Br. J. Anaesth. (1982), **54**, 1151

REPETITIVE ADMINISTRATION OF PANCURONIUM AND VECURONIUM (Org NC 45, NORCURON) IN PATIENTS UNDERGOING LONG LASTING OPERATIONS

W. BUZELLO AND G. NÖLDGE

SUMMARY

Fifty-one patients undergoing surgical procedures which required at least 2 h of anaesthesia were randomly divided into two groups receiving either pancuronium or vecuronium (Org NC 45) as a muscle relaxant under evoked twitch tension control. In the absence of halogenated inhalation anaesthetics, both drugs were administered by initial bolus injection of 0.1 mg kg^{-1}, followed by increments of 0.025 mg kg^{-1} when twitch height had recovered to 25% of control. In all cases the initial dose produced total neuromuscular blockade and satisfactory intubation conditions within 2–4 min. The time of onset was slightly shorter with vecuronium than with pancuronium. The mean duration from the end of injection to 25% recovery of the initial and the maintenance doses was three and four times longer with pancuronium than with vecuronium, respectively. The average drug requirement per hour to maintain at least 75% block was one maintenance dose of pancuronium 0.025 mg kg^{-1} and four maintenance doses of vecuronium 0.1 mg kg^{-1}. The overall recovery time (25% to 75% twitch height) irrespective of the number of maintenance doses was 40 ± 14 min with pancuronium and 15 ± 8 min with vecuronium (mean ± SD). Some cumulation was observed with pancuronium, particularly in terms of prolonged recovery time. With vecuronium, both duration of action of maintenance doses and recovery time did not depend on the number of maintenance doses. In both groups of patients no cardiovascular or other side-effects were observed. It is concluded that vecuronium is a true intermediate-acting non-depolarizing muscle relaxant. Its lack of cumulation favours the maintenance of profound neuromuscular blockade until close to the end of operation without the risk of an unduly long recovery time.

In addition to atracurium (Payne and Hughes, 1981), pipecurium (Classen and Schramm, 1980), the "bulky esters" (Savarese and Wastila, 1979) and chandonium (Gandiha, Marshall and Paul, 1975), vecuronium (Org NC 45, Norcuron) represents one of the recent approaches to develop a muscle relaxant meeting the requirements listed in table I. Chemically, vecuronium is a monoquaternary pancuronium analogue. After favourable results of both animal experiments and clinical pilot studies (Bowman and Norman, 1980) the drug has now been subjected to a multi-centre clinical trial. In this context the present paper reports a comparative study of repetitive administration of pancuronium and vecuronium in long-lasting operations.

PATIENTS AND METHODS

Fifty-one adult patients of both sexes, ASA class I–II, undergoing surgical procedures requiring at least 2 h of anaesthesia were investigated. Informed consent had been obtained in all cases. The patients were randomly divided into two groups receiving either pancuronium ($n = 22$) or vecuronium ($n = 29$) as muscle relaxant. Patients under 20 and over 60 yr of age and those with neuromuscular, renal and hepatic disease were excluded from the study.

All patients were premedicated with atropine 0.01 mg kg^{-1}, fentanyl 0.0015 mg kg^{-1} and droperidol 0.07 mg kg^{-1} i.m. Anaesthesia was induced with thiopentone 200–300 mg, fentanyl 0.3–0.5 mg and droperidol 5–10 mg. The trachea was intubated after muscle relaxation with pan-

TABLE I. *Properties desirable in an ideal muscle relaxant (Savarese and Kitz, 1973)*

(1)	Rapid onset of action (30–45 s)
(2)	Short duration of block (10–20 min)
(3)	No cumulative effects
(4)	Reversal of block by suitable antidote
(5)	No pharmacologically active or toxic metabolites
(6)	High potency
(7)	No histamine release
(8)	No cardiovascular side-effects

W. BUZELLO, M D ; G. NÖLDGE, M.D ; Department of Anaesthesiology, University Hospital, Hugstetter Strasse 55, D-7800 Freiburg, Federal Republic of Germany.

