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Comparison of Suxamethonium and Rocuronium on time to Oxygen Desaturation during Apnoea Following Rapid Sequence Induction- A Randomized Controlled Trial

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Abstract
Hypoxia and hypoxic related injuries remain the main cause of anaesthesia related death and serious morbidity. The study has been focused on maximising the intrapulmonary oxygen reserve to prolong non-hypoxic apnoea duration. Various technique of preoxygenation including rebreathing with high fresh gas flow, application of positive airway pressure during preoxygenation, nasopharyngeal oxygen insufflation following preoxygenation can delay the onset of arterial desaturation during apnoea. The present study was carried out with the primary objective of comparing between suxamethonium and rocuronium as agent for rapid sequence induction with respect to the time required for oxygen saturation to decrease to 92% in seconds following apnoea. It was hypothesized that suxamethonium would be associated with shorter time to desaturate from administration until oxygen saturation was 92%.
In the present studies 66 patients were divided into two groups: Group S (n=33) for suxamethonium and Group R (n=33) for rocuronium and their datas was analysed.
Significant difference was detected in the time taken for oxygen saturation to decreased to 92% between the two group (p=0.042). Haemodynamic parameters both at intubation and post-intubation at 2minutes were comparable and showed no significant differences.
Keywords: *safe apnea, suxamethonium, rocuronium, rapid sequence intubation.*

Introduction

Patients scheduled for elective surgeries are usually in optimal physical and mental condition with a definitive surgical diagnosis. In contrast, the patient with the surgical emergency may have an uncertain diagnosis and uncontrolled coexisting disease.

Vomiting or regurgitation of gastric contents followed by aspiration while the protective laryngeal reflexes are obtunded is one of the commonest and devastating hazards of emergency anaesthesia. The presence of vomitus above the vocal cord causes spasm in lighter plane resulting in apnoea which may persist and results to severe hypoxemia or even cardiac arrest. Even if the spasm does resolves, aspiration may occur unless a supraglottic debris has been cleared before resumption of ventilation.

Rapid-sequence induction (RSI) is the technique most frequently used for a patient with full stomach as it minimizes the duration of time between loss of consciousness and tracheal intubation during which the patient is at greater risk of aspiration.

The traditional technique of RSI as described in the original publication[1] entails administration of a precalculated dose of induction agents followed immediately by a neuromuscular blocking agent after adequate preoxygenation. Cricoid pressure at 20-40 N is applied before loss of consciousness. After the jaw relaxes and succinylcholine associated fasciculation ceased, the trachea is intubated and cuff inflated. Positive pressure ventilation is avoided before tracheal intubation[1,2]. After the tube positioninga and adequate seal are confirmed cricoid pressure is released. However, differences have been noted in the perception and execution of RSI among amaesthesiologist[3] and might reflect the current controversy regarding some of the technique in traditional components. This may be the reason for failure to establish a standard RSI protocol.

Traditionally, succinylcholine which is also known as suxamethonium has been the neuromuscular blocking drugs (NMBD) of choice for RSI because of its two desirable properties: a rapid onset of action which facilitates speedy intubation, thereby minimizes the risk of aspiration, while a short duration of action allows for quicker onset of spontaneous respiration in the event of failed intubation.

However, it causes a number of adverse effects which includes increased serum potassium concentration, myalgia, and rarely malignant hyperthermia. Myalgia caused by suxamethonium is due to fasciculations which increases the whole-body oxygen consumptions.[4,5] Increased oxygen consumption is one of the factors that may have a major effect on time to oxygen desaturation following apnoea during induction of anaesthesia[6]. High dose of rocuronium (0.9-1.2 mg/kg) has been suggested as an alternative for RSI as it achievesa intubating condition in a comparative time as suxamethonium[7,8,26] but its use has been limited by a more prolonged duration of action. However, the availability of the sugammadex enables high dose rocuronium to be used a s an alternative to suxamethoniumin RSI. Sugammadex allows a rapid reversal through encapsulation of the rocuronium molecule. Studies have shown that non-depolarizing NMBD do not alter oxygen consumption in anaesthetized patient[4,5,6,9] since the muscular tone is already reduced by GA.

Apnoea is always present during RSI in GA. Maintaining haemoglobin saturation during airway management is critical for patient's safety. Desaturation to below 70% puts patient at risk of dysrhythmia, hemodynamic decompensation, hypoxic brain injury and death[10,11]. It is potentially life threatening if it is inadequately managed.

