



COMPARATIVE EFFECTIVENESS OF ROCURONIUM VERSUS VECURONIUM ON ONSET TIME FOR INTUBATION, INTUBATION CONDITIONS AND DURATION OF ACTION: A RANDOMIZED, CONTROLLED STUDY ON PATIENTS UNDERGOING GENERAL ANESTHESIA.

KEYWORDS

Intubation condition, Neuromuscular blockade, rocuronium. Rapid onset

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ABSTRACT

Background and Aim: Due to paucity of data, we compared onset time, intubation conditions and duration of action of Rocuronium versus Vecuronium.

Methods: 60 patients matching study inclusion were randomly divided in group R(rocuronium, n=30) or V(Vecuronium, n=30). Onset times, scale of intubating conditions and duration of action were measured in both groups and compared. We also assessed hemodynamic responses post induction in both groups.

Results:

Out of total 60 patients, group R showed lesser time taken for intubation i.e. within 60 and 90 secs only as compared to group V(i.e. extended upto 120 and 150 sec). In group R, intubating conditions were excellent in 24 patients (80%) whereas 11 patients (36.6%) in group V. In both groups, hemodynamic difference was statistically non-significant.

Conclusion:

Considering proven superiority for desired clinical outcomes, rocuronium could be a considerable option for neuromuscular blockade.

INTRODUCTION:

Rapid Onset of a neuromuscular blocking agent is one of the important properties to be considered for its choice in endotracheal intubation. For a long period, "Suxamethonium" – a muscle relaxant was practised as the gold standard for its rapid onset, brief duration and good intubation conditions. However, its side effects (Vervloet D Fau - Nizankowska et al.) associated with its mechanism of action posed a clinical need of newer research molecules without such side effects. This led to advent of "Vecuronium" and "Atracurium" with shorter onset times (Pasko-Majewska, Owczuk R Fau - Wujtewicz, & Wujtewicz). However, these drugs were less efficient to facilitate rapid sequence intubation (Davison KI Fau - Holland & Holland) – the endowed characteristic of its successor research drug named – Rocuronium (Patanwala, Stahle Sa Fau - Sakles, Sakles Jc Fau - Erstad, & Erstad). It is a non-depolarizing monoquaternary aminosteroid compound. Due to paucity of data on comparative effectiveness of R versus V, we aimed to investigate non-inferiority of R in onset time, intubation conditions and duration of action compared to V. We also aimed to evaluate comparative hemodynamic difference induced by both drugs.

MATERIALS AND METHODS:

After obtaining institutional approval at Dhiraj General Hospital, Pipariya, sixty (n=60) consented patients of ASA I&II of both sexes, aged 18 to 60 years, weighing 42 to 80 kgs undergoing general anesthesia and surgery were included in double blinded parallel-group randomized fashion with two equal sized (n=30 in each group) groups: Group R (Rocuronium intubating dose 0.6mg/kg and maintenance dose 0.15mg/kg) and Group V (Vecuronium intubating dose 0.1mg/kg and maintenance dose 0.02mg/kg). The patients with neuromuscular disease or disorder, increased risk of pulmonary aspiration, Mallampatti grade III & IV, medication known to influence neuromuscular function, anticipated difficult intubation, previous administration of antihistaminic or antibiotics 24 hrs before surgery were excluded from study. Pregnant female patients were also excluded from the study.

Clinical Intervention:

A. Patient Preparation:

After detailed pre-anesthetic evaluation with all patients taking no oral intake 6-8 hours prior induction, peripheral venous line was secured with 18 Gauge venous cannula and I.V infusion was started. Baseline H/R, BP, SpO₂ were recorded and ECG was monitored using BPL Excello Pro monitor followed by premedication with Inj.

Glycopyrrolate 0.2 mg, Inj. Ondansetron 4 mg, Inj Midazolam 1mg and Inj Tramadol 1.5 mg/kg I.V. 10 min before induction.

B. Induction and maintenance:

All patients were pre-oxygenated with 100% O₂ for 3 minutes. Surface electrode were fixed on ulnar side of volar surface of wrist and connected to peripheral nerve stimulator. All patients were induced with Thiopentone 5-7 mg/kg I.V. After the loss of consciousness (i.e. loss of eyelid reflex), Train of Four (TOF) reading was obtained with peripheral nerve stimulator (INMED make, model Ns100).

