# Reports of Investigation

# Cumulation characteristics of cisatracurium and rocuronium during continuous infusion

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**Purpose:** The dissimilar pharmacokinetic properties of cisatracurium (CIS) and rocuronium (ROC) predict different potential for drug cumulation when these drugs are administered by continuous infusion. A study was therefore undertaken to compare cumulation potential of CIS and ROC during surgical procedures of relatively long duration (2-4 hr).

**Methods:** Sufentanil/propofol-$N_2O$ anesthesia was administered to 40 ASA I and II adults. In a double-blind protocol, patients were randomly allocated to receive a continuous *iv* infusion of either CIS or ROC, titrated in progressive increments or decrements as required to achieve and maintain 95 ± 5% depression of the T1 response of the adductor pollicis muscle, using a Datex NMT-100 Relaxograph EMG monitor applied at the wrist. At the end of surgery, 60 $\mu g \cdot kg^{-1}$ neostigmine plus 15 $\mu g \cdot kg^{-1}$ atropine were administered for reversal.

**Results:** The duration of infusion was 104 ± 33 min in group CIS and 110 ± 23 min in group ROC ($P$=NS). In both groups, a progressive decrease in potency-adjusted infusion rates was observed after 30 min, then stabilized beyond 60 min. When allowing for an initial period of stabilization, mean potency-adjusted infusion requirements were: CIS 0.81 ± 0.02 $\mu g \cdot kg^{-1} \cdot min^{-1}$ and ROC 5.58 ± 1.94 $\mu g \cdot kg^{-1} \cdot min^{-1}$. There were no differences between groups at any time with regard to potency-adjusted infusion requirements necessary to maintain 90-99% block ($P$=NS). However, drug costs/hr for maintenance of neuromuscular block were less with CIS ($3.57 ± 0.09) than with ROC ($6.03 ± 0.27), $P < 0.001$.

**Conclusion:** When adjusted to equipotency, infusion requirements of CIS and ROC vary at similar rates during general anesthesia. Despite pharmacokinetic differences, neither drug demonstrates cumulation for infusion lasting up to 3.5 hr.

**Objectif :** Les propriétés pharmacocinétiques différentes du cisatracurium (CIS) et du rocuronium (ROC) laissent présager un potentiel différent d'accumulation lorsqu'on les administre en perfusion continue. Une étude a donc été menée pour comparer le potentiel d'accumulation de CIS et de ROC pendant des interventions chirurgicales de durée relativement longue (2-4 h).

**Méthode :** Une anesthésie à base de sufentanil/propofol-$N_2O$ a été administrée à 40 adultes d'état physique ASA I et II. Selon un protocole à double insu, les patients ont été répartis de façon aléatoire et ont reçu une perfusion *iv* continue de CIS ou de ROC en doses progressives ou dégressives comme l'exigent la réalisation et le maintien d'une dépression de 95 ± 5 % de la réponse à T1 du muscle adducteur du pouce, en utilisant un moniteur Datex NMT-100 Relaxograph EMG appliqué au poignet. À la fin de l'opération, 60 $\mu g \cdot kg^{-1}$ de néostigmine et 15 $\mu g \cdot kg^{-1}$ d'atropine ont été administrés pour renverser le bloc.

**Résultats :** La perfusion a duré 104 ± 33 min dans le groupe CIS et 110 ± 23 min dans le groupe ROC ($P$=NS). Dans les deux groupes, une baisse progressive des vitesses de perfusion ajustée en fonction de la puissance a été observée après 30 min, puis stabilisée après 60 min. En tenant compte d'une période initiale de stabilisation, les besoins de médicaments perfusés ajustés à la puissance ont été : 0,81 ± 0,02 $\mu g \cdot kg^{-1} \cdot min^{-1}$ de CIS et 5,58 ± 1,94 $\mu g \cdot kg^{-1} \cdot min^{-1}$ de ROC. Il n'y a pas eu de différence intergroupe de médicaments perfusés nécessaires au maintien de 90-99 % du bloc ($P$=NS). Cependant, pendant le maintien du blocage neuromusculaire, le coût /h a été moindre avec le CIS (3,57 $ ± 0,09) qu'avec le ROC (6,03 $ ± 0,27), $P < 0,001$.

