Fair	Difficult
Jaw relaxation	Relaxed	Not fully relaxed	Poor relaxation
Resistance to blade	None	Slight	Active
Vocal cord position	Abducted	Intermediate	Closed
Vocal cord movement	None	Moving	Closing
Reaction to insertion of tracheal tube and/or cuff inflation (movement of the limps/coughing)	None	Slight/Diaphragm	Vigorous/ Sustained (>10 s)

Excellent when all variables were excellent; good when all variables were excellent or good; poor in the presence of a single poor variable. Laryngoscopy accepted as easy, when jaw was relaxed and there was no resistance to blade insertion; fair, when there was slight resistance to blade insertion; difficult, in case of poor jaw relaxation and active resistance. Reaction to insertion of tracheal tube and/or cuff inflation was accepted as good, when one or two weak contractions of movement for less than 5 s; poor, in case of more than two contractions and/or movement for less than 5 s.

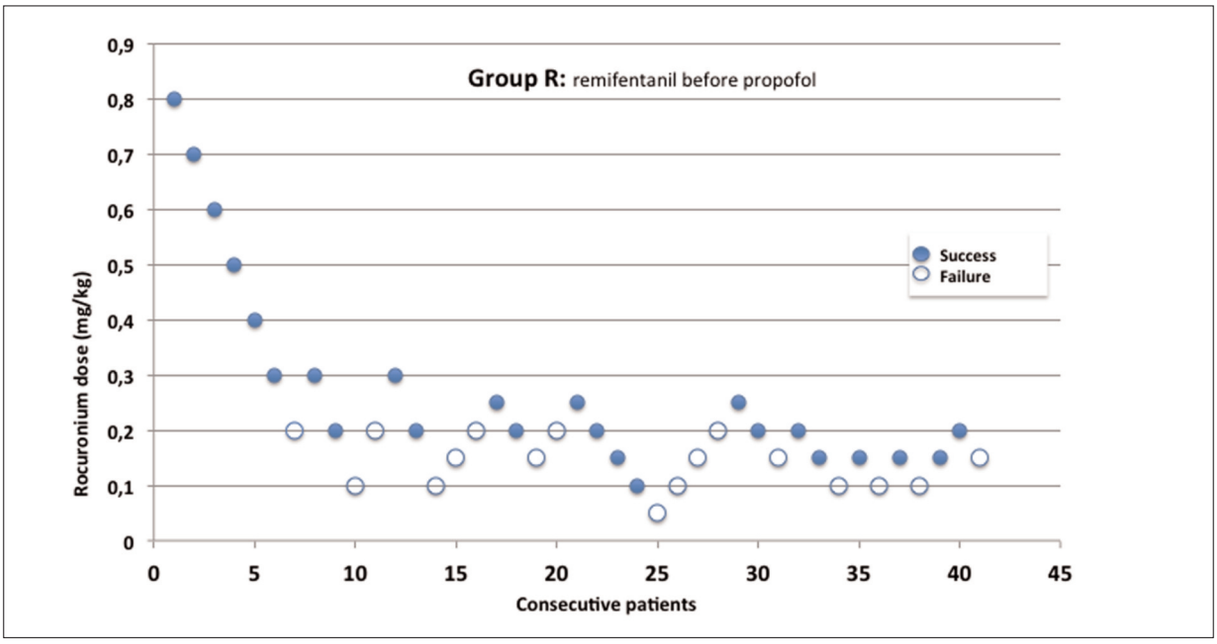

Figure 3. Individual dose-response associations in Group R.

pendent samples t-test and data were expressed as mean±SD. Differences in gender, ASA status, postoperative recall, postoperative sore throat and intubation conditions were analyzed using the chi-square test or Fisher's Exact test, where applicable, and the data were given as numbers and percentage. MAP and HR values were analyzed using repeated measures analysis of variance, and Bonferroni test was used to evaluate the differences between the groups. Point estimates of ED_{50} and ED_{95} target dose levels were calculated by using the Pooled Adjacent Viola-