The response to stimulation of ulnar nerve at the wrist was monitored using surface electrodes placed after cleaning the skin. A supramaximal stimulus was delivered using frequency of 2 Hz and a current strength ranging 30-50 mA. The number of responses of adductor pollicis following ulnar nerve stimulation at the wrist was counted. After recording baseline TOF reading, the test neuromuscular blocking drug was injected. The patients randomly received an injection of equivalent doses of either Rocuronium 0.6 mg/kg (Group -R) or Vecuronium 0.1mg/kg (Group-V) for tracheal intubation. The response of adductor pollicis to a TOF stimulation every 15 seconds was monitored.

After administration of muscle relaxant endotracheal intubation was attempted every 30s in beginning, 60s after drug administration until intubation could be achieved with good or excellent condition and TOF count was noted at the time of intubation. The intubating condition was evaluated and score on a scale based on Cooper et al (Gupta & Kirubahar, 2010) grading was noted. Systolic BP, diastolic BP, HR were recorded at 1,5,10,15 minutes after intubation and thereafter every 15 minutes throughout the surgery in both groups.

Table - 1 : Cooper et al. Score of Intubating conditions' scales

Score (Cooper et al) (Cooper, Mirakhur Rk Fau - Clarke, Clarke Rs Fau - Boules, & Boules)	Jaw relaxation	Vocal cords	Diaphragmatic response
Excellent	Complete	Open	None
Good	Moderate	Slight moving	Slight movement
Fair	Minimal	Closing	Coughing
Poor	None	Closed	Bucking

All patients were intubated with appropriate size cuffed portex oral ET tube. The ET tube was secured in place after checking for adequate air entry in both lung fields and the cuff was inflated. Thereafter anaesthesia was maintained with N₂O, O₂ & Isoflurane using Bain circuit. Neuromuscular function was monitored once in 15 seconds with TOF. When the 2nd twitch of TOF recover, a further increment of Rocuronium 0.15 mg/kg in Group R and Vecuronium 0.02 mg/kg in Group V was given. Thereafter TOF was recorded once in 60 seconds.

Duration was taken as the time from the end of inj. of Neuromuscular blocker (NMB) to recovery of 2nd response to TOF. Surgical relaxation was maintained at loss of 3 responses to TOF and at the appearance of 2nd response to TOF. The maintenance dose of NMB was supplemented in dose of rocuronium 0.15 mg/kg or vecuronium 0.02 mg/kg.

C. Recovery:

At the end of surgery and after recovery of 3rd response to TOF, patients were administered Inj. Neostigmine 0.05mg/kg and Inj Glycopyrrrolate 0.008mg/kg. Extubation was done after satisfactory reversal and throat suction. Adequate recovery from NMB was judged by clinical observation like ability to open eyes widely, protrusion of tongue; sustain head lift for 5 seconds, hand grip and ability to cough. Adequate NM recovery was assessed by number of twitch present to TOF at the end of 5 minutes after administration of reversal. Any clinical signs of histamine release (rashes, bronchospasm or hypotension) were observed throughout the surgical period. All patients were monitored for next 24 hours post operatively in surgical ICU. Any untoward effects were noted and recorded.

Data Analysis:

The collected data was analysed using the Statistical software namely SPSS 11.0 and Microsoft Word and Microsoft Excel were used generate graphs and tables for analytics presentation. The inferences based on 'p' value were made as follows:

p>0.05 – Not significant
p<0.05 – Significant
p<0.01 – Highly significant
p<0.001 – Very highly significant

RESULTS:

Demographics:

Both groups (Group R and Group V) were found comparable in terms of age, weight distribution and gender with no statistical significant difference (p>0.05).

Table 2 : Baseline Characteristics – Age, Gender and Weight(N-Not Significant)

	Group R	Group V	P value
Mean age	40.43±11.02	42.43±11.22	0.4889(NS)
Mean wt.	57.97±9.76	57.13±8.39	0.7241(NS)
Sex(M/F)	12/18	15/15	1.000(NS)

Time taken for Intubation in secs:

Patients in group R were found to have lesser time taken for intubation ie. within 60 and 90 secs only as compared to those in group V (i.e. extended upto 120 and 150 sec). Also, major proportion of patients with accomplished intubation (n=22/30) were found in group R compared to only one patient (n=1/30) in group V within first 60 secs post induction. Another important observation was delayed accomplishment in intubation in major proportion of patients in group V (n=19/30 and n=7/30 within 120 and 150s respectively).

