Comparison of Different Induction Doses of Rocuronium and Vecuronium in Neuroanaesthesia Practice

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Objective: To evaluate the efficiency of use of rocuronium and vecuronium in different dose regimens in neuroanaesthesia practice in terms of intubation time and first additional dose requirement.

Methods: Sixty-eight neurosurgery patients with intracranial mass that were operated on were included in our study. Patients were randomly divided into 4 groups according to the induction dose of neuromuscular blocker (NMB) as: Group 1: Vecuronium 0.1 mg kg⁻¹, Group 2: Priming, 20% of total vecuronium (0.1 mg kg⁻¹) needed for induction injected 5 minutes before induction and then the rest used for induction, Group 3: Rocuronium group: 0.6 mg kg⁻¹, Group 4: Rocuronium with rapid-sequence induction dose (RSID) (1.2 mg kg⁻¹). TOF (Train of four) test was used to decide on intubation and an additional NMB dose during surgery. Intubation quality, time from induction to intubation, time until the first additional NMB dose and subsequent NMB dose intervals were recorded.

Results: The RSID of rocuronium provided a significantly shorter time period for intubation against the other groups. Also, the time period from induction to first additional NMB requirement was significantly longer in the RSID group than the others. There were no statistically significant differences between the groups' in terms of time period for monitorisation, positioning and start of surgery.

Conclusion: With the use of RSID of rocuronium, it was seen that excellent intubation quality is provided at around 1 minute and, with its longer duration of action until a first additional dose, it covers the time period for monitorisation, positioning and start of surgery. Because of these effects, we think that RSID of rocuronium may be a better choice of dose regimen for neuroanaesthesia practice.

Key Words: Rocuronium, vecuronium, neuromuscular blockade, priming, neurosurgery

Introduction

Patients who are submitted to surgery for intracranial space-occupying lesions generally have high intracranial pressure. Therefore, reduction of the intracranial pressure and decreasing the volume of brain tissue and cerebrospinal fluid are among the most important goals of anaesthesiologist to avoid brain damage while cranium and dura mater are opened and to achieve easy access to the lesion that is to be resected (1). Maintaining the hemodynamic stability in the period from anaesthesia induction to the beginning of the surgery is of importance in achieving this goal. Choosing the right neuromuscular blocking agent (NMBA) and method of administration are the key points for successful management of this period.

For the close follow-up of hemodynamic status and fluid balance of the patient, invasive monitoring for arterial blood pressure, central venous pressure and urine output are usually required during neurosurgery operations (1). Establishing invasive monitoring, positioning the patient and placing sterile drapes before the operation, requires a long period of time. Although patients may be exposed to painful stimuli during this period, as the operation has not yet begun, a state of mild anaesthesia is usually required to maintain the physiological functions of the patient. The time from the induction of anaesthesia to the onset of surgery is the period that the anaesthesiologist works most intensely, and a common and unwanted condition during this period is the movement of the patient due to changes in the depth of anaesthesia. This may increase brain blood flow and cause further increase in intracranial pressure which makes it difficult to prepare the brain for surgery. Furthermore, this may cause herniation, permanent neurologic deficits and even death. Therefore, it is of crucial importance to prevent movement during both induction and maintenance of anaesthesia in patients with high intracranial pressure. It is possible to increase the quality of intubation by using different NMBA application methods. There have been studies showing that administration of 20% of NMBA induction dose about 3-5 minutes before induction (defined as rapid sequ-

ence induction or priming) not only shortens the duration for achieving complete blockage but also increases the quality of intubation (2-7).

In the present study, we aimed to test the benefits of priming and rapid sequence induction of vecuronium and rocuronium, which are the most commonly preferred non-depolarizing NMBA, by comparing them with doses used in standard practice during anaesthesia induction of neurosurgery operations. For this purpose, we compared the time from anaesthesia induction to the development of complete block and to the first maintenance dose. These were interpreted together with the time to establish invasive monitoring, patient positioning time and the time to surgery, and the benefits, these approaches brought to the anaesthesia practice, were evaluated.