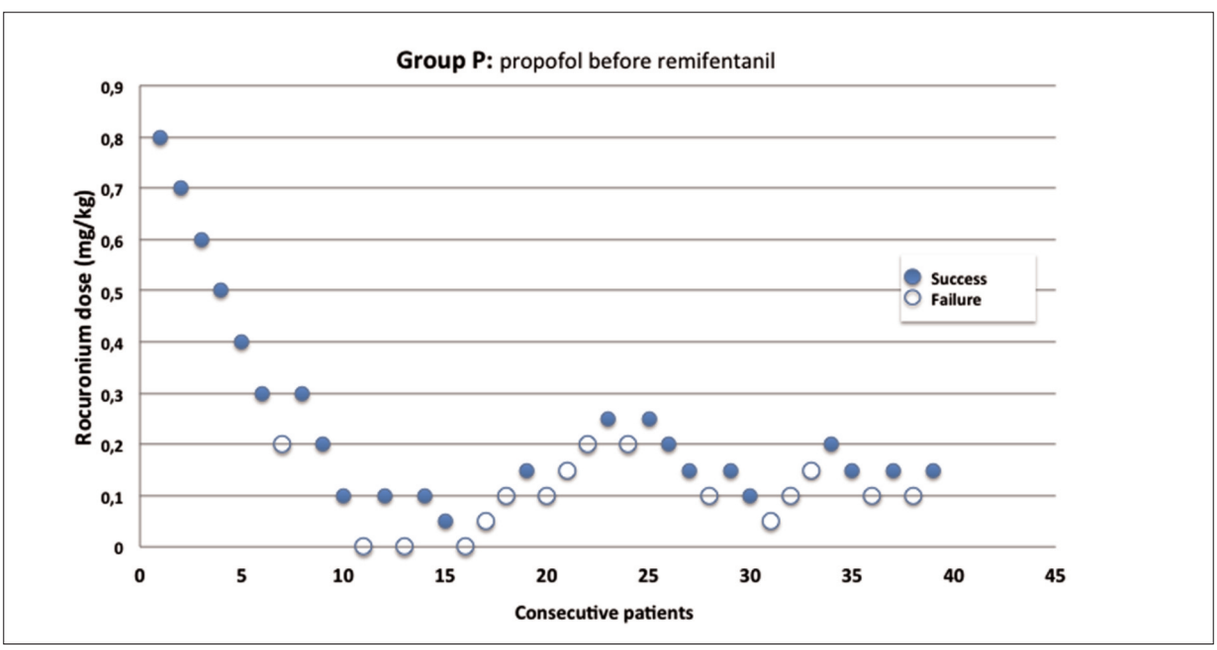

Figure 4. Individual dose-response associations in Group P.

tors Algorithm (PAVA) in isotonic regression. Bootstrapping is used to create the 95% confidence interval (CI) on the estimators[13]. A p value of < 0.05 was considered statistically significant.

Results

A total of 84 patients were enrolled and randomly allocated into two groups, Group R (n = 43) and Group P (n = 41). One patient in Group R was excluded from the study due to an error in drug administration sequence. Additionally, 1 patient in Group R and 2 patients in Group P were excluded because of the miscalculation of rocuronium dosages. Therefore, the results of a total of 80 patients (41 patients in Group R, and 39 patients in Group P) were evaluated (Figure 1). The first patient received 0.8 mg/kg rocuronium in both groups, and the consecutive patients received the dose determined according to modified Dixon's up-and-down method[12]. Characteristics of the patients included are presented in Table II. Accordingly, the two groups were similar with respect to age, gender, ASA physical status, height, weight and BMI ($p > 0.05$).