Table 3 : No. of patients with accomplished intubation based on time taken for intubation

Time(within n secs)	Group R		Group V	
	No	%	No	%
60	22	73	1	3
90	8	26	3	10
120	0	0	19	63
150	0	0	7	23

Intubation conditions

In group R, intubating condition were excellent in 24 patients (80%) whereas only 11 patients (36.6%) in group V.

Table 4: Comparative intubation conditions in both study (group R) and control group (group V).

Group	Excellent	Good	Fair	Poor
Rocuronium	24(80%)	6(20%)	0	0
Vecuronium	11(36.6%)	14(46.6%)	4(13.3%)	1(3.3%)

Train of Four

In group R, till first twitch out of 4, 7 patients (%), underwent successful neuromuscular blockade at adductor pollicis, whereas none in case of group V. Considering failure of blockage, no of patients were more in group V (n=15) as compared to those in group R (n=6).

Table 5 : Comparative response to TOF for both groups (Group R and V)

TOF	Group R		Group V	
	No	%	No	%
0 / 4	2	6.6	-	
1 / 4	5	16.6	-	
2 / 4	8	26	4	13.3
3 / 4	9	27	11	36.6
4 / 4	6	20	15	50

Hemodynamic Changes:

In both groups, heart rate, systolic and diastolic blood pressure showed statistically non-significant difference at 5 mins post intubation.

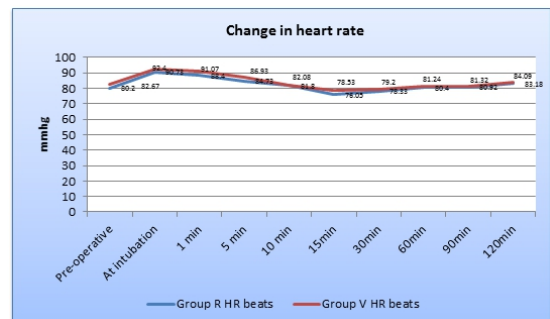


Fig 1: Comparative HR trend in both groups

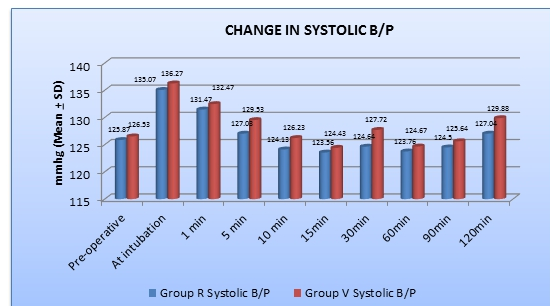


Fig2: Comparative SBP trend in both groups

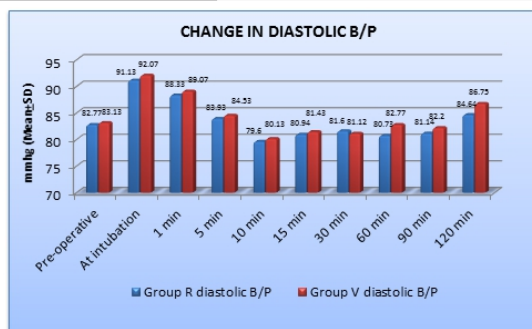


Fig 3: Comparative DBP trend in both groups

DISCUSSION:

Advent of neuromuscular blocking agent has expanded new horizons in anaesthetic practice and led the modern era of surgery in field of cardiothoracic, neurological and organ transplantation sciences. In 1983, all the requirements of an ideal neuromuscular block was mentioned (Krieg N Fau - Mazur, Mazur L Fau - Booi, Booi Lh Fau - Crul, & Crul), which included rapid onset time, excellent intubation conditions and shorter duration of action. Though vecuronium and rocuronium demonstrated promising clinical benefit, no robust data was found to determine either one's superiority. Present study was a comparative effectiveness study between rocuronium and vecuronium on their onset times, intubation conditions category and duration of action during general anesthesia.

To rationalize use of muscle relaxants in correlation with proper assessment of neuromuscular transmission during induction and maintenance, we adopted "Train of Four" stimulation of ulnar nerve at wrist along with monitoring of neuromuscular function as per recommendations in previous evidence (Ali). Moreover, evaluation approach for intubation conditions was similar to that adopted in previous studies (De Haes, Eleveld Dj Fau - Wierda, & Wierda), (Mazurek et al.) i.e. within 60 secs, first attempt of intubation and afterwards at every 30 secs interval with attempt of intubation, continual assessment of intubation conditions. Additionally, there was no administration of inhalational anesthetic or opioid after muscle relaxant administration till intubation.