0007–0912/82/111151–07 $01.00

curonium 0.1 mg kg^{-1} or vecuronium without the aid of suxamethonium. Anaesthésia was maintained with increments of fentanyl according to the individual requirements under mechanical ventilation with oxygen in nitrous oxide 1:2 in the absence of halogenated inhalation anaesthetics. One-quarter of the initial dose of the appropriate muscle relaxant was repeated when neuromuscular transmission had recovered 25% of control. Neuromuscular function was assessed by recording evoked twitch tension of the adductor pollicis muscle. Train-of-four supramaximal square pulses (0.2 ms, 2 Hz, 30 s apart) were delivered to the ulnar nerve at the wrist by a battery-operated Myotest nerve stimulator (Viby-Mogensen et al., 1980). The resulting twitch tension was quantitated by a boomerang force displacement transducer (Walts, Lebowitz and Dillon, 1968) and recorded on a polygraph. Table II gives the parameters taken from the tracings. Recovery time was measured in both the absence and presence of neostigmine. In the latter conditions (eight patients receiving pancuronium and eight receiving vecuronium) neostigmine 0.02 mg kg^{-1} was administered with atropine 0.015 mg kg^{-1} when twitch tension had recovered 25% of control. In seven patients who received pancuronium and eight who received vecuronium, recovery time was not measured because these patients were either transferred to the intensive care unit for mechanical ventilation before twitch tension had recovered 75% of control, or neostigmine had been given at a later stage of recovery than 25% twitch height.

Clinical observations included intubation conditions, arterial pressure (RIVA-ROCCI), heart rate, e.c.g., and signs of histamine release (skin reactions, bronchoconstriction).

All variables were calculated as means and standard deviations ($\bar{x} \pm$ SD). Student's *t* test was used to assess statistical significance. Linear regressions were calculated after the least squares method.

TABLE II. *Variables of time course of neuromuscular blockade*

Onset	Time from end of injection to maximum block
DUR_{25}	Duration from end of injection of initial dose to 25% recovery
DUR_{90}	Duration from end of injection of initial dose to 90% recovery
$DUR_{rep.25}$	Duration from end of injection of maintenance dose to 25% recovery
Recovery time	Time from 25% to 75% recovery after the last maintenance dose or after the initial dose in the absence of maintenance doses

RESULTS

The duration of anaesthesia was 161 ± 47 and 171 ± 76 min in the pancuronium and vecuronium group, respectively. In all cases the initial doses of both muscle relaxants produced total neuromuscular blockade with smooth intubation conditions. Particularly with vecuronium, it was our experience that in some patients the muscles of the vocal cords were completely paralysed when active movement of the arms and hands was still present. Cardiovascular side-effects, skin reactions and bronchoconstriction did not occur.

The variables describing the time course of neuromuscular blockade produced by pancuronium and vecuronium are summarized by figure 1. Additionally, figure 2 shows the evoked mechanomyograms of one representative case from each group. In detail, the following results were obtained:

(i) The *time of onset* tended to be shorter with vecuronium than with pancuronium (3.5 ± 2.7 *v.* 2.5 ± 1 min without statistical significance).

(ii) The *mean duration of the initial dose* (DUR_{25}) was three times longer with pancuronium than with vecuronium; this was statistically significant.

(iii) The requirement of *maintenance doses* is illustrated in table III. Nearly a quarter of the patients who received pancuronium did not need any maintenance dose and, with one exception only, not more than three increments had to be given to the remaining 16 patients. Mean $DUR_{rep.25}$ ranged between 20 and 150 min. In the vecuronium group, 70% of patients required five to 15 maintenance doses. Accordingly, $DUR_{rep.25}$ ranged between 8 and 25 min which is about one-quarter of that of pancuronium. On average, one maintenance dose of pancuronium or four maintenance doses of vecuronium per hour were required to maintain neuromuscular transmission less than 25% of control (0.015 *v.* 0.10 mg kg^{-1} h^{-1}). Some *cumulation*, in terms of increasing duration of action with increasing number of maintenance doses, may be suspected from three patients of four who received three or more maintenance doses of pancuronium and from eight patients of 28 receiving up to nine maintenance doses of vecuronium (table IV). However, this tendency is not reflected by the overall values of figure 1.