**Conclusion :** Après ajustement pour «équipuissance», les besoins perfusionnels du CIS et du ROC ont varié de façon similaire pendant l'anesthésie générale. Malgré des différences pharmacocinétiques, aucun des médicaments n'a montré d'accumulation pendant la perfusion qui pouvait durer jusqu'à 3,5 h.

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Presented in part at the 56th Annual Meeting, Canadian Anesthesiologists' Society; Calgary Alberta; June, 1999.
Funded in part by a research grant from Glaxo-Wellcome, Inc. Canada
*Accepted for publication July 8, 2000.*

WITH widespread availability of programmable syringe infusion pumps for intraoperative use, it has become increasingly common to administer intermediate-duration neuromuscular blocking drugs (NMBDs) by continuous infusion. While recognizing that the majority of anesthetized patients only require intense block at particular times, in comparison to intermittent bolus injections, infusions provide greater stability of drug concentration, and hence clinical effect, for procedures scheduled to last longer than one to two hours.[1] Infusion techniques also have the potential to provide costs savings and increased safety via faster recovery or more facile reversal. As a guide to therapy, infusion requirements of the newer intermediate duration relaxants cisatracurium (CIS) and rocuronium (ROC) have been established.[2–9] However, despite wide inter-patient variability in drug requirements, previous studies have not specifically addressed how infusion rates need to be adjusted as a function of time, during the conduct of anesthesia.

We recently demonstrated that vecuronium begins to cumulate after the second hour of infusion, when adjusted to maintain a constant level of neuromuscular block between 90-95% depression of the T1 response of the first dorsal interosseous muscle.[10] In contrast, infusion requirements of atracurium (when potency-adjusted), remain constant for the same level of block. This observation implies absence of cumulation with atracurium, due to the much shorter elimination half-life of this drug ($t_{1/2}\beta$=20-25 min *vs* 60-70 min for vecuronium). While context- sensitive half times of these drugs have not been compared, it appears that elimination half lives become the more important factor governing the spontaneous termination of drug effect, the longer a drug is given.

By the same line of reasoning, we hypothesized that the newer intermediate NMBDs cisatracurium and rocuronium would also demonstrate different cumulation potentials. Whereas neuromuscular function recovers more rapidly following a single bolus of ROC compared with CIS, this results from the short distribution time of ROC. However, ROC also has a considerably longer elimination half-life than CIS ($t_{1/2}\beta$=60-70 min for ROC, 22- 26 min for CIS).[4,7] The present study was therefore designed to compare the time to onset of action, time-related infusion requirements, drug costs, and cumulation potential of CIS *vs* ROC during procedures of relatively long duration.

## Methods

This randomized, double-blind, parallel design study was approved by the hospital Research Ethics Board, and written informed consent was obtained from each subject. Forty patients of both sexes who were scheduled for elective surgery under general anesthesia were enroled. Patients were randomly allocated in equal numbers to receive either cisatracurium (Group CIS) or rocuronium (Group ROC). Assignment was done using a computer-generated randomization schedule, and the hospital pharmacist who prepared the study medications in coded syringes was provided a series of sealed envelopes specifying group allocation.

Enrolment consisted of patients undergoing elective orthopedic, abdominal, plastic, or gynecological surgery expected to last two to four hours. Subjects were ASA Class I or II, and aged 18-70 yr. Excluded was anyone with a history of renal, hepatic or neuromuscular disease. In addition, an anticipated difficult airway, body mass index <20 or > 30 $kg \cdot m^{-2}$, or history of hypersensitivity or allergy to any of the study medications also resulted in exclusion.