Methods

After the study was approved by the Ethics Committee of Istanbul University Istanbul Medical Faculty (Approval date: 01.08.2008, 2008/51) and Ministry of Health Drug Control Committee (21-7-2008, 046766), 68 patients, hospitalized in Neurosurgery clinic, who were scheduled for surgery for intracranial space-occupying lesions under general anaesthesia, ranging in age from 18 to 70 years, were included in the study. Informed consents of the patients were obtained before the study procedures were started. Patients with advanced liver and renal failure, pregnant patients, patients who had a history of long-term antiepileptic use and those who did not give consent to take part in the study were excluded. Anaesthesia was induced with midazolam at a dose of 0.04-0.1 mg kg⁻¹, propofol at a dose of 2 mg kg⁻¹ and fentanyl at a dose of 1-2 mcg kg⁻¹ in all patients. Dose calculations were based on patients' body weights. The patients were randomly allocated into two groups by sealed-envelope technique and they received NMBA according to the group they were assigned. Maintenance of anaesthesia was performed using 40-50% of oxygen-air mixture and 1-2% of sevoflurane and remifentanyl infusion at a rate of 0.01-0.1 mcg kg⁻¹ min⁻¹. The patients were assessed in 4 groups based on the type and dose of NMBA they received.

Group 1: Vecuronium group: Induction was performed with a dose of 0.1 mg kg⁻¹.

Group 2: Vecuronium, priming group: The patients received 20% of the total Vecuronium dose (0.1 mg kg⁻¹), calculated according to the body weight, 5 minutes before the induction of anaesthesia and the rest of the dosage was given after the administration of the hypnotic agent.

Group 3: Rocuronium group, Induction was performed with a dose of 0.6 mg kg⁻¹.

Group 4: Rocuronium, rapid-sequence induction group; induction was performed using rocuronium at a dose of 1.2 mg kg⁻¹.

Table 1. Goldberg's scale for evaluation of intubation

Score	Description
Excellent	(1) Easy tracheal tube insertion, immobile open vocal cords, no reactive cough
Good	(2) Open vocal cords, mild reactive cough
Poor	(3) Moderate reactive cough, resistance in vocal cords
Impossible	(4) Uncontrolled cough with closed vocal cords, resistance against tube

Neuromuscular monitoring was performed using acceleromyography (Datex Neuromuscular Transmission Monitor "NMT", Helsinki, Finland). Monitoring was performed by the same anaesthesia technician who was experienced in neuromuscular monitoring in all patients. Sensor was placed at midline on the distal anterior part of the thumb and adductor pollicis muscle was prepared for recording. After the hand and forearm were placed in supine position, the positive and negative nerve stimulating electrodes were placed on the skin over the ulnar nerve with the positive electrode at the distal.

Standard monitoring included electrocardiography (ECG), non-invasive arterial pressure and pulse oximetry. During spontaneous breathing with 100% oxygen through a face-mask, the patients were sedated with midazolam and fentanyl at doses described above. After sedation, train-of-four (TOF) test was performed (used as the reference value). Thereafter 2 mg kg⁻¹ of intravenous propofol was administered and after the loss of the eyelash reflex, NMBA was administered. Upon disappearance of responses to TOF stimuli (TOF: 0) the patients were underwent orotracheal intubation. The time interval between the administration of NMBA and disappearance of responses in TOF test was defined as "time to complete block". Quality of intubation was scored using Goldberg's scale (Table 1) (8).

Maintenance dose of NMBA was set at one third of the initial dose and repeated upon reversal of >20% of the blockade in TOF measurements, performed in one minute intervals. Time to first NMBA requirement after induction and subsequent intervals for repeated doses were determined based on reversal of >20% of blockade in TOF measurements. The intervals were recorded and averaged for each group. Invasive arterial blood pressure, oxygen saturation, ECG, CVP, end-tidal carbon dioxide (ETCO₂) and body temperature were monitored.