(iv) In the pancuronium group the *recovery time* irrespective of the previous number of maintenance doses (fig. 1) was 40 ± 14 min ($n = 7$) in the absence, and 11 ± 4 min in the presence of neostigmine ($n = 8$). With vecuronium, the corresponding fig-

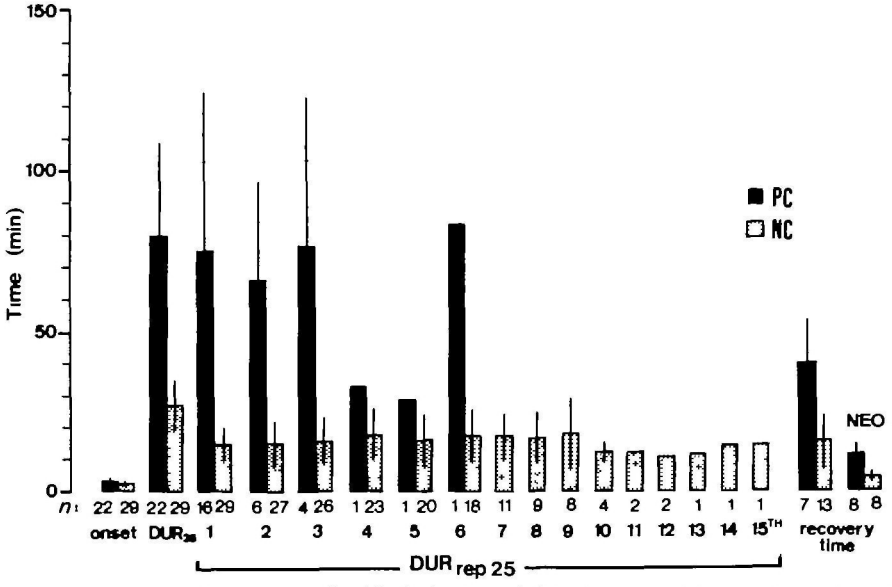

FIG. 1. Time course of neuromuscular blockade (mean ± SD) from repetitive administration of pancuronium (PC) and vecuronium (NC). NEO = recovery time after neostigmine 0.02 mg kg^{-1} given at 25% recovery. n = number of patients.

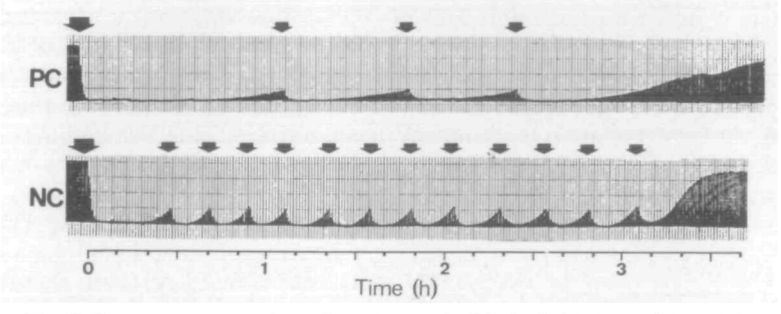

FIG. 2. Representative tracings of neuromuscular blockade from repetitive administration of pancuronium (PC) and vecuronium (NC). Large arrows = 0.1 mg kg^{-1}; small arrows = 0.025 mg kg^{-1}.

