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Clinical observations on the use of the muscle relaxant rocuronium bromide in the dog

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Abstract

This study was designed to evaluate the effectiveness of neuromuscular blockade with rocuronium bromide (rocuronium) in eighty dogs anaesthetised for a variety of surgical procedures. Rocuronium 0.3 or 0.6 mg/kg (G03 and G06) was administered intravenously (IV) and neuromuscular function was monitored with an acceleromyograph. Lag time (LT) was >1 min in both groups. Onset time (OT) was 2 ± 0.9 and 1.1 ± 0.6 min in the groups given 0.3 and 0.6 mg/kg, respectively. There was a significantly longer time of action with 0.6 mg/kg in contrast to 0.3 mg/kg rocuronium. Time of no response (TonR) was 9.1 ± 4.9–16.9 ± 6.1 min in the groups given 0.3 and 0.6 mg/kg, respectively. The time from the end of injection until 25% recovery of the first twitch from the baseline value ($T1_{25}$) was 13.8 ± 5.5 and 22.3 ± 6.7 min in the groups given 0.3 and 0.6 mg/kg, respectively. $T1_{25–75}$ was similar in both groups. Total recovery to baseline values was achieved in 23.8 ± 6.6 and 31.9 ± 6.5 min in the groups given 0.3 and 0.6 mg/kg, respectively ($P < 0.05$). Premedication, maintenance agent, body position and stimulation site had no significant influence on the pharmacodynamic parameters in both groups. It was concluded that rocuronium is an effective non-depolarising muscle relaxant in the dog under clinical conditions.

Keywords: Dog; Anaesthesia; Neuromuscular blocking agents; Rocuronium

1. Introduction

The introduction of muscle relaxants to human anaesthesia in 1942 was a major advance, since any desired degree of relaxation could be produced irrespective of the depth of anaesthesia (Griffith and Johnson, 1942). The first reports of the use of muscle relaxants in dogs were described by Pickett (1951) using curare and with the depolarising agent succinylcholine (Hall, 1952) and a number of non-depolarising muscle relaxants including pipecuronium, atracurium, pancuronium and vecuronium have been introduced in veterinary anaesthesia in recent years (Jones, 1987, 1992; Jones and Clutton, 1984; Jones and Seymour, 1985). The latest addition, rocuronium bromide (ORG 9426) (rocuronium), derived from vecuronium, became available in 1995.

The main indication for the use of muscle relaxants is to relax skeletal muscles to make surgical access easier, to prevent movement during ophthalmic, orthopaedic and