In order to provide hemodynamic stability during placement of the pin head holder, 0.5 mg kg⁻¹ of intravenous esmolol was given in one minute. The infusion was repeated at the same dose but more slowly (within 4 minutes) in patients who still had high blood pressure and tachycardia. Time between induction and achievement of complete block, the time to completion of all catheterization procedures (invasive blood pressure, CVP, temperature, hourly urine output) and the time to completion of patient positioning and the time to onset of surgery were also recorded.

Statistical analysis

Data were presented as mean±standard deviation. GraphPad Prism 5.01 statistical software was used for analyses. Male/female and ASA values were compared using chi-square test and the remaining data were compared using non-parametric Kruskal Wallis ANOVA test. When the difference was found significant, Dunn's test was used to determine which groups were different from each other. The differences were considered significant if the p value was less than 0.05.

Results

A total of 68 patients, 17 patients in each group, were analysed in the present study. There was no significant difference between the groups in regard to age and body weight (Table 2)

There was a significant difference among the groups in regard to time interval between induction and achievement of complete block ($p=0.0001$). Intergroup comparisons revealed that time to achievement of complete blockade was signifi-

cantly shorter in Group 4 than that in all the other groups but there was no significant difference among groups other than group 4 (Table 3).

Similarly, the time interval from induction to first NMBA requirement was significantly different among the groups, and the time to first NMBA requirement was significantly longer in Group 4 than that of Group 3 (Table 3). The time to first NMBA requirement was almost equal to the time to onset of surgery in vecuronium groups (Group 1 and 2), whereas the interval was approximately 15 minutes longer than the time to onset of surgery in Group 4 and it was quite shorter than the time to onset of surgery in group 3.

Intubation was performed upon disappearance of all responses to TOF testing, and there was no significant difference among groups with regards to the quality of intubation, which was tested using Goldberg's scale (Table 3).

There was no significant difference among groups in terms of monitoring time, positioning time and time to onset of surgery

Table 2. Patient characteristics

	Group 1 Vecuronium 0.1 mg kg ⁻¹	Group 2 Vecuronium Priming	Group 3 Rocuronium 0.6 mg kg ⁻¹	Group 4 Rocuronium RSI- 1.2 mg kg ⁻¹	p
Patient (n)	17	17	17	17	
Male/Female	7/10	7/10	8/9	9/8	0.65
Age (years)	40.1±14.1	43.6±27.5	44.5±16.1	45.1±16.3	0.70
Weight (kg)	64.1±11.7	62.0±23.1	66.9±10.2	67.2±14.1	0.96
ASA physical status I/II	9/8	8/9	8/9	7/10	0.92
RSI: Rapid sequence induction					

Table 3. Time to achievement of complete block, quality of intubation and intervals for curare requirement

	Group 1 Vecuronium 0.1 mg kg ⁻¹	Group 2 Vecuronium Priming	Group 3 Rocuronium 0.6 mg kg ⁻¹	Group 4 Rocuronium RSI- 1.2 mg kg ⁻¹	p
Time to achievement of complete block (TOF:0) (second)	168.7±49.2	151.6±64.3	125.9±45.1	75.6±47.4*	0.0001
Goldberg's scale for intubation	1.44±0.63	1.33±0.48	1.40±0.63	1.35±0.60	0.09
Time to first dose requirement (TOF:0-TOF 20%) (min)	61.1±22.0	57.0±30.4	34.2±14.7	79.0±38.6**	0.001
Repeated dose intervals TOF: 0-TOF: 20% (min)	52.4±15.3	62.3±11.7	37.8±9.6	51.9±21.6	0.08
n	17	17	17	17	
Dunn's post-test: *: $p<0.01$; Group 4 vs. the other groups. **: $p<0.05$; Group 3 vs. Group 4; RSI: Rapid sequence induction					