TABLE III. *Distribution of numbers of maintenance doses of pancuronium (PC) and vecuronium (NC). DUR_{an} = duration of anaesthesia (min) (mean ± SD); n = number of patients*

	Number of maintenance doses												
Drug	0	1	2	3	4	5	6	7	9	10	12	15	Total
PC													
n	5	11	2	3			1						22
%	22 7	50	9	13.6			4.5						100
DUR_{an}	134 ± 30	179 ± 70	272	387 ± 162			265						161 ± 4
NC													
n		2	1	3	2	3	6	4	4	2	1	1	29
%		6.9	3 4	10.4	6.9	10.4	20.7	13.8	13.8	6.9	3.4	3.4	100
DUR_{an}		125	195	105 ± 21	105	220 ± 83	143 ± 46	115 ± 84	233 ± 80	163	220	200	174 ± 75

compared with vecuronium. The effect of repetitive administration was not studied systematically.

In the present study as in previous investigations (Crul and Booij, 1980; Fahey et al., 1981b; Kalina et al., 1981) both drugs were administered in equal doses on a mg per kg basis. Recent findings in man indicate that vecuronium is 1.3 to 1.7 times more potent than pancuronium (Buzello et al., 1980; Crul and Booij, 1980; Krieg, Crul and Booij, 1980). Hence, the slightly shorter time of onset of vecuronium which was also reported by Crul and Booij (1980), Agoston and colleagues (1980) and Krieg, Crul and Booij (1980), may be the result of some relative overdosage. In itself, the 2.5 min onset time of vecuronium is not very attractive clinically, because it is still considerably longer than that of suxamethonium. However, the onset of action may be accelerated by increasing the initial dose which, contrary to pancuronium, is unlikely to prolong the recovery time significantly. Further investigation is required to decide whether, in crash induction, vecuronium may become an alternative to suxamethonium.

Excessive individual variation is a common problem in the clinical use of non-depolarizing muscle relaxants (Katz, 1967). This is reflected by the large relative standard deviations of both DUR_{25} and $DUR_{rep.25}$ of pancuronium, ranging between ± 18 and $\pm 63\%$ of the mean (fig. 1). In absolute figures, $\bar{x} \pm SD$ covers a range from 30 to 90 min. With vecuronium, too, the relative standard deviations may exceed $\pm 50\%$ of the mean. However, in absolute terms, this represents a range as little as 10–15 min, which is not likely to create major clinical problems in the period immediately after anaesthesia.

Cumulation of successive doses is a regular finding when pancuronium or other traditional curare derivatives are used. With pancuronium, Fahey and others (1981b) found an increasing duration of block as a result of repeated administration of up to four 0.02-mg kg^{-1} doses. This phenomenon was minimal or absent if vecuronium was given, even in up to five doses of 0.04 mg kg^{-1} each. In the study of Kalina and colleagues (1981), in which both pancuronium and vecuronium were administered in a 0.05-mg kg^{-1} initial bolus followed by increments of 0.015 mg kg^{-1} at 25% recovery, $DUR_{rep.25}$ of both drugs remained fairly constant (about 20–25 min with pancuronium and 10 min with vecuronium), and no signs of cumulation were noticed. In the present study, with twice the initial and maintenance doses, we found moderate cumulation with pancuronium, namely in terms of prolonged recovery time, and no cumulation with vecuronium (fig. 2). Apparently, with pancuronium the evidence of cumulation is dose-dependent, and 0.015–0.025 mg kg^{-1} h^{-1} represents the maintenance dose of a 75% block. This is different with vecuronium which, even in greater doses, does not accumulate. Buzello and others (1980) reported that, after recovery from a 0.075 mg kg^{-1} bolus followed by 10 maintenance doses (0.015 mg kg^{-1} each), another 0.0375 mg kg^{-1} dose produced only 33 min (DUR_{25}) neuromuscular block, which was not different in duration from that after a single 0.075-mg kg^{-1} dose. In the present study no signs of cumulation were seen up to a total dose of 0.5 mg kg^{-1} (= 38 mg) of vecuronium within 3 h 20 min (= 9.4 mg h^{-1}). In the patients listed in table IV, systemic or local hypothermia may have contributed to the increasing duration of block.