### *Anesthesia protocol*

Patients received their usual medications up to, and including, the morning of surgery, but were not premedicated. In the operating room, two peripheral intravenous lines were established; one for the muscle relaxant infusion and the other for all other intravenous medication. Patients then received 0.03 $mg \cdot kg^{-1}$ midazolam *iv* for sedation. Standard monitoring was applied, consisting of ECG, pulse oximetry and non-invasive arterial pressure. In addition, a Datex NMT-100 Relaxograph EMG monitor was applied over the ulnar nerve at the wrist using surface electrodes. The monitor was set to deliver a train-of-four (TOF at rate of 2 Hz, for two seconds), every 20 sec throughout the study, using supra-maximal current. Skin surface electrodes were applied over the thenar eminence to record the electromyographic response to the adductor pollicis muscle following stimulation of the ulnar nerve. To avoid patient discomfort, calibration of the apparatus was done after induction of anesthesia, but prior to administration of the muscle relaxant.

Anesthesia was induced with a combination of 0.3 $\mu g \cdot kg^{-1}$ sufentanil *iv* followed by 1.5-2.0 $mg \cdot kg^{-1}$ propofol *iv*. Upon loss of consciousness, positive pressure ventilation was provided with $O_2$ 100% while calibration of the Datex Relaxograph was performed. The patient's trachea was intubated, and anesthesia was maintained with $N_2O/O_2$ in a 2:1 ratio; sufentanil infusion, 0.15-0.25 $\mu g \cdot kg^{-1} \cdot hr^{-1}$, and propofol, 50-150 $\mu g \cdot kg^{-1} \cdot min^{-1}$ *iv*, titrated according to individual patient requirements and the level of surgical stimulation. Potent inhaled anesthetics were avoided, to eliminate

the neuromuscular potentiating effects of these drugs as a confounding variable. The infusion regimen of the neuromuscular blocking drugs is described below. Towards the end of surgery, infusions of both sufentanil and muscle relaxant were discontinued, and neuromuscular block was reversed with a combination of 60 $\mu g \cdot kg^{-1}$ neostigmine plus 15 $\mu g \cdot kg^{-1}$ atropine. Reversal was administered without allowing any time for spontaneous recovery, where the $T_4/T_1$ ratio was between 5-10% of baseline. When neuromuscular function recovered to a $T_4/T_1$ ratio 0.7, propofol and $N_2O$ were also discontinued, $FiO_2$ was set at 1.0, and the patient's trachea was extubated when the subject was awake and breathing spontaneously. The remainder of the postoperative clinical course was left to the discretion of the attending anesthesiologist.

*Study drug infusion protocol*

The study drug was administered from two separate coded labeled syringes, each prepared on the study day by the hospital clinical trials pharmacist. To maintain blindness, commercially-provided vials of both CIS and ROC were diluted in normal saline to final concentrations which were equipotent on a volumetric basis, assuming a potency ratio of CIS/ROC = 6:1. In each group, the first 5 mL syringe contained the loading dose, equivalent to $2xED_{95}$, which was administered as a single *iv* bolus over 30 sec. The second 60 mL syringe contained drug at the same concentration, and was infused to provide maintenance of neuromuscular block. The loading dose, initial infusion rates, and maintenance rates of infusion are shown in Table I. When the $T_1$ amplitude was depressed to 10% of baseline, the trachea was intubated under direct laryngoscopy. The study drug infusion was started once evidence of recovery from the initial bolus ($T_1 \geq 1\%$ of baseline) was demonstrated. Throughout surgery, adjustments in the rate of infusion were made in increments or decrements of 0.03 $mL \cdot kg^{-1} \cdot hr^{-1}$ at intervals no less frequently than every five minutes, in order to maintain 95 ± 5% $T_1$ block throughout surgery. Relaxant infusions were discontinued five to ten minutes before the end of surgery, after which reversal drugs were administered in the above-stated doses.