This study was planned to give an idea about the rapidity with which desaturation occurs with the two NMBD- suxamethonium and rocuronium. It was designed to compare the time taken by both the drug to desaturate till 92% during apnoea following RSI and was hypothesized that suxamethonium would be associated with a shorter time to desaturate.

Materials and Methods

The prospective randomized control double-blind study was conducted after getting approval from the hospital ethic committee. Patient within the age of 23-60 years; height within the range of 140-165 cm; weight between 50-70 kg and belonging to ASA physical status grade I and II scheduled for elective surgery were included in the study. Exclusion criteria included patient not willing to participate in the study, pregnant patients, history of significant pulmonary pathology or significant cardiovascular disease, person with BMI > 26 kg/m^2, anticipated difficult intubation, patients having a history of malignant hyperthermia, recent burnt, abdominal sepsis and prolonged immobilization.

If any difficulty was encountered during induction or intubation, appropriate action was taken by the

anaesthesiologist to optimize the patient and the patient was excluded from the study.

The number of patients in each group was calculated to be 30, by considering type 1 error α=0.005 and the power of the study (1-β) to be 80%, where type 2 error (β=0.20). A 30 second difference was considered clinically relevant[12] and standard deviation was taken to be 34 seconds from a pilot study conducted earlier. Considering a drop-out rate of 20% a sample size of 72 patients was considered. A P value < 0.05 was considered significant. A sample size of 72 patients was initially taken considering the inclusion and exclusion criteria. Out of them, 4 patients opted out of the studies, finally 68 patients were randomized into two groups of 34 each to receive either SCH 1mg/kg (group S) or injection Rocuronium 1mg/kg (group R). Two patients developed complications after induction and had to be excluded from the studies so data from 62 patients was available for analysis; group S (n=33) and group R (n=33).

After admission of the patients, a repeat preanesthetic check up was done where they were explained about the procedure in their own vernacular language and written informed consent was taken. The patients were advised oral Ranitidine 150 mg the night before the surgery, on the day of surgery, 18G IV cannula was established and infusion commenced. After shifting the patient to the operating room, they were allocated two different room by lottery method subsequently the monitor (NIBP, SPO2) were attached. Baseline haemodynamic variables (HR, MAP) were recorded. All patients received premedication with 0.02mg/kg midazolam IV before induction. Anaesthesia was administered by an experienced anaesthesiologist. To minimise bias an independent investigator was assigned to record the data who was called after the administration of the NMBD. Thus, both the patient and the investigator were blinded to the study.

Patient were preoxygenated with 100% oxygen in the supine position using a tight fitting non-rebreathing facemask[13] with the bag for 3 minutes[14,15] and the patient was asked to breath normally. Anaesthesia was then induced using the RSI technique.

For induction, injection propofol (2mg/kg) was administered over 20 seconds accompanied by injection fentanyl (2mcg/kg). Either injection SCH (1mg/kg) or rocuronium (1mg/kg) were given upon loss of verbal contact. The facemask was removed 60secs after the administration of NMBD[16,17] and was followed by laryngoscopy and tracheal intubation. Stop watch was started from the time the facemask was removed[12]. The tracheal tube was left open to air until oxygen saturation decline to 92%, at this point the stopwatch was stopped. Oxygen saturation was continuously monitored, once it declined to 92%, the patient was connected to the ventilator. Anaesthesia was maintained with the muscle relaxant as required. The time from onset of apnoea to the time that oxygen saturation reached 92% was compared among the two group. The mean arterial pressure and heart rate at intubation and 2 mins post-intubation was also recorded and compared.