The data for ED_{50} and ED_{95} are given in Table III. Accordingly, when the induction of general anesthesia started with administration of 2 μg/kg remifentanil followed by 2 mg/kg propofol (in Group R), the dose of rocuronium for successful RSI in 50% of the patients (ED_{50}) was calculated as 0.182 mg/kg with a 95% CI of 0.142-0.210 using the PAVA estimators. The estimated ED_{95} dose was found to be 0.244 mg/kg (95% CI: 0.195-NA). In Group P, where the induction of general anesthesia started with administration of 2 mg/kg propofol followed by 2 μg/kg remifentanil, the dose of rocuronium for successful RSI in 50% of the patients (ED_{50}) was calculated as 0.121 mg/kg with a 95% CI of 0.044-0.203 using the PAVA estimators. The estimated ED_{95} dose was found to be 0.243 mg/kg (95% CI: 0.200-NA). According to 95% CI of the estimates there was no statistically significant differences with respect to both ED_{50} and ED_{95} doses of rocuronium in Group R and Group P.

Figure 3 and 4 showed the individual dose-response associations according to the up-and-down sequence in each group. The overall assessment of intubation-related data and prevalence of complications are summarized in Table IV. Endotracheal intubation was possible in all the patients, and there was no statistically significant difference between the Group R (56.1%) and Group P (59%) regarding the rate of clinically acceptable intubation conditions ($p = 0.795$). Intubation success scores were comparable between the two groups (15.5 ± 2.5 in Group R and 14.8 ± 2.5 in Group P, $p = 0.189$). The time interval between the initiation of the intubation procedure and the first recognizable end-tidal CO_2 on the patient monitor in Group P (43.7 sec) was slightly, but not significantly, longer than that of Group R (41.9 sec) ($p = 0.667$).

Hemodynamic data in response to endotracheal intubation are presented in Figure 5 and 6. Baseline values for both MAP and HR before the induction of general anesthesia were comparable between Group R and Group P ($p > 0.05$). The statistically significant decrease in HR was observed 1 min after the end of anesthesia induction (before intubation) as compared to the baseline values and the other consecutive measurements except for 10th minutes after endotracheal intubation in both groups ($p < 0.001$). The statistically significant decrease in MAP was detected in every measurement points as compared to the baseline MAP value ($p < 0.001$). The maximum decrease in MAP was observed 1 min after the end of anesthesia induction. There was no statistically significant difference in any measurement

Table II. Patient demographics.

	Group R (n = 41)	Group P (n = 39)	*p*-value
Gender, male/female	20/21	19/20	0.996
ASA physical status, I/II	33/8	29/10	0.512
Age, years	39.2 ± 12.6	37.1 ± 12.3	0.449
Weight, kg	71.9 ± 10.9	74.4 ± 11.4	0.313
Height, cm	168.9 ± 8.2	170.4 ± 8.9	0.457
BMI, kg/cm^2	24.9 ± 2.7	25.5 ± 2.8	0.345

Group R: Group Remifentanil; Group P: Group Propofol; Values are given as mean ± SD, or number of patients. ASA, American Society of Anesthesiologists; BMI, body mass index.

Table III. Data of estimated ED_{50} and ED_{95} of rocuronium.

	Group R (n = 41)	Group P (n = 39)
ED_{50} (mg/kg) of rocuronium	0.182 ± 0.018 (0.142 – 0.210)	0.121 ± 0.038 (0.044 – 0.203)
ED_{95} (mg/kg) of rocuronium	0.244 ± 0.138 (0.195 – NA)	0.243 ± 0.136 (0.200 – NA)

Group R: Group Remifentanil; Group P: Group Propofol; Values are given as estimated values ± standard error (95% confidence interval). NA, not applicable.

Table IV. Output of RSI and incidence of complications.