*Measurements*

The primary response variable was the potency-adjusted infusion rate during the course of surgery. The following secondary efficacy variables were also assessed:

(i) time to onset of action following initial bolus administration, defined as the time to reach 90% twitch depression ($T_1$) and to reach maximal depression or complete abolition of the single twitch height;

TABLE I Muscle relaxant infusion regimens

| | *Cisatracurium (n=20)* | *Rocuronium (n=20)* |
|---|---|---|
| Drug Concentration ($mg \cdot mL^{-1}$) | 0.5 | 2.5 |
| Loading Dose ($mg \cdot kg^{-1}$) ($2xED_{95}$) | 0.1 | 0.6 |
| Initial Infusion Rate ($\mu g \cdot kg^{-1} \cdot min^{-1}$) * | 1.7 | 10.2 |

* Titrated to maintain $T_1$ = 5-10% of control

(ii) number of infusion rate adjustments per hour required to maintain 95 ± 5% single twitch depression;

(iii) time for return of $T_4/T_1 \geq 70\%$ and single twitch height to recover to 70% of baseline value.

In addition, the point at which patients were able to maintain head lift for greater than five seconds was documented. Each study was considered terminated when full recovery of neuromuscular function was achieved, and the post-treatment evaluation was complete.

Finally, hourly costs for maintenance of neuromuscular block were calculated as follows: *Cost/hr ($Can) = Infusion Rate ($\mu g \cdot kg^{-1} \cdot min^{-1}$) x Body Weight (kg) x 60 $min \cdot hr^{-1}$ x Unit Price Cost.* For these calculations, representative infusion rates were the mean rates of infusion for each group beyond the second hour of administration (at which time stabilization had been achieved). Unit price drug costs at the time of the study were: CIS: $19.95/20 mg vial; ROC: $12.75/50 mg vial.

*Statistical considerations*

As the primary response was the potency-adjusted infusion rate required to maintain 95 ± 5% single twitch depression, calculation of sample size was based upon the following assumptions for the primary response: (1) in group ROC the required infusion rate was between 0.24-0.30 $mg \cdot kg^{-1} hr^{-1}$ with a standard deviation of 0.15, and (2) a treatment difference of 30% is statistically significant. Using a two-sided test, a study with 18 patients in each group would provide 80% power to detect statistically significant treatment differences. Allowing for drop-outs for technical reason and/or non-evaluable subjects, the total sample size was therefore adjusted to 40 patients.

Potency-adjusted infusion rates were compared using repeated-measures ANOVA. For purposes of the analysis, time t=0 was chosen as the time of the initiation of the infusion (following recovery from the loading dose). Where group-time interactions were identified, ANOVA or paired Student's t tests were applied post-hoc. Time to onset variables were analyzed using ANOVA or Wilcoxon rank sum tests, depending upon the distributions. Throughout the text and tables,

results of continuous response variables are presented as mean ± SD, and $P < 0.05$ was considered to be statistically significant.

## Results

Patient characteristics, as well as the duration of surgery and mean durations of infusion were similar in both groups (Tables II, III). While some procedures continued beyond three hours, the number of observations decreased progressively after the second hour. Accordingly, statistical comparisons were applied only to data up to 130 min from the start of the infusion.

Onset time (to achieve $T_1$<10%) was faster in group ROC than in group CIS ($P < 0.05$). However, once established, the infusions of both drugs allowed stable levels of block (90-99% depression of $T_1$ amplitude) to be achieved and maintained throughout surgery (Figure 1). In both groups, potency-adjusted infusion rates were observed to decrease by approximately 50% during the first hour, and stabilized thereafter (Figure 2). Similarly, the number of infusion rate adjustments decreased with time, but remained similar at corresponding 30 min intervals (Table III). More importantly, there were no group-time interactions with respect to mean infusion requirements throughout the

TABLE II Patient characteristics

| | *Cisatracurium (n=20)* | *Rocuronium (n=20)* |
|---|---|---|
| Age (Yr) | 37.3 ± 12.0 | 35.9 ± 12.8 |
| Sex (m/f) | 6/14 | 7/13 |
| Weight (kg) | 72.3 ± 11.6 | 71.5 ± 10.6 |
| ASA (I/II/III) | 10/9/1 | 16/4/0 |