Table 4. Monitoring time, positioning and surgery times

	Group 1 Vecuronium 0.1 mg kg ⁻¹	Group 2 Vecuronium Priming	Group 3 Rocuronium 0.6 mg kg ⁻¹	Group 4 Rocuronium RSI-1.2 mg kg ⁻¹	p
Monitoring time (min)	24.2±8.3	25.6±4.0	24.6±8.2	27.1±6.4	0.34
Positioning time (min)	11.8±4.3	16.0±6.5	18.6±10.9	13.4±5.2	0.52
Time to the onset of surgery (min)	58.5±10.6	56.0±7.9	55.3±20.1	64.4±13.2	0.21
Operation time (min)	299.2±109.1	366.7±61.1	368.4±163.2	374.9±99.2	0.18
Body temperature (C°)	35.4±0.8	35.4±0.5	35.6±0.7	35.7±0.5	0.25
n	17	17	17	17	
RSI: Rapid sequence induction					

and NMBA requirement intervals. Body temperature values were similar throughout the operation in all groups (Table 4).

Discussion

In the present study, it was observed that patients who underwent surgery for intracranial mass under general anaesthesia, treated with rapid-sequence induction with rocuronium had a significantly shorter time to achievement of complete block than those who received anaesthesia with or without priming. In addition, the time to requirement of the first dose of NMBA was prolonged till the onset of surgery. The patients who received rapid sequence induction with rocuronium and those who received priming with vecuronium had better intubation quality scores than those in the other groups, although the difference was not statistically significant.

Although the quality of intubation was better in the priming group, the time to achievement of complete block was not shortened. The reason for this may be that priming shortens the time to onset of action and contributes to rapid-sequence induction, but does not affect the time needed to achieve complete NMBA effect, as previously demonstrated by other studies (9). However, when viewed from the perspective of neuroanaesthesia, priming dose seems not to have any additional benefits in conditions where rapid-sequence anaesthesia is not required. Double vision, focusing problems and occasional respiratory distress has been reported in patients who received priming doses (10). No such problems were encountered in our study, as the priming dose was given under sedation and while receiving oxygen via a facemask.

Advanced age, dental prosthesis, leanness and collapsed cheeks are common features observed in neuroanaesthesia patients, especially in those with intracranial tumours. Although less frequently observed, big arched noses and facial abnormalities are features that make mask ventilation difficult. Due to such reasons, problems with mask ventilation are encountered in 1.6-5% of anaesthesia cases (11, 12). Therefore, in some patients, intubation may be required to be performed before complete NMBA action is achieved. This may lead to movement of the patients during intubation and may further increase intracranial pressure, which is already at critical levels, especially in neurosurgery patients. As a result, it may become difficult to reduce intracranial pressure during the operation and patient may become subject to increased operative risk. In studies where rapid-sequence induction with rocuronium was evaluated, succinylcholine was compared with rocuronium at a dose of 1.2 mg kg⁻¹ and muscle paralysis, quality of intubation and time to onset of action were evaluated. While excellent intubation scores were achieved by both drugs, time to apnoea onset was not significantly different. However, it was observed that patients who received succinylcholine had faster recovery than those who received rocuronium (2-5). Although the prolonged action of rocuronium in rapid sequence induction doses, despite good intubation conditions, is considered as troublesome, this pro-

longation may be advantageous in long lasting neurosurgery operations, as was observed in our study.

Mogarian et al. (2) in their study, in which they compared rocuronium at different doses, vecuronium at a dose of 0.1 mg kg⁻¹ and succinylcholine at a dose of 1 mg kg⁻¹, found that the onset of action of rocuronium (at a dose of 1.2 mg kg⁻¹), measured by TOF, was 55±14 seconds. This time interval was slightly longer in our study (75.6±47.4 seconds). This difference may be attributed to the fact that most of our patients had been started on acute anticonvulsant therapy before the operation (for a week or a shorter duration). In the study mentioned above, time to onset of action of rocuronium at a dose of 0.6 mg kg⁻¹ and vecuronium at a dose of 0.1 mg kg⁻¹ was 89±33 seconds and 144±39 seconds, respectively. In our study, the corresponding figures were 125.9±45.1 seconds and 168.7±49.2 seconds, respectively. Although the above-mentioned study reported statistically significant differences in time intervals, only rocuronium given at a dose of 1.2 mg kg⁻¹ produced statistically significant difference in our study. Similar to our study, the duration of action of rocuronium was reported to increase to two-folds when it was given at a dose of 1.2 mg kg⁻¹ compared to 0.6 mg kg⁻¹.