Result and Analysis

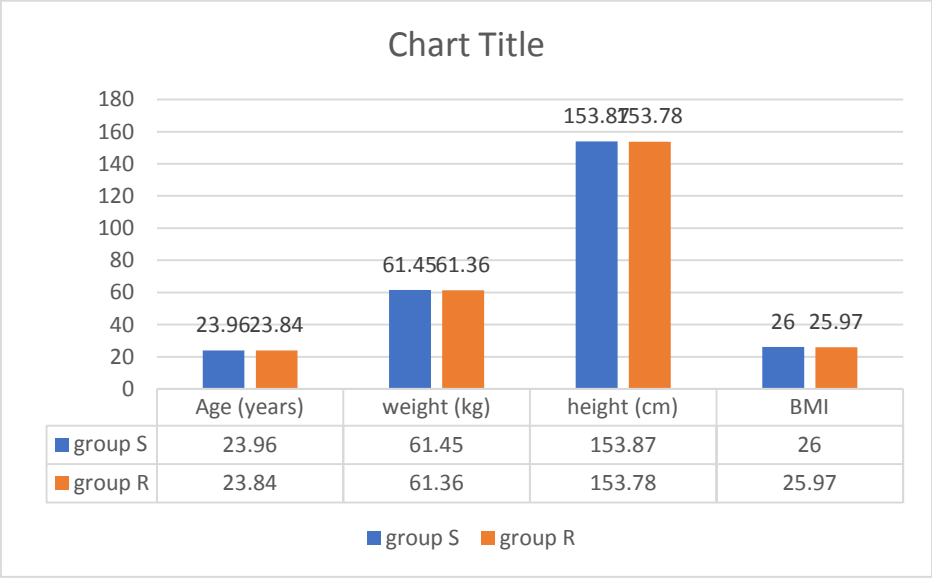
A sample size of 72 patients was initially taken considering the inclusion and exclusion criteria. Out of them, 4 patients opted out of the studies, finally 68 patients were randomized into two groups of 34 each to receive either SCH 1mg/kg (group S) or injection Rocuronium 1mg/kg (group R). Two patients developed complications after induction and had to be excluded from the studies so data from 66 patients was available for analysis; group S (n=33) and group R (n=33).

Observations were tabulated in an excel sheets and analysed. Continuous data were expressed as mean± SD. Discrete categorical data were presented as number of patients [n(%)]. comparison of continuous data with a normal distribution were performed using the independent student's t test. Categorical data were analysed with contingency tables using Pearson Chi-square

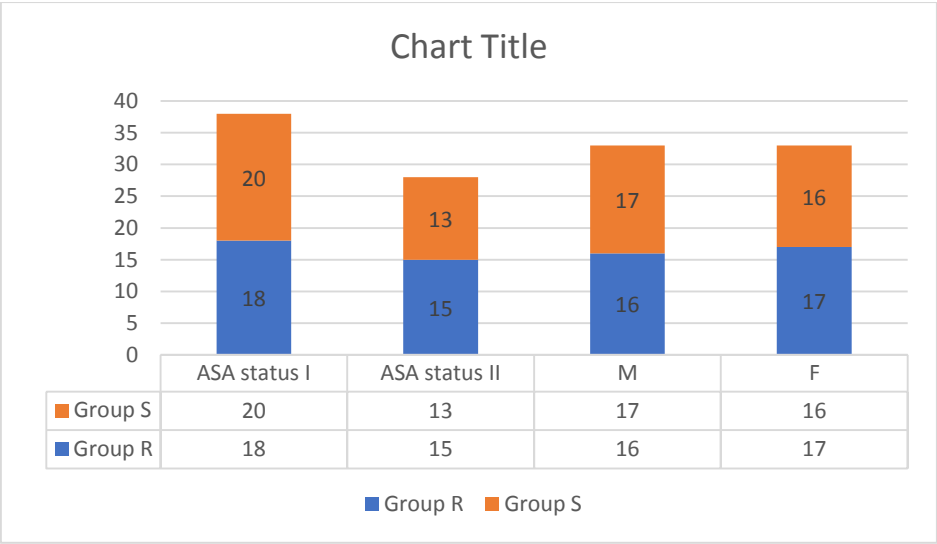
test. Statistical test was considered significant when p value <0.005. All analysis was conducted using SPSS for window (version 19.0; SPSS Inc., Chicago, IL)

Table 1 Demographic variables of the patients

Parameter		Group S (n=33)	Group R (n=33)	P value
Age (years)	Mean	23.96	23.84	0.871(NS)
	SD	±2.82	±3.23	
Weight (kg)	Mean	61.45	61.36	0.903(NS)
	SD	±2.03	±3.78	
Height(cm)	Mean	153.87	153.78	0.915(NS)
	SD	±3.29	±3.62	
BMI (kg/m^2)	Mean	26.0	25.97	0.961(NS)
	SD	±1.63	±1.91	
ASA status	I	20	18	0.969(NS)
	II	13	15	
M:F	M	17	16	0.996(NS)
	F	16	17	



Bar diagram showing distribution of patients according to age(years), weight(kg), height(cm), BMI in Group S and Group R.