	Group R (n = 41)	Group P (n = 39)	*p*-value
Clinically acceptable intubation	23 (56.1%)	23 (59.0%)	0.795
Intubation success score*	15.5 ± 2.5	14.8 ± 2.1	0.189
End tidal CO_2 monitoring time, sec	41.9 ± 19.9	43.7 ± 15.1	0.667
Hypotensive episode	37 (90.2%)	33 (84.6%)	0.513
Severe hypotensive episode	27 (65.9%)	24 (61.5%)	0.688
Bradycardia	6 (14.6%)	2 (5.1%)	0.265
Vasoactive medication	14 (35.9%)	9 (22.0%)	0.168
Postoperative recall (%)	0 (0)	0 (0)	NA
Postoperative sore throat (%)	5 (12.2%)	4 (10.3%)	1.000

Values are given as mean ± SD or number of patients, percentage. NA, not applicable. *Calculated according to Table I with 3 points for excellent, 2 points for good and 1 point for poor variables.

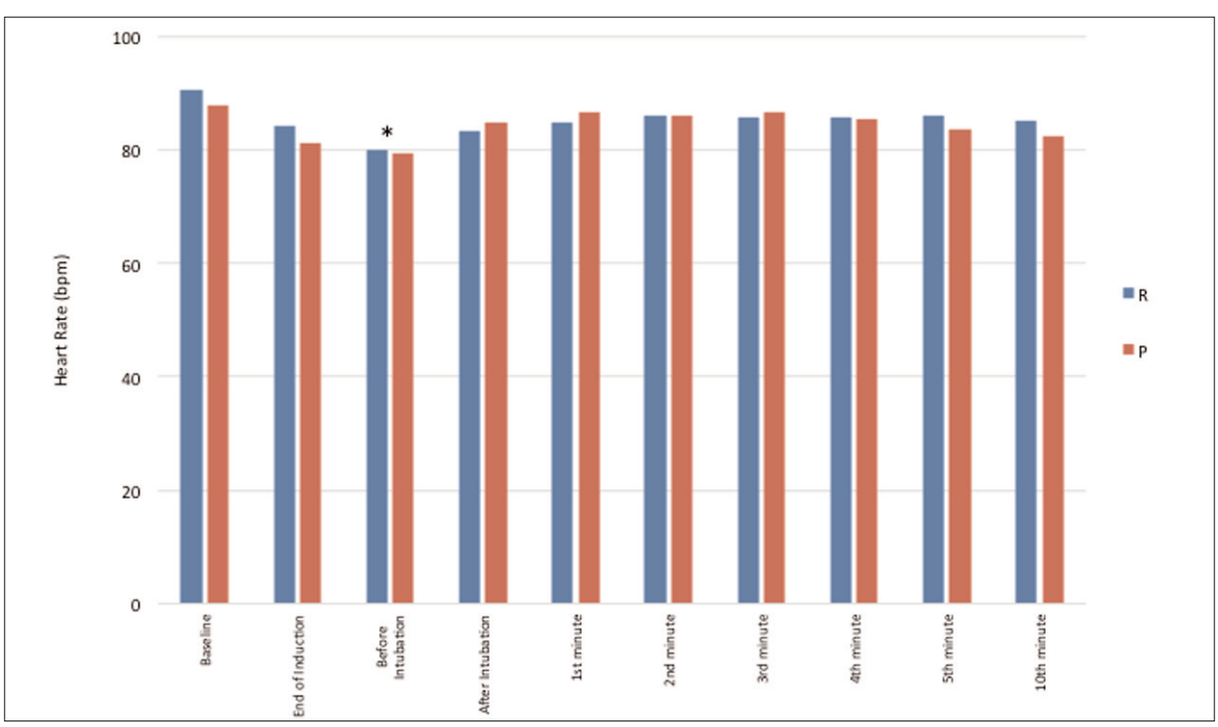

Figure 5. Changes in heart rate.

