Effects Of Smoking On Neuromuscular Blockade For Rocuronium

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Abstract

The purpose of the present study is to investigate the interaction of chronic smoking and the neuromuscular effects of rocuronium.

Twenty non-smokers were compared with 20 smokers who have been smoking >24 cigarettes per day for 10 years. Anesthesia was induced with propofol 2 mg kg^{-1} iv and fentanyl 2 µg kg^{-1} iv. Endotracheal intubation was performed with rocuronium 0.6 mg kg^{-1} iv.

The onset time, 25 % recovery time and recovery index were investigated. The mean onset times in the Group smokers and Group non -smokes were 61 ± 5.32 sec and 66 ± 4.12 sec respectively ($p<0.05$). The mean times of 25 % recovery in the Group smokers and Group non-smokers were 9.4 ± 1.48 min, and 14.15 ± 1.5 min respectively ($p<0.05$). The mean times of recovery index of neuromuscular blockade in the group smokers and group non-smokers were 8.5 ± 2.1 min, and 14.55 ± 2.18 min respectively ($p<0.05$).

In conclusion, smoking can change neuromuscular block effects of rocuronium.

INTRODUCTION

The primary actions at the neuromuscular transmission are acetylcholine release after an electrical stimulus from the neuromuscular junction, interaction with receptors and finally degradation of acetylcholine with acetylcholine esterase. Nicotine is an agonist-acting alkaloid substance on the nicotinic-cholinergic receptors like acetylcholine. Continuous agonistic stimuli lead to a “down regulation” and a decrease in the number of the receptors ($_1$, $_2$).

Chronic smoking leads to an increase in the concentration of blood nicotine levels. High blood nicotine levels can cause down regulation and will have an influence on neuromuscular block. Rocoroniun is a non-depolarization neuromuscular drug recently available in our daily practice.

In this study we compared the neuromuscular block duration of rocuronium between chronic smokers and non-smoking patients.

MATERIAL AND METHODS

This study was approved by the hospital ethics committee, and informed consent was obtained from the patients. Forty ASA group I-II patients who were scheduled for elective abdominal surgical operation were included. Patients with neuromuscular disease, patients using neuromuscular acting drugs, radiotherapy patients , chemotheraphy patients, patients with malnutrition and alcoholics were excluded from this study.

The patients were divided into two groups; Group Smokers (n=20) and Group non-smokers (n=20). Patients with a smoking history of more than 24 cigarettes day^{-1} and more than 10 years were included in the smokers group.

As a premedication,0.07 mg kg^{-1} im midozolam was administered 30 minutes before the operation. We monitored the patients' heart rate, invasive blood pressure, peripheral oxygen saturation (SpO_2), and end tidal carbon dioxide pressure ($EtCO_2$) by Millenia device (Millenia, Orlando, USA) perioperatively.

During the operation, patients were monitored with a TOF Guard apparatus (Organon technica, Belguim) in addition to classic monitoring. The musculus adductor pollicis muscle and nervus ulnaris were used for neuromuscular monitorization. Train of four (TOF) and Single twitch (ST) stimulis were used in this study. Every 10 seconds, 4 TOF stimuli was performed with 2 hertz submaximal frequency and a 0.2 msn time interval.

Anesthesia was induced with propofol 2 $mg.kg^{-1}$ iv and fentanyl 2 µg, kg^{-1} iv. After the induction of the anesthesia, before the administering of rocuronium, the TOF Guard was calibrated. The temperature of the hand that monitored with the TOF Guard was held at over 33°C and was increased when needed. Following the Rocuronium 0.6 $mg.kg^{-1}$ administration, when ST was blocked 100 %, the trachea was entubated. During the operation, every 5 minutes TOF stimulation was used repeatedly.

Both of the groups were mechanicaly ventilated with FiO_2; %50, oxygen and air mixture; tidal volume of 10 $ml.kg^{-1}$and a respiration frequency of 10 sec^{-1}. Anesthesia was maintained with 1-2 % Sevoflurane. During the operation, the 0.1$mg.kg^{-1}$ rocuronium and 1 $mgr.kg^{-1}$ fentanil were repeated .

At the end of the operation, in order to reverse the neuromuscular blockade 0.01 $mg.kg^{-1}$ atropin and 0.02 $mg.kg^{-1}$ neostigmin were administered.

In both groups, neuromuscular blockade (NMB) onset time (interval between rocuronium administration and 100 % blockade of ST stimuli), 25 % recovery time (time interval between the rocuronium administration and the time interval that T1 response recovery 25 %) and recovery index (time interval between 25 % to 75 %) were recorded.