Bar diagram showing distribution of patients according to sex (male: female) and ASA status (I and II)

Table 2 Distribution of patients according to Hb (gm/dL), baseline MAP (mm of Hg), baseline heart rate (beats per minute)

Parameter		Group S (n=33)	Group R (n=33)	P value
Hg (gm/dL)	Mean	12.85	12.45	0.067(NS)
	SD	±0.78	±0.93	
Baseline MAP (mmHg)	Mean	90.27	91	0.357(NS)
	SD	±3.06	±3.30	
Baseline heart rate (bmp)	Mean	85.42	84	0.299(NS)
	SD	±5.45	±5.60	

Table 3 Comparison of SO_2(%) for group S and group R and their statistical analysis

	Group S (n=33)	Group R (n=33)	P value
Mean	97.57	97.48	0.751(NS)
SD	±1.22	±1.09	

Table 4 Comparison of mean arterial pressure (MAP) at intubation and 2mins post intubation for group S and group R and their statistical analysis

Parameter		Group S (n=33)	Group R (N=33)	P value
MAP at intubation (mmHg)	Mean	82.09	82.15	0.934(NS)
	SD	±2.97	±2.99	
MAP at 2 mins (mmHg)	Mean	77.87	78.27	0.630(NS)
	SD	±3.21	±3.39	

Table 5 Comparison of Heart rate at intubation and 2 minutes post intubation for group S and group R and their statistical analysis

Parameter		Group S (n=33)	Group R (N=33)	P value
HR at intubation (mmHg)	Mean	90.21	90.60	0.768(NS)
	SD	±5.39	±5.44	
HR at 2 mins (mmHg)	Mean	88.12	88.33	0.863(NS)
	SD	±4.92	±5.08	

Table 6-Comparison of time for oxygen saturation to reach 92% (in seconds) for group S and Group R with their statistical analysis

	Group S (n=33)	Group R (n=33)	P value
Mean	292.24	315.78	0.042(S)
SD	±63.77	±4.59	

Discussion

Anaesthesia for emergency surgery can be termed unplanned as the patients are not evaluated preoperatively for the surgery. Most of these patients who need emergency surgery have compromised vital function and hence are at greater risk of developing life-threatening complications like hypoxia, dysrhythmia, shock, cardiac arrest and even death. Careful selection of anaesthesia technique, drugs and dosage depending on the patient's clinical conditions are thus vital components for the safe conduct of anaesthesia. Full stomach should be assumed in such patient. RSI is an anaesthesia technique designed to facilitated rapid tracheal intubation at high risk of aspiration. The main objective of the technique is to minimize the time interval between the loss of protective airway reflexes and tracheal intubation since the airway is unprotected during this time, it is the most critical period during which aspiration of gastric content is likely to occur1. Hypoxia usually occurs during apnoea in

RSI, and is more pronounced in patients with uncontrolled coexisting diseases.

Hypoxia and its related injuries remain the main cause of anaesthesia related death and serious morbidity. Current studies have been focused on maximising the intra-pulmonary oxygen reserve to prolong non-hypoxic apnoea duration. Various technique of ‘’pre-oxygenation”, including deep breathing with high fresh gas flow of oxygen[18], application of positive airway pressure during preoxygenation[19,20] and nasopharyngeal oxygenation following preoxygenation[21,22] which can delay the onset of arterial oxygen desaturation during apnoea have been developed. The head up position has been recommended to optimise pre-oxygenation[23-26].

Succinylcholine is the most commonly used depolarizing NMBD in RSI because of its fast onset and short duration. Unfortunately, it increases muscle oxygen consumption as a result of skeletal muscle fasciculation[27] and it cause serious side-effect such as malignant hyperthermia in some sensitive cases. Rocuronium, an intermediate acting non-depolarizing muscle relaxant, has an onset of action that is more rapid than others. It is well-documented alternative to succinylcholine for intubation in RSI[7,8]. With the introduction of sugammadex, its action can be reversed within 3 minutes. Though succinylcholine provides better intubating conditions in minimum time[28,29], it causes more rapid desaturation as documented in previous studies[12]. Hypoxia resulting from this rapid desaturation becomes detrimental more so in the patients posted for emergency surgeries. Non hypoxic apnoea duration also known as period of safe apnoea is the time till the oxygen saturation reaches 88-90%. When patients desaturate below this level, their status in on the steep portion of the oxy-haemoglobin dissociation curve and can decrease to critical levels (70%) within seconds[30]. The present study investigated the non-hypoxic apnoea duration during induction of general anaesthesia using RSI technique.