Similar studies by Alvarez-Go`mez et al. (Alvarez-Gomez et al.), Van De Brock et al. (van den Broek, Hommes Fd Fau - Nap, Nap HJ Fau - Wierda, & Wierda) David G. Whalley et al. (Whalley, Maurer Wg Fau - Knapik, Knapik Al Fau - Estafanous, & Estafanous), found rocuronium effective to facilitate excellent intubation conditions at 60 secs i.e. early intubation vs 120 secs with vecuronium with the same dose i.e. 0.6 mg/kg rocuronium or 0.1 mg/kg vecuronium, which matched with our findings. Consistent superiority like previous studies (England, Margaron Mp Fau - Feldman, & Feldman), (Chatrath, Singh I Fau - Chatrath, Chatrath R Fau - Arora, & Arora) in facilitating "excellent" intubation conditions in more number of patients in rocuronium group than those in vecuronium group was also found in our study. Not only more number of patients, but also major proportion of patients in R group was found to have "excellent" intubation conditions. Our results coincided with those presented by Meistelman et al. and Donati et al. (Donati, Meistelman C Fau - Plaud, & Plaud) that there was less patients having failure in achieving complete neuromuscular blockade at 4th twitch of train of four (TOF) in rocuronium group compared to those in vecuronium group. Except study with maintenance dose using enflurane (Kim, Joshi Gp Fau - White, White Pf Fau - Johnson, & Johnson) with duration of action of initial dose of rocuronium upto 45 mins vs 52 mins in case of vecuronium, our study showed longer duration of action of initial dose of rocuronium i.e. ranging from 26 to 35 mins, which was consistent with similar evidences (Whalley et al.), (Xue et al., 1998), (Swen et al.), (Suzuki et al.), (Gan et al.) previously published. This also was followed by no further increase in maintenance dose,

which was comparable to Lambalk LM et al. (Lambalk, De Wit Ap Fau - Wierda, Wierda Jm Fau - Hennis, Hennis Pj Fau - Agoston, & Agoston), Tannieres-Ruffie ML et al. (Tannieres-Ruffie ML Fau - Vourc'h & Vourc'h) and Fahey et al. (Fahey Mr Fau - Morris et al.).

The two intermediate acting steroidal drugs, Vecuronium and Rocuronium could be considered to offer good cardiovascular stability. Similar findings to those demonstrated by Maddineni VR et al. (Maddineni, McCoy Ep Fau - Mirakur, Mirakur Rk Fau - McBride, & McBride) Hudson ME et al. (Hudson, Rothfield Kp Fau - Tullock, Tullock Wc Fau - Firestone, & Firestone) and Levy JH et al. (Levy, Davis Gk Fau - Duggan, Duggan J Fau - Szlam, & Szlam) were obtained in terms of no change in heart rate with given dose of rocuronium. However, similar trend in vecuronium was also observed rendering the statistical difference between heart rate change in both groups over the time interval statistically non-significant, which was consistent with findings from Wierda JMKH et al. (Wierda et al.), Robertson EN et al. (Robertson En Fau - Booi, Booi Lh Fau - Fragen, Fragen Rj Fau - Crul, & Crul) and Kaufman JA (Kaufman, Dubois My Fau - Chen, Chen Jc Fau - Lea, & Lea). Similar non-significant trend observed in change in systolic and diastolic blood pressure also in both group showed cardiovascular stability of both rocuronium and vecuronium.

Moreover, there were no side effects or adverse events noted in any of both groups. Another major observation was found in terms of ease of reversal in both groups, where rocuronium proved to be superior with demonstrated clinical impact.

For evidence based safe and effective anaesthesia, it is must to have neuromuscular blocking agent with rapid onset time, excellent/good intubation conditions and also longer duration of action of initial dose of anesthetic drug. From our study, it is proven that rocuronium is superior in facilitating rapid onset time, excellent intubation conditions and duration of action as compared to those in vecuronium. However, we would like to acknowledge the bias that might have skewed the distribution graph due to small sample size. As a future scope, interdose comparison of rocuronium and associated clinical effects with more number of subjects i.e. bigger sample size could be planned to have concrete idea before hospital system integration.