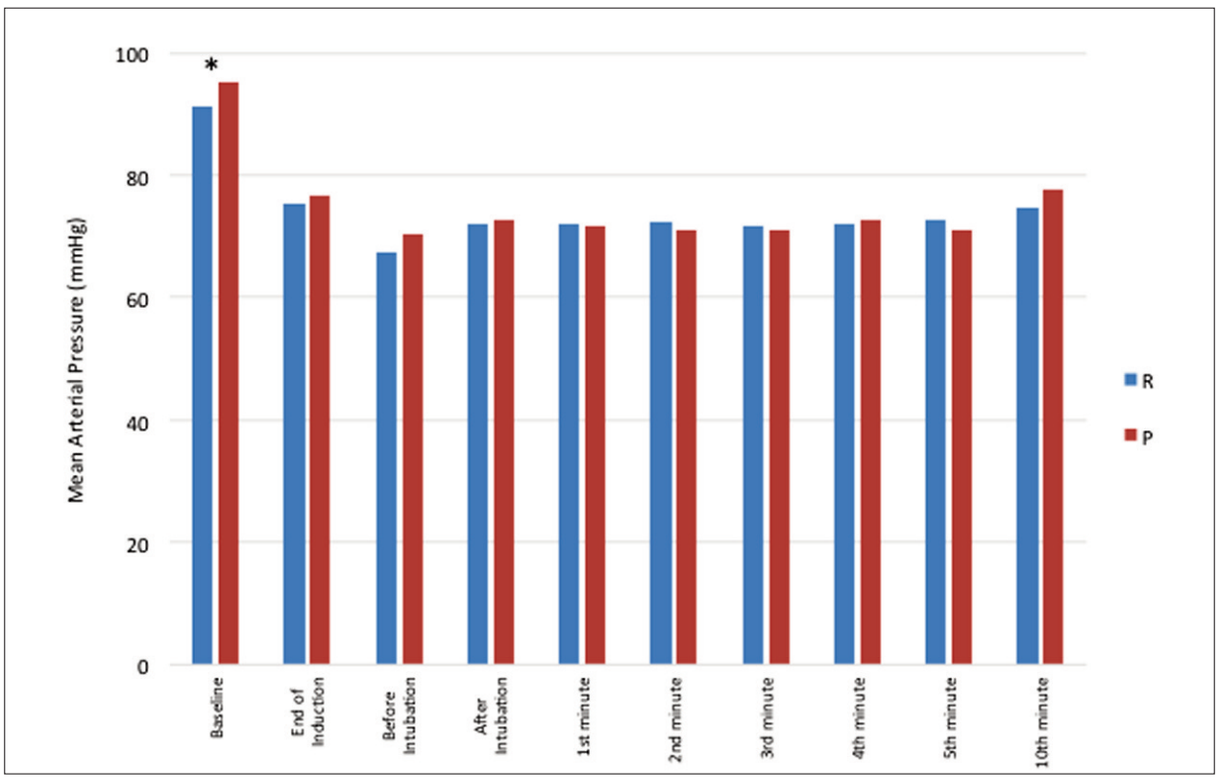

Figure 6. Changes in mean arterial pressure.

points between the two groups in terms of MAP and HR values. In addition, no difference was recorded between the two groups with respect to the incidence of complications such as hypotensive episode, severe hypotensive episode, bradycardia, and requirement for vasoactive medication ($p > 0.05$ for all). None of the patients reported postoperative recall in both groups, and the overall incidence of a sore throat was 5 and 4% in Group R and Group P, respectively, again with no significant difference between the two groups ($p = 0.784$) (Table IV).

Discussion

This prospective, parallel-group, double-blind, randomized study was designed to compare the effect of administration sequence of conventional induction doses of propofol (2 mg/kg) and remifentanil (2 μg/kg) on estimated ED_{50} and ED_{95} of rocuronium by using an up-and-down sequential study design to provide acceptable intubation conditions in a RSI model. The results indicated that the choice of administration sequence of propofol and remifentanil does not have an impact on estimated ED_{50} and ED_{95} of rocuronium in providing acceptable intubation conditions in RSI technique.