In our study 66 patients were randomly allocated into 2 groups of 33 each to receive either injection suxamethonium (group S) or injection Rocuronium (group R) following induction with propofol and fentanyl. Sixty seconds after administration of neuromuscular blocking drug, face mask was removed and the patient was intubated. The tracheal tube was left open to air till saturation reached 92%. Time to desaturate was calculated from the time when the face mask was removed. The 2 groups were comparable with respect to age, sex, weight, height, BMI, Hb%, ASA status and baseline oxygen saturation.

The main finding of the study was that safe apnoea time was significantly shorter for suxamethonium 292.24±63.77 seconds compared to rocuronium 315.78±4.59 seconds (p=0.042). The rapid desaturation caused by suxamethonium may be attributed to the increased muscle oxygen consumption due to fasciculations. The result of our study corroborated with the results obtained from studies conducted by Taha et al[31](2010) and Tang et.al[12](2011).

There was no statistically significant difference between the HR immediately after intubation between group S 90.21±5.39 beats/min and group R 90.60±5.44 beats/min (p+0.768). there was no significance between group S 88.12±4.92 beats/min and group R 88.33±5.08beats/minwith respect to heart rate 2 mins post intubation.

No significance difference (p=0.934) was noted between the MAP immediately after intubation which was 82.09±2.97 mm Hg for group S and 82.15±2.99 mm Hg for group R, MAP at 2 mins post intubation 77.87±3.21 mm Hg for group S and 78.27±3.39 for group R which was statistically non-significant (p=0.630). Our results corroborated with the findings of the study conducted in 2010 by Taha et al[31].

In the present study, no intubation surge in respect to HR and MAP was noted in respect to both the groups. The supplementation of fentanyl as an agent may have resulted in the stable hemodynamic in both groups. Similar study was conducted in a study by Harris CE et al[32], who

found that administration of fentanyl 2 mcg/kg before thiopental, propofol or etomidate plus succinylcholine resulted in more stable hemodynamic profile than seen without the use of fentanyl.

According to previous studies, we constructed a desaturation model and ensured that the procedure were under control and safe[31,25], for our study we considered the safe apnoea time from the administration of the NMBD to the time when oxygen desaturation declined to 92%. It was considered as a safe end point in normal patient not at risk of developing hypoxemia because at that saturation arterial oxygen tension was acceptable and there was no significant Carbon dioxide accumulation[12].

In the present study, we used injection Propofol as the induction agent. In the original description of rapid sequence induction, Stept and Safar[1]used thiopental in 80 patients with satisfactory results. However, rapid administration of thiopental can result in serious hemodynamic side effects[33]. Dobson et al.[34] compared propofol and thiopental for RSI with rocuronium 0.6 mg/kg and found better intubating conditions in the propofol group.

Barr and Thornley[35] compared the total time to intubation when thiopental and succinylcholine were given either in rapid succession or by titration to loss of consciousness and found that the titration group had a shorter mean time to intubation (70vs78 seconds). In our study we used sleep dose technique and titrated the induction agent till loss of consciousness was achieved.

We co-administered inj. Fentanyl 2µg/kg with inj. propofol during induction. Administration of fentanyl 2µg/kg before thiopental, propofol or etomidate plus succinylcholine resulted in more stable hemodynamic than seen without the use of fentanyl[32].

Conclusion

In the emergency department, most of the patients are in a decompensated state. The effect of shunting, increased metabolic demand, anaemia, volume depletion and decreased cardiac output are synergistic in reducing the functional capacity and thereby shortening the period of safe apnoea in critically ill patient. In these cases, the neuromuscular blocking drug which causes more desaturation becomes important. From our study it was concluded that succinylcholine related muscle fasciculations has been cited as the most probable reason for this finding. Hence, in patients at high risk of desaturation rocuronium may provide a longer duration of safe apnoea and so may be a better choice as NMBD over succinylcholine.

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