The particular kinetic properties of vecuronium induced neuromuscular blockade are readily explained by the high plasma clearance of the drug 123 ± 41 ml min^{-1} (Somogyi, Shanks and Triggs, 1976). The reason for the rapid decay of the plasma concentration of vecuronium is still unknown. Five (McLeod, Watson and Rawlins, 1976) and 123 ± 41 ml min^{-1} (Somogyi, and Triggs, 1976). The reason for the rapid decay of the plasma concentration of vecuronium is still unknown. Five possible mechanisms have to be discussed: renal and biliary elimination, metabolic and chemical degradation, and redistribution. Although vecuronium has not been determined in the urine, renal excretion can be excluded as a principle limiting the duration of block, since Fahey and others (1981a) found almost equal plasma clearances in anephric and normal patients. The monoquaternary structure of vecuronium renders the molecule less polar than its bisquaternary analogue pancuronium. This may favour its biliary excretion. For pancuronium, this pathway only accounts for about 10% of the administered dose during 24 h (Agoston et al., 1973; Buzello, 1975) and does not contribute to the plasma clearance during spontaneous recovery of neuromuscular transmission under ordinary clinical conditions. It appears reasonable to assume that with vecuronium, even the possibly increased biliary excretion is still far from influencing the duration of block. The same has to be expected from metabolic 3- and 17-desacetylation which for pancuronium accounts for only 10% of the dose during

the first 6 h after administration (Agoston et al., 1973; Buzello, 1975). Savage, Sleigh and Carlyle (1980) advocated pH-dependent chemical hydrolysis of the acetyl groups because of the monoquaternary structure of the molecule as a pathway of particular relevance for the pharmacokinetics of vecuronium. In man its role has still to be investigated. The last possible principle is the uptake of the drug by inactive tissues. In kinetic terms this requires a very large total volume of distribution. A synthesis of the findings of McLeod, Watson and Rawlins (1976) and Somogyi, Shanks and Triggs (1976) on pancuronium and Van der Veen and Bencini (1980) and Fahey and colleagues (1981a) on vecuronium does not support this view, since the total volumes of distribution of both drugs are not significantly different. Further investigations in the field of pharmacokinetics and drug metabolism are required to elucidate the fate of vecuronium in man.

Recovery time is an index with major clinical implications, because neuromuscular transmission between 25 and 75% represents a stage between acceptable surgical conditions (twitch tension $< 25\%$) and full recovery, which in most instances is unsatisfactory for both the surgeon and the anaesthetist. Therefore, for the ideal muscle relaxant, the recovery time should be as short as possible and not depend on the dose. Pancuronium does not meet this requirement. Recovery time after one single 0.1-mg kg^{-1} bolus is 34 ± 10 min, and it may increase over 50 min with the second maintenance dose (table IV). In contrast, vecuronium offers the advantage of a very small level of residual neuromuscular transmission by numerous maintenance doses until close to the end of surgery while still keeping the recovery time as brief as 10–25 min. This property, together with the short $DUR_{rep.25}$, suggests the infusion technique as a convenient mode of administration. This technique is now under investigation in our department.

We conclude that, in comparison with pancuronium, the introduction of vecuronium represents a remarkable step toward the "ideal muscle relaxant" according to table I. It is not yet the "non-depolarizing suxamethonium", but in our experience it is the first true intermediate-acting non-depolarizing muscle relaxant which will certainly fill a gap in the anaesthetist's neuromuscular armamentarium.

REFERENCES

Agoston S., Salt, P., Newton, D., Bencini, A., Boomsma, P., and Erdmann, W. (1980). The neuromuscular blocking activities of Org NC 45, a new pancuronium derivative in anaesthetized patients. *Br. J. Anaesth.*, 52, 53S.

—— Vermeer, G. A., Kersten, U. W., and Meijer, D. K. F. (1973). The fate of pancuronium bromide in man. *Acta Anaesthestol. Scand.*, 17, 267

Bowman, W. C., and Norman, J. (eds) (1980). Symposium on Org NC 45. *Br. J. Anaesth.*, 52, (Suppl. 1).