In induction of general anesthesia, propofol may be preferred as the first line drug to provide fast hypnosis, and remifentanil may be added to prevent potential hemodynamic response to laryngoscopy. However, the injection pain associated with propofol may be a concern related with its usage, and recently, Choi et al[14] suggested that pretreatment with remifentanil could be used as an efficient way of preventing propofol injection pain. On the other hand, clinically we experienced that most of the anesthesiologists have traditions in selecting the administration sequence for propofol and remifentanil, and use the same sequence in their RSI practice. Aside from hypnotic and opioid agents, rocuronium is also an essential component of RSI to provide acceptable intubation conditions. Some prior reports demonstrated that the onset time of rocuronium might be changed with the pretreatment of different adjuncts such as ephedrine or esmolol[15,16]. It has been postulated that the influence of these drugs on onset time of rocuronium depends on the changes of CO and, therefore, muscle perfu-

sion and the exposure speed of rocuronium to the effect side. Furthermore, there are a few studies evaluating the administration sequence of hypnotic and adjunct agents on the effectiveness of NMBAs. Na et al[10] demonstrated that the onset time of rocuronium was prolonged by early administration of remifentanil during target-controlled infusion of propofol and remifentanil due to decreased CO. It is well-known that the hemodynamic consequences of anesthesia induction, especially decrease in CO, may be exaggerated due to the nature of RSI procedure. Rocuronium onset and, therefore, acceptable intubation conditions from a clinical point of view may be influenced by the administration sequence of propofol and remifentanil. However, to our best of knowledge, there is no study comparing the effect of administration sequence of propofol and remifentanil on rocuronium ED_{50} and ED_{95} doses in providing acceptable intubation conditions.

The classical definition of effective dose in pharmacology is the amount of drug that produces the required effect in a certain percentage of patients being exposed to this drug. In another word, ED_{50} and ED_{95} are the doses that demonstrate the quantal dose-response relationship in 50% and 95% of patients, respectively. In their studies with 28 patients, Oh et al[8] reported the lowest dose of rocuronium for successful RSI in 50% of the patients (ED_{50}) after induction of anesthesia with conventional doses of remifentanil (2 μg/kg) and propofol (2 mg/kg) as 0.20 mg/kg with a 95% CI of 0.17-0.23 using the modified Dixon's up-and-down method. Based on their results, the authors suggested to use remifentanil and propofol administration sequence. In the present study, during the induction of general anesthesia with administration of 2 μg/kg remifentanil followed by 2 mg/kg propofol (in Group R), as in the study by Oh et al[8], the dose of rocuronium for successful RSI in 50% of the patients (ED_{50}) was found to be 0.182 mg/kg (95% CI: 0.142-0.210). Although we did not conduct a dose finding study, the ED_{50} of rocuronium was found to be similar in these two studies based on a sequential study design. The ED_{95} of rocuronium was calculated as 0.244 mg/kg (95% CI: 0.195-NA) in Group R (Table III). In the present study, we also evaluated the ED_{50} and ED_{95} of rocuronium with administration sequence of propofol and remifentanil (in Group P) as 0.120 mg/kg (95% CI: 0.044-0.203), and that of ED_{95} as 0.243 mg/kg (95% CI: 0.200-NA). It is important to note that according to %95 CI of the estimates there was no statistically significant difference in terms of ED_{50} and ED_{95} of rocuronium between Group R and Group P (Table III).

Propofol is accepted as an appropriate induction agent for RSI due to its high degree of lipophilicity that allows rapid onset time. Opioids as an adjunct are generally combined with propofol to achieve better intubation conditions even without NMBAs. Remifentanil, an ultrashort duration opioid, has become an excellent option to blind autonomic responses associated to endotracheal intubation[17]. Rational use of presented drugs should provide excellent tracheal intubation conditions, promote fast onset and return to consciousness and spontaneous ventilation in case of intubation failure[18]. McNeil et al[19] demonstrated that propofol and remifentanil combination without succinylcholine was an effective way to perform endotracheal intubation in RSI technique. The combination of these drugs may be an alternative to the use of NMBAs for procedures requiring endotracheal intubation, but not muscle relaxation during surgery, and in situations where the use of NMBAs is contraindicated. Recently, Siddik-Sayid et al[9] showed the effectiveness of 0.3 mg/kg administration of rocuronium before lidocaine (1.5 mg/kg), and coadministration of remifentanil (2 mg/kg) and propofol (2 mg/kg) in providing excellent intubating conditions (90% in 92 patients) with a total induction time of 100 s. In the present study endotracheal intubation was possible in all the patients, and there was no statistically significant difference between the Group R (56.1%) and Group P (59%) regarding the rate of clinically acceptable intubation conditions ($p = 0.795$). The higher success rate of intubation demonstrated in the study of Siddik-Sayyid et al[9] might be due to the prior administration of rocuronium before propofol and remifentanil, and longer induction time compared with the present study.