For the statistical analysis of the collected data, Student's t and chi square tests were used. Values of $p< 0.05$ were accepted as statistically significant. Results were given as the mean ± standard deviation.

Power analyses were done before the study to determine the minimum patient number. We determined the patient number as a minimum of 16 with ?: 0.05 and ?: 95 %.

RESULTS

Patients and operation characteristics are shown in Table I and the neuromuscular effects are shown in Table II .

Figure 1

Table I: Patients and operation (medium ± standard deviation)

	Group smokers (n=20)	Group nonsmokers (n=20)
Age (year)	32.3 ± 4.46	33.1 ± 4.39
Weight (kg)	65.5 ± 9.09	64.8 ± 8.5
Sex (F/M)	8/12	11/9
Operation duration (min)	75± 11	81± 14

Figure 2

Table II: Comparison of the neuromuscular effects of the groups (mean ± standard deviation)

	Group smokers (n=20)	Group Nonsmokers (n=20)
Onset time (sec)	61 ± 5.32*	66 ± 4.12
25 % recovery time (min)	9.4 ± 1.48*	14.15 ± 1.5
Recovery index (min)	8.5 ± 2.1*	14.55 ± 2.18

p<0.05*

In both groups age, sex, weight information and operation duration times were similar and had no statistical difference.

The mean time of onset in the Smokers Group and the Non-smokers Group was 61 ± 5.32 sec and 66 ± 4.12 sec respectively ($p<0.05$). The mean time of 25 % recovery time in the Smokers Group and the Non-smokers Group was 9.4 ± 1.48 min, and 14.15 ± 1.5 min respectively ($p<0.05$). The mean times of recovery index of neuromuscular blockade in the Smokers Group and the Nonsmokers Group were 8.5 ± 2.1 min, and 14.55 ± 2.18 min respectively ($p<0.05$).

CONCLUSION

Excessive smoking habit is described as a habit of having smoked for more than 10 years and more than 24 cigarettes per day. ($_3$). In 1988 in our country percentages of smoking habits were; for citizens over 15 years of age: males: 62.8 %, females: 24.3 %, the whole population: 43.6 % ($_4$). Chronic smoking habit has a bad influence on respiratory and circulatory as well as all other systems. Smoking can influence liver drug metabolism by causing enzyme induction and has harmful effects on the blood vessels and

liver blood stream ([5]).

Rocuronium is a steroid structured non-depolarizing NMB and has been recently available in our country. Even we do not have enough knowledge about the drug elimination, the 33 % of the drugs removal from the kidneys led us to believe that the remaining part is metabolized by the liver ([6]).

Teiria et al ([7]) compared the doses of the verocuronium that maintains the NM blockade around 90-98 % and the verocuronium's ED95 at the propofol-alfentanil-N2O anesthesia between smoker and non-smoker patients. ED95 61.38 mg.kg–1 was found in smoker group and 47.49 mg.kg –1 was found in the non-smoker group. The doses of the verocuronium that maintains the neuromuscular blockade around 90-98 % were found to be 96.80 mg.kg –1hour^{-1} and 72.11 mg.kg –1 hour^{-1} in the smoker group and non-smoker group respectively. In the smoker group, after the decrease in the verocuronium's clinical effect interval, they noticed a 25 % increase in the verocuronium's maintenance dose. They think the reason may be an alternation in the receptor level or the verocuronium's liver metabolism.

Rautoma et al ([8]) showed a 20% increase in hourly rocuronium administration. Puura et al ([9]) found lower maintenance doses of atracurium in smokers than non-smokers. In these studies the differences between neuromuscular blockers may be attributed to the atracurium's free and ester hydrolises from liver and Hoffmann elimination. On the other hand, steroide structured rocuronium and verocuroniums could be eliminated by liver cytocrome 450. In our study rocuronium's neuromuscular effect, onset time, 25 % recovery time, and the recovery indexes all decreased in the smoker group when compared with the non-smoker group. Chronic smoking state causes an elevation in blood nicotine levels and these increased levels may lead to a continuous agonistic effect and thus will lead to a down regulation in the nicotinic receptors. As a result, in the smoker group lower nicotinic receptors in the neuromuscular junction can be blocked by rocuronium more rapidly than non-smoker group. We attributed the short clinic effect interval of the rocuronium in the smoker group to the induction of the liver enzymes and the increase of the metabolism of the drug in the liver.

As a conclusion, smoking habit may have an influence on neuromuscular block. We pay attention to clinic practice with rocuronium, intubation conditions can obtain rapidly in smoker patients. However in contrast to that action, because of the shortness in clinic effect interval, excessive doses in maintenance levels may be needed.

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