Prolonged action of rocuronium in rapid sequence induction was evaluated in patients on chronic anticonvulsant treatment. In one study, where rocuronium was given at doses of 0.6 mg kg⁻¹ and 1.2 mg kg⁻¹, it was observed that recovery was extremely faster at doses of 0.6 mg kg⁻¹. Therefore, it was proposed that patients who receive anticonvulsants should be given rocuronium at doses of 1.2 mg kg⁻¹ under close monitoring (13).

Hepatic metabolism of non-depolarizing steroidal NMBAs increases in patients who receive anticonvulsants (especially phenytoin and carbamazepine) as cytochrome p450 is induced in the liver. Therefore, these patients may require higher doses at frequent intervals. Because of the fact that most of the patients who require intracranial interventions receive anticonvulsants, induction with high-dose rocuronium not only improves the quality of intubation but also prolongs the time to the initial NMBA dose owing to its prolonged time of action. We think that this fact provides an important advantage in long lasting operations such as intracranial operations.

Using rocuronium at doses of 1.2 mg kg⁻¹ in induction, the anaesthesiologist may benefit from working without the need of giving additional doses of NMBAs during monitoring and positioning of the patient until the operation starts. The time from induction until the onset of surgery is longer in neurosurgery than that in most other type of operations. During this period in which surgical stimuli does not occur, attenuation of anaesthesia is inevitable to achieve hemodynamic stability and movements of the patient might be avoided by the use of NMBAs under neuromuscular monitoring. The placement of pin head holders creates a strong stimulus and

causes hypertension in patients with intracranial masses. At this stage, additional doses of opioids and/or NMBAs are mostly required. In our study, in addition to short-acting opioid infusion which was started after induction, we also used a short-acting beta blocker, esmolol, during the placement of the head holder. Hemodynamic stability during positioning was provided in this way. As we used neuromuscular monitoring, the NMBA requirements of the patients were noticed earlier and repeat doses were administered. No movement was observed in the patients during positioning and none of the patients needed additional doses of NMBAs. Although about 43% of the patients included in the study, required NMBAs before the operation started, NMBAs were required by only 17.6% of the patients receiving rapid-sequence induction with rocuronium. Thus, using neuromuscular monitoring and rapid sequence induction with rocuronium before neurosurgery operations, the problems related with patient movement may be decreased 2.5 fold.

Our study has important limitations. These include lack of evaluation of problems that could arise from unwanted patient movements during the operation and anticonvulsant use of the patients. The problems that can arise from unwanted patient movements vary in individual patients and may range from a mild increase in intracranial pressure to development of permanent neurological deficits. By the virtue of medical ethics, we could only make speculative comments about the elimination of this unwanted effect which was provided by the use of neuromuscular monitoring. Considering the anticonvulsant treatment, the patients who are admitted to hospital for intracranial surgery are often initiated on such treatment, at least for prophylactic purposes. Although treatment with anticonvulsants changes the duration of action of NMBAs when the treatment lasts more than one month, effects of short term use is still unknown (14). This uncertainty may be seen in the differences of the standard deviations of the groups regarding the time to achievement of complete block and the time until the first requirement of NMBA.

Conclusion

Among the non-depolarizing NMBAs, rocuronium stands out by having the shortest onset of action. In our study we observed that rocuronium shortened the time to achievement of complete block and provided a good intubation quality. Again, owing to its prolonged duration of action at this dose, it may cover the preparation stage until the start of the operation (although it may vary according to the conditions in individual clinic); we think that rocuronium may be an appropriate option in neuroanaesthesia practice.

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Informed Consent: Written informed consent was obtained from patients who participated in this study.

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