References:

- Ali, H.H. Monitoring of neuromuscular function. (0544-0440 (Print)).
- Alvarez-Gomez, J. A., Fabregat J Fau - Estelles, M. E., Estelles Me Fau - Brugger, A. J., Brugger Aj Fau - Aguilar, R., Aguilar R Fau - Perez, F., & Perez, F. [Speed of intubation using a new neuromuscular blocker. Rocuronium bromide (ORG 9426)]. [Rapidez de intubación de un nuevo bloqueador neuromuscular. Bromuro de rocuronio (ORG 9426)]. (0034-9356 (Print)).
- Chatrath, V., Singh I Fau - Chatrath, R., Chatrath R Fau - Arora, N., & Arora, N. Comparison of intubating conditions of rocuronium bromide and vecuronium bromide with succinylcholine using "timing principle". (2231-2730 (Electronic)). doi: D - NLM: PMC3087261 OTO - NOTNLM
- Cooper, R., Mirakur Rk Fau - Clarke, R. S., Clarke Rs Fau - Boules, Z., & Boules, Z. Comparison of intubating conditions after administration of Org 9246 (rocuronium) and suxamethonium. (0007-0912 (Print)).
- Davison KI Fau - Holland, M. S., & Holland, M. S. A comparison study of vecuronium bromide and atracurium besylate for rapid sequence induction. (0094-6354 (Print)).
- De Haes, A., Eleveld Dj Fau - Wierda, J. M., & Wierda, J. M. The relationship between rate of administration of an intubating dose of rocuronium and time to 50% and 90% block at the adductor pollicis muscle. (1387-1307 (Print)).
- Donati, F., Meistelman C Fau - Plaud, B., & Plaud, B. Vecuronium neuromuscular blockade at the adductor muscles of the larynx and adductor pollicis. (0003-3022 (Print)).
- England, A. J., Margaron Mp Fau - Feldman, S. A., & Feldman, S. A. Tracheal intubation conditions after one minute: rocuronium and vecuronium, alone and in combination. (0003-2409 (Print)).
- Fahey Mr Fau - Morris, R. B., Morris Rb Fau - Miller, R. D., Miller Rd Fau - Sohn, Y. J., Sohn Yj Fau - Cronnelly, R., Cronnelly R Fau - Gencarelli, P., & Gencarelli, P. Clinical pharmacology of ORG NC45 (NorcuronTM): a new nondepolarizing muscle relaxant. (0003-3022 (Print)).
- Gan, T. J., Madan R Fau - Alexander, R., Alexander R Fau - Jhaveri, R., Jhaveri R Fau - El-Moalem, H., El-Moalem H Fau - Weatherwax, K., Weatherwax K Fau - Glass, P. S., & Glass, P. S. Duration of action of vecuronium after an intubating dose of rapacuronium, vecuronium, or succinylcholine. (0003-2999 (Print)).
- Gupta, S., & Kirubakar, R. (2010). A comparative study of intubating conditions of rocuronium bromide and suxamethonium in adult patients. *Anesthesia, Essays and Researches*, 4(1), 15-19. doi: 10.4103/0259-1162.69300
- Hudson, M. E., Rothfield Kp Fau - Tullock, W. C., Tullock Wc Fau - Firestone, L. L., &