Buzello, W. (1975). Der Stoffwechsel von Pancuronium beim Menschen. *Anaesthesist.*, 24, 13.

—— Bischoff, G., Kuhls, E., and Noldge, G. (1980). The new non-depolarizing muscle relaxant Org NC 45 in clinical anaesthesia: preliminary results *Br. J. Anaesth.*, 52, 62S.

Classen, H. G., and Schramm, V. (eds) (1980). Pipecurium bromide (Arduan). *Drug. Res.*, 1, 341.

Crul, J. F., and Booij, L. D. H. J. (1980). First clinical experiences with Org NC 45. *Br. J. Anaesth.*, 52, 49S.

Fahey, M. R., Morris, R. B., Miller, R. D., Nguyen, T. L., and Upton, R. A. (1981a). Pharmacokinetics of Org NC 45 (Norcuron) in patients with and without renal failure. *Br. J. Anaesth.*, 53, 1049.

—— —— —— Sohn, Y. J., Cronelly, R , and Gencarelli, P. (1981b). Clinical pharmacology of Org NC 45 (Norcuron). *Anesthesiology.*, 55, 6.

Gandiha, A., Marshall, I. G., and Paul, D. (1975). Some actions of chandonium iodide, a new short acting muscle relaxant, in anaesthetized cats and on the isolated muscle preparation. *Clin. Exp. Pharm. Physiol.*, 2, 159.

Kalina, K., Fitzal, S., Schwarz, S., Zadrobilek, E., and Steinbereithner, K. (1981). Erste Ergebnisse einer Vergleichsstudie von Org NC 45 und Pancuronium. Proceedings, 10th International Anaesthesia Postgraduate Course, Vienna, 1981, p. 87.

Katz, R. L. (1967). Neuromuscular and electromyographic effects of d-tubocurarine, edrophonium and neostigmine in man. *Anesthesiology.*, 28, 327.

Krieg, N., Crul, J. F., and Booij, L. H. D. J. (1980). Relative potency of Org NC 45, pancuronium, alcuronium and tubocurarine in anaesthetized man *Br. J. Anaesth.*, 52, 783.

McLeod, K., Watson, M. J., and Rawlins, M. D. (1976). Pharmacokinetics of pancuronium in patients with normal and impaired renal function. *Br. J. Anaesth.*, 48, 341.

Payne, J. P., and Hughes, R. (1981). Evaluation of atracurium in anaesthetized man. *Br. J. Anaesth.*, 53, 45.

Savage, D. S., Sleigh, T., and Carlyle, I. (1980). The emergence of Org NC 45, 1- (2 , 3 , 5 , 16 , 17) -3, 17-bis (acetyloxy)-2- (1-piperidinyl)-androstan-16-yl) -1-methylpiperidinium bromide, from the pancuronium series. *Br. J. Anaesth.*, 52, 3S.

Savarese, J. J., and Katz, R. J. (1973). The quest for a short-acting non-depolarizing neuromuscular blocking agent. *Acta Anaesthesiol. Scand.* (Suppl.) 53, 43.

—— Wastila, W. B. (1979). Pharmacology of BW785U: a short-acting non-depolarizing neuromuscular blocking agent. *Anesthesiology*, 51, S277.

Somogyi, A. A., Shanks, C. A., and Triggs, E. J. (1976). Clinical pharmacokinetics of pancuronium bromide. *Eur. J. Clin. Pharmacol.*, 10, 367.

Van der Veen, F., and Bencini, A. (1980). Pharmacokinetics and pharmacodynamics of Org NC 45 in man. *Br. J. Anaesth.*, 52, 37S.

Viby-Mogensen, J., Hansen, P. H., Jørgensen, B. C., Ørding, H., Kann, T., and Fries, B. (1980). A new nerve stimulator (Myotest). *Br. J. Anaesth.*, 52, 547.