RSI is commonly related with negative hemodynamic consequences due to rapid injection of hypnotic and adjuvants that potentially cause cardiovascular system depression. Propofol alters the baroreflex mechanism that results in a smaller increase in HR for a particular decrease in blood pressure. Remifentanil also causes hypotension and decrease in HR depending on the injected dose[20]. McNeil et al[19] demonstrated that postinduction MAP values were decreased from baseline by 21% in their RSI model generated with propofol and remifentanil combination. In our study, the decrease in postinduction MAP values

was similar to the study by McNeil et al[19]. While MAP values were decreased immediately after induction from baseline by 18% and 20% in Group R and Group P, respectively, there was no difference between the two groups. There are some conflicting results regarding the effects of RSI with remifentanil and propofol combination on postinduction HR. Hanna et al[21] found that propofol and remifentanil, when used as the same dose as in this study, did not cause any significant change in HR. However, McNeil et al[19] demonstrated that the same induction model decreased the postinduction HR values compared with baseline by 14% with statistically significant difference. We also found a similar decrease in postinduction HR values compared with baseline in both Group R [(12% decrease ($p < 0.001$)] and Group P [(10% decrease ($p < 0.001$)]. O'Hare et al[22] showed that remifentanil injection with a dose of 1.25 μg/kg was associated bradycardia in 50% of patients undergoing RSI. The results of this study, however, disagree with O'Hare et al[22]. There was no requirement of atropine administration due to bradycardia in our study. This finding can be explained by the duration of remifentanil injection (over 30 seconds), which may be the key factor for avoiding bradycardia. However, ephedrine was used in 14 patients (35.9%) in Group R and 9 patients (22%) in Group P due to severe hypotension defined as 30% decrease in baseline MAP. The MAP and HR returned to baseline values after the end of endotracheal intubation. There was no difference between two groups related with hemodynamic consequences of RSI.

We acknowledge some limitations. Although we obtained both ED_{50} and ED_{95} of rocuronium, the statistical way of evaluating the ED_{95} using the estimated dose-response outcome is not valid due to our study design. CI values were very wide because some subjects assigned to a dose near the ED_{95} was likely to be very few. We acknowledge that for a design to estimate the ED_{95}, the mass of rocuronium doses should be in the vicinity of the ED_{95}. In fact, we represented the results related with ED_{95} because we believe that our study will give others an estimate of ED_{95} to be used in setting the study dose levels in further studies. We designate clinically acceptable or unacceptable intubation conditions as successful or failed intubation, respectively. However, RSI is a procedure that excellent intubation conditions are always preferred. Therefore, the design of this study might not be performed in the patients that have real indications of performing RSI. In addition to this, we did not evaluate the onset time of rocuronium using an objective neuromuscular blockade monitorization technique. We only used clinical end-points to decide the success or failure of intubation. Finally, only patients with ASA physical status I and II with an age range from 18 to 65 years were included in the study, considering the difference in hemodynamic tolerance in ASA III and IV patients and the change in pharmacokinetics and pharmacodynamics of rocuronium with age, the results obtained from this study may be invalid in the elderly.

Conclusions

We demonstrated that there is no difference in terms of rocuronium requirement to provide similar endotracheal intubation conditions, even in different propofol and remifentanil administration sequence in a RSI model.

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Conflict of Interest

The Authors declare that there are no conflicts of interest.

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