- Firestone, L. L. Haemodynamic effects of rocuronium bromide in adult cardiac surgical patients. (0832-610X (Print)).
13. Kaufman, J. A., Dubois My Fau - Chen, J. C., Chen Jc Fau - Lea, D. E., & Lea, D. E. Pharmacodynamic effects of vecuronium: a dose response study. (0952-8180 (Print)).
 14. Kim, D. W., Joshi Gp Fau - White, P. F., White Pf Fau - Johnson, E. R., & Johnson, E. R. Interactions between mivacurium, rocuronium, and vecuronium during general anesthesia. (0003-2999 (Print)).
 15. Krieg N Fau - Mazur, L., Mazur L Fau - Booi, L. H., Booi Lh Fau - Crul, J. F., & Crul, J. F. Intubation conditions and reversibility of a new non-depolarizing neuromuscular blocking agent, Org-NC45. (0001-5172 (Print)).
 16. Lambalk, L. M., De Wit Ap Fau - Wierda, J. M., Wierda Jm Fau - Hennis, P. J., Hennis Pj Fau - Agoston, S., & Agoston, S. Dose-response relationship and time course of action of Org 9426. A new muscle relaxant of intermediate duration evaluated under various anaesthetic techniques. (0003-2409 (Print)).
 17. Levy, J. H., Davis Gk Fau - Duggan, J., Duggan J Fau - Szlam, F., & Szlam, F. Determination of the hemodynamics and histamine release of rocuronium (Org 9426) when administered in increased doses under N2O/O2-sufentanil anesthesia. (0003-2999 (Print)).
 18. Maddineni, V. R., McCoy Ep Fau - Mirakur, R. K., Mirakur Rk Fau - McBride, R. J., & McBride, R. J. Onset and duration of action and hemodynamic effects of rocuronium bromide under balanced and volatile anesthesia. (0001-5164 (Print)).
 19. Mazurek, A. J., Rae B Fau - Hann, S., Hann S Fau - Kim, J. L., Kim Ji Fau - Castro, B., Castro B Fau - Cote, C. J., & Cote, C. J. Rocuronium versus succinylcholine: are they equally effective during rapid-sequence induction of anesthesia? (0003-2999 (Print)).
 20. Pasko-Majewska, M., Owczuk R Fau - Wujtewicz, M., & Wujtewicz, M. [Comparison of atracurium, cisatracurium and vecuronium during anaesthesia for laparoscopic surgery]. [Ocena porównawcza atrakurium, cisatracurium i wekuronium podczas znieczulenia ogólnego do operacji laparoskopowych.]. (0209-1712 (Print)).
 21. Patanwala, A. E., Stahle Sa Fau - Sakles, J. C., Sakles Jc Fau - Erstad, B. L., & Erstad, B. L. Comparison of succinylcholine and rocuronium for first-attempt intubation success in the emergency department. (1553-2712 (Electronic)).
 22. Robertson En Fau - Booi, L. H., Booi Lh Fau - Fragen, R. J., Fragen Rj Fau - Crul, J. F., & Crul, J. F. Clinical comparison of atracurium and vecuronium (Org NC 45). (0007-0912 (Print)).
 23. Suzuki, T., Munakata K Fau - Watanabe, N., Watanabe N Fau - Katsumata, N., Katsumata N Fau - Saeki, S., Saeki S Fau - Ogawa, S., & Ogawa, S. Augmentation of vecuronium-induced neuromuscular block during sevoflurane anaesthesia: comparison with balanced anaesthesia using propofol or midazolam. (0007-0912 (Print)).
 24. Swen, J., Rashkovsky Om Fau - Ket, J. M., Ket Jm Fau - Koot, H. W., Koot Hw Fau - Hermans, J., Hermans J Fau - Agoston, S., & Agoston, S. Interaction between nondepolarizing neuromuscular blocking agents and inhalational anesthetics. (0003-2999 (Print)).
 25. Tannieres-Ruffie Ml Fau - Vourc'h, G., & Vourc'h, G. [Comparison of the clinical effects of vecuronium and pancuronium bromide in general surgery]. [Comparaison des effets cliniques du vecuronium et du bromure de pancuronium en chirurgie generale.]. (0750-7658 (Print)).
 26. van den Broek, L., Hommes Fd Fau - Nap, H. J., Nap Hj Fau - Wierda, J. M., & Wierda, J. M. Rocuronium- and mivacurium-induced neuromuscular block and intubating conditions: a comparison with vecuronium. (0952-1941 (Print)).
 27. Vervloet D Fau - Nizankowska, E., Nizankowska E Fau - Arnaud, A., Arnaud A Fau - Senft, M., Senft M Fau - Alazia, M., Alazia M Fau - Charpin, J., & Charpin, J. Adverse reactions to suxamethonium and other muscle relaxants under general anesthesia. (0091-6749 (Print)).
 28. Whalley, D. G., Maurer Wg Fau - Knapik, A. L., Knapik Al Fau - Estafanous, F. G., & Estafanous, F. G. Comparison of neuromuscular effects, efficacy and safety of rocuronium and atracurium in ambulatory anaesthesia. (0832-610X (Print)).
 29. Wierda, J. M., Mastrone E Fau - Bencini, A. F., Bencini Af Fau - Boyer, A., Boyer A Fau - Rashkovsky, O. M., Rashkovsky Om Fau - Lip, H., Lip H Fau - Karliczek, R., ... Agoston, S. Haemodynamic effects of vecuronium. (0007-0912 (Print)).
 30. Xue, F. S., Liao, X., Tong, S. Y., Liu, J. H., An, G., & Luo, L. K. (1998). Dose-response and time-course of the effect of rocuronium bromide during sevoflurane anaesthesia. *Anaesthesia*, 53(1), 25-30. doi:10.1111/j.1365-2044.1998.00278.x