Walts, L. F., Lebowitz, M., and Dillon, J B. (1968). A means of recording force thumb adduction. *Anesthesiology*, 29, 1054.

ADMINISTRATIONS REPETEES DE PANCURONIUM ET DE VECURONIUM (ORG NC 45, NORCURON) CHEZ DES PATIENTS SOUMIS A DES INTERVENTIONS DE LONGUE DUREE

RESUME

Cinquante et un patients adultes subissant des actes chirurgicaux, qui nécessitaient au moins 2 h d'anesthésie, ont été divisés au hasard en deux groupes recevant soit du pancuronium soit du vécuronium (Org NC 45) comme myorelaxant, sous surveillance de la pression provoquée par le twitch. En l'absence d'anesthésiques halogénés inhalés, les deux agents étaient administrés avec une injection directe initiale de 0,1 mg kg^{-1} suivie d'injections complémentaires de 0,025 mg kg^{-1} lorsque la hauteur du twitch était revenue à 25% de la valeur témoin. Dans tous les cas, la dose initiale a entrainé un block neuromusculaire complet et des conditions d'intubation satisfaisantes en 2–4 min. Le délai d'installation était légèrement plus bref avec le vecuronium qu'avec le pancuronium. La durée moyenne comprise entre la fin de l'injection et la récupération de 25% du twitch avec injection de la dose d'entretien était trois à quatre fois plus longue avec le pancuronium qu'avec le vecuronium. La dose de produit moyenne nécessaire par heure pour maintenir un block d'au moins 75% était une dose d'entretien de pancuronium (0,025 mg kg^{-1}) et quatre doses d'entretien de vecuronium (0,1 mg kg^{-1}). Le temps de récupération globale (25 à 75% de hauteur du twitch) était 40 ± 14 min avec le pancuronium et 15 ± 8 min avec le vecuronium quel qu'ait été le nombre des réinjections. Une certaine accumulation a été observée avec le pancuronium, particulièrement en termes de prolongation du temps de récupération. Avec le vecuronium, ni la durée d'action de la dose d'entretien ni le temps de récupération ne dépendraient du nombre de doses d'entretien. Dans aucun des groupes n'ont été observés d'effets secondaires cardiovasculaires ou autres. Nous en concluons que le vécuronium est un agent myorelaxant non dépolarisant vraiment intermédiaire. L'absence d'accumulation favorise la maintenance d'un bloc neuromusculaire profond presque jusqu'à la fin de l'intervention sans risque de réveil indûment retardé.