TABLE III Characteristics of the muscle relaxant infusions

| | *Cisatracurium* | *Rocuronium* |
|---|---|---|
| Surgery Duration (min) | 134.0 ± 34.5 | 136.0 ± 26.4 |
| Onset Time to $T_1$ < 10% (min) | 4.1 ± 0.9 | 1.8 ± 0.5* |
| Time after bolus to infusion start (min) | 32.1 ± 5.5 | 27.5 ± 8.4 |
| Infusion Duration (min) | 104.3 ± 32.5 | 110.5 ± 22.9 |
| Infusion Rate Adjustments (n/30 min) | | |
| t = 0 - 30 | 2.3 ± 1.3 | 2.3 ± 1.1 |
| t = 30- 60 | 2.4 ± 1.4 | 1.9 ± 0.8 |
| t = 60- 90 | 1.6 ± 1.5 | 1.4 ± 1.1 |
| t = 90- 120 | 0 | 0.8 ± 0.9 |
| Mean Infusion Rates ($\mu g \cdot kg^{-1} \cdot min^{-1}$) | | |
| t = 0 - 30 | 1.66 ± 0.10 | 10.06 ± 0.43 |
| t = 30- 60 | 1.09 ± 0.14 | 7.43 ± 0.69 |
| t = 60- 90 | 0.81 ± 0.02 | 5.58 ± 0.42 |
| t = 90- 120 | 0.86 ± 0.03 | 5.45 ± 0.17 |
| Cumulative Infusion | | |
| Drug Dose (mg) | 8.6 ± 2.4 | 58.3 ± 15.5 |
| Recovery Time to $T_4/T_1 > 0.7$ | | |
| Post-reversal (min) | 8.9 ± 3.4 | 6.5 ± 2.2* |
| Drug Costs | | |
| Cumulative infusion drug cost ($Can) | 8.58 ± 2.78 | 14.85 ± 3.87* |
| Cost/hr after 1st hr ($Can) | 3.57 ± 0.09 | 6.03 ± 0.27† |

* $P < 0.05$, different from group CIS
† $P < 0.001$, different from group CIS

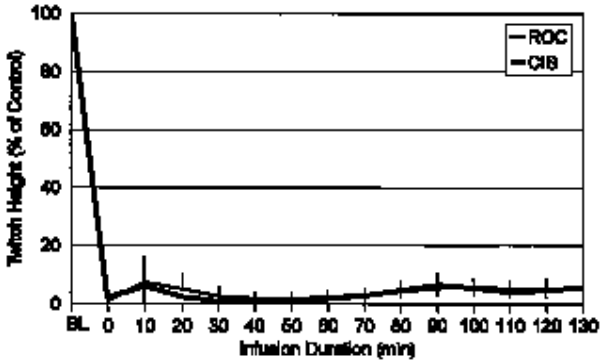


FIGURE 1 Single twitch heights (expressed as per cent of control) during continuous infusions of cisatracurium and rocuronium. Loading doses were administered at t=0 min. Adjustments of the infusion rates of cisatracurium and rocuronium allowed the depth of neuromuscular block to be maintained at a level representing 95 ± 5% $T_1$ suppression throughout surgery with both neuromuscular blocking drugs.

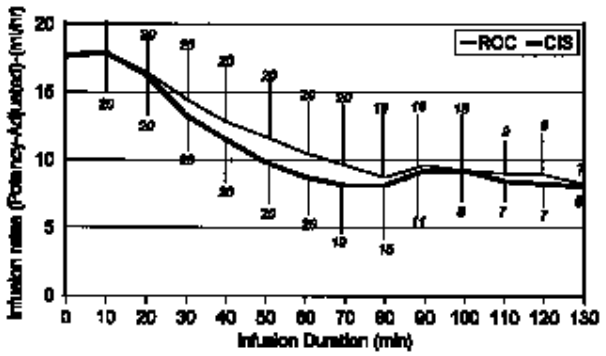


FIGURE 2 Mean infusion rates of cisatracurium and rocuronium required to maintain 95 ± 5% $T_1$ suppression of the single twitch height during balanced anesthesia. An initial decrease in infusion requirements of both drugs represents a stabilization period, after which potency-adjusted infusion requirements were similar with both drugs. The number of patients (observations) for each group and time period are displayed above and below the corresponding standard deviation bar.

course of the study ($P$=NS). However, drug costs/hr for maintenance of neuromuscular block were less with CIS ($3.57 ± 0.09) than with ROC ($6.03 ± 0.27), $P < 0.001$. The total cumulative dose of CIS (during infusion) was 8.6 ± 2.4 mg compared with 58.3 ± 15.5 mg for ROC. Finally, mean times to recovery ($T_4/T_1>0.7$) following administration of neostigmine were shorter in group ROC (6.5 ± 2.2 min) than with group CIS (8.9 ± 3.4 min, $P < 0.05$).

All patients recovered from anesthesia uneventfully. There was no evidence of untoward effects attributable to the muscle relaxant in either group, nor was there clinical evidence of residual neuromuscular block in the PACU.

## Discussion

The key finding of this study is a demonstrated absence of cumulation of both cisatracurium and rocuronium, when administered by continuous infusion to maintain a clinically relevant degree of neuromuscular block (95 ± 5% $T_1$ suppression). When allowing for an initial period of stabilization, mean potency-adjusted infusion requirements were cisatracurium 0.81 ± 0.02 $\mu g \cdot kg^{-1} \cdot min^{-1}$ and rocuronium 5.58 ± 1.94 $\mu g \cdot kg^{-1} \cdot min^{-1}$. Variability in dose requirements during the course of infusion was consistent with observations from other clinical trials. Reversal times were on average, three minutes faster following infusion of rocuronium than of cisatracurium, following a standardized dose of neostigmine. At current Canadian prices, costs to *maintain* neuromuscular block with cisatracurium are less than the costs of rocuronium.

The rationale for this trial took into consideration the distinct pharmacokinetic characteristics of cisatracurium and rocuronium, and how these attributes influence potential for drug cumulation. Interpatient pharmacokinetic and pharmacodynamic variability can pose clinical challenges when titrating drug requirements to the desired level of clinical effect. Volumes of drug distribution, rate constants and elimination half lives vary in a physiological manner, while pathological processes and drug interactions may further alter drug requirements. It is now widely appreciated that the importance of elimination half-life in predicting duration of effect for anesthetic drugs is quite limited, as most drugs are rarely given for sufficient duration to achieve steady state. Cisatracurium, like atracurium, is cleared by Hofmann elimination, a pathway which does not depend on the usual organs of elimination (liver, kidney).[4] Accordingly, Fisher has pointed out that pharmacokinetic models to describe the disposition of this drug must determine the rate constant for both the plasma and non-organ pathways.[11] Kisor *et al.* demonstrated that only 23% the elimination of cisatracurium occurs via organs, in contrast to 90-95% dependency for rocuronium.[12,13] Accordingly, it could be reasoned that, during the course of an anesthetic, rocuronium might tend to accumulate at receptor sites (neuromuscular junction) to an extent that infusion requirements would have to be progressively decreased to maintain the same level of neuromuscular block. The fact that this was not observed in our study might be because the infusions were not administered for sufficient duration to saturate body clearance systems. It has been suggested that this may result in distribution processes contributing progressively less and less to reductions in plasma concentrations.

The findings of the current study contrast with those from our previous comparison of atracurium and vecuronium administered by continuous infusion.[10] In that trial, maintenance requirements of atracurium were unaltered during a similar period of infusion. On the other hand, infusions of vecuronium had to be decreased by more than 50% over two hours to prevent progressive deepening of the level of neuromuscular block. It was concluded from this study that a constant infusion of vecuronium titrated to maintain $T_1$ near 5% of control provided clear evidence of cumulation with this intermediate-duration NMBD. However, one subtle difference between the former and current studies is the mean age of patient populations being investigated. The patient age in the vecuronium study was 65.4 ± 6.6 yr, compared with a mean age of 35.9 ± 12.8 yr in the rocuronium group of the current investigation. While the rates of plasma clearance of vecuronium and rocuronium decline dramatically in the elderly,[14] the pharmacokinetic profile of cisatracurium is essentially unaffected by increasing age.[15,16] One could only speculate as to whether or not a comparison of cisatracurium and rocuronium infusions in an older patient population would demonstrate an analogous time-related discrepancy in infusion requirements, as observed in the earlier trial.

An additional note of explanation is made regarding the design of the infusion regimens. A standard approach to the design of manual infusion regimens is to administer a loading dose followed by a continuous infusion.[1] In general, administration of an appropriate bolus at the start of an infusion permits a gradual increase in plasma concentration from the infusion to be matched by exponentially declining drug concentrations from the bolus. This will result in an early, but not immediate plateau. Generally speaking, the longer the interval between the loading dose and the start of the infusion, the greater the dose of additional relaxant required to "catch up". In the current study, an infusion was not started immediately, as the standard

loading doses (equivalent to 2xED95) necessary to facilitate intubation of the trachea, resulted in complete paralysis for approximately one half-hour in both groups. Our approach permitted return of neuromuscular function to a detectable level ($T_1$>1%) in the most rapid manner possible, at which point the infusion was started. The rationale was to mimic a standard approach to infusion of cisatracurium and rocuronium, whereby the muscle relaxant infusion is initiated upon return of a single twitch (as determined by the train-of-four response). At the end of the infusion, no period of spontaneous recovery was permitted before reversal with neostigmine. While in the usual clinical setting muscle relaxant infusions are commonly discontinued some minutes prior to completion of surgery, it was deemed more important in this study to compare reversal times from deep and equivalent levels of block (90-99% depression of $T_1$). In this regard, the drugs behaved in a similar manner. Spontaneous recovery indices of these two relaxants have been reported elsewhere.

Finally, to put the issue of drug costs into perspective, we observe that neuromuscular blocking drugs constitute a substantial proportion of expenditures of any given class of anesthetic drugs for most hospital pharmacies.[17] Muscle relaxant expenditures are between 20-40% of the cumulative anesthesia drug budget. This study shows that once a stable level of neuromuscular block is achieved, hourly maintenance costs of CIS ($3.57 ± 0.09) are less (approximately 40%) than hourly costs of rocuronium ($6.03 ± 0.27). However, at present the cost of an intubating dose of cisatracurium ($14.38 @2x$ED_{95}$/72 kg) is greater than an intubating dose of rocuronium ($11.02 @2x$ED_{95}$/72 kg). Taking into consideration the more rapid onset time of rocuronium, this drug is cost-effective for rapidly achieving relaxation to facilitate intubation of the trachea for procedures where muscle relaxation will not be maintained beyond one to two hours, and for rapid-sequence induction. However, when relaxation is to be continued for longer than two hours, cisatracurium may be a more cost-effective alternative. Ultimately, the clinician must decide whether a cost differential of a few dollars per hour (once stability has been achieved) is important, and takes into consideration the total number of ampules per hour used. It can certainly be argued that, within limits, pharmacological properties are of greater importance.

In summary, we found no greater propensity for drug cumulation with either cisatracurium or rocuronium when infused for up to three hours, to maintain a 95 ± 5% level of neuromuscular block during propofol/nitrous oxide/narcotic anesthesia. When allowing for an initial period of stabilization, mean potency-adjusted infusion requirements were: cisatracurium 0.81 ± 0.02 $\mu g \cdot kg^{-1} \cdot min^{-1}$ and rocuronium 5.58 ± 1.94 $\mu g \cdot kg^{-1} \cdot min^{-1}$. Neostigmine was equally effective in accelerating recovery from deep neuromuscular block produced from either muscle relaxant. It is concluded that, for intraoperative use, the infusion pharmacodynamics of cisatracurium and rocuronium are similar.

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