REPETITIVE ANWENDUNG VON PANCURONIUM UND VECURONIUM (ORG NC 45, NORCURON) BEI PATIENTEN MIT LANGDAUERNDEN OPERATIONEN

ZUSAMMENFASSUNG

Funfzig erwachsene Patienten, die sich Operationen unter mindestens 2 Stunden dauernder Narkose unterzogen, wurden radomisiert in zwei Gruppen aufgeteilt. Von ihnen erhielt die eine Pancuronium and die andere Vecuronium (Org NC 45) als Muskelrelaxans. Die neuromuskulare Übertragung wurde durch das evozierte Mechanomyogramm uberwacht. Halogenierte Inhalationsnarkotika wurden nicht verwandt. Beide Muskelrelaxantien wurden in gleicher Dosierung verabreicht, und zwar in Form eines initialen Bolus von 0,1 mg kg^{-1} gefolgt von Widerholungsdosen von 0,025 mg kg^{-1} bei Erholung der Kontraktionskraft auf 25% der Kontrollwerte. In allen Fallen führte die Initialdosis innerhalb 2–4 Minuten bei totaler neuromuskulärer Blockade zu guten Intubationsbedingungen. Vecuronium hatte eine etwas kürzere Anschlagszeit als Pancuronium. Die mittlere Wirkungsdauer der Initial- bzw. Erhaltungsdosen, gerechnet vom Ende der Injektion bis 25% Erholung, was nach Pancuronium drei- bzw. viermal langer als nach Vecuronium. Der durchschnittliche stündliche Relaxansbedarf zur Aufrechterhaltung einer mindestens 75%igen neuromuskulären Blockade betrug eine Erhaltungsdosis Pancuronium (0,025 mg kg^{-1}) bzw. vier Erhaltungsdosen Vecuronium (0,1 mg kg^{-1}). Die Erholungszeit (Zeit von 25 bis 75% Erholung) ohne Rücksicht auf die Anzahl der vorangegangenen Erhaltungsdosen betrug bei Pancuronium 40 ± 14 Minuten und bei Vecuronium 15 ± 8 Minuten ($\bar{x}$ ± SD). Eine geringe Kumulation wurde bei Pancuronium beobachtet, vorrangig in Form einer verlängerten Erholungszeit. Bei Vecuronium ließ weder die Wirkungsdauer der Erhaltungsdosen noch die Dauer der Erholungszeit eine Abhängigkeit von der Anzahl der Erhaltungsdosen erkennen. Cardiovaskuläre oder andere Nebenwirkungen wurden in keiner Patientengruppe beobachtet. Vecuronium kann hiernach als ein wirkliches mittellang wirksames Muskelrelaxans eingestuft werden. Das weitgehende Fehlen von Kumulationserscheinungen begunstigt die Aufrechterhaltung einer tiefen Muskelrelaxation nahezu bis zum Operationsende ohne die Gefahr einer übermäßig langen Erholungszeit. Die Substanz ist allerdings nicht so kurz wirksam, daß sie Succinylcholin vollstandig ersetzen konnte.

ADMINISTRACIÓN REPETIDA DE PANCURONIO Y DE VECURONIO (ORG NC 45, NORCURON) A PACIENTES SOMETIDOS A OPERACIONES DE LARGA DURACIÓN

SUMARIO

Se repartió al azar cincuenta y un pacientes adultos sometidos a operaciones quirúrgicas que necesitaban por lo menos 2 h de anestesia en dos grupos a los cuales se administró ya sea pancuronio ya sea vecuronio (Org NC 45) como relajante muscular bajo control de tensión de contracción evocada. En la ausencia de anestéticos halogenados de inhalación, se administró ambas substancias mediante una inyección de bolo inicial de 0,1 mg kg^{-1}, seguida por incrementos de 0,025 mg kg^{-1}, cuando el tope de la contracción había vuelto al 25% del control. En todos los casos, la dosis inicial produjo un bloqueo neuromuscular total y condiciones de intubación satisfactorias dentro de 2–4 min. El momento en que se inició la acción del vecuronio se produjo ligeramente más rápido que para el pancuronio. El periodo medio que media entre el fin de la inyección y una recuperación del 25% de las dosis iniciales y de mantenimiento fue tres y cuatro veces más largo con el pancuronio que con el vecuronio, respectivamente. La cantidad media de dichas substancias que se necesitaba cada hora para mantener un bloqueo de por lo menos un 75% correspondía a una dosis de mantenimiento de pancuronio (0,025 mg kg^{-1}) y cuatro dosis de mantenimiento de vecuronio (0,1 mg kg^{-1}). El tiempo global de recuperación (25% al 75% del tope de contracción), sin tener en cuenta el número de dosis de mantenimiento, fue de 40 ± 14 min con el pancuronio y de 15 ± 8 min con el vecuronio (media ± SD). Se observó alguna acumulación con el pancuronio, en particular en cuanto a la prolongación del periodo de recuperación. En lo que se refiere al vecuronio, tanto la duración de acción de las dosis de mantenimiento como el tiempo de recuperación no dependieron del número de dosis de mantenimiento. En ambos grupos de pacientes, no se observó ningún efecto secundario cardiovascular o de otra índole. Se concluye que el vecuronio constituye un verdadero relajante muscular nodepolarizante de acción intermedia. Su falta de acumulación propicia el mantenimiento de un bloqueo neuromuscular profundo hasta casi el fin de la operación sin el riesgo de causar un periodo de recuperación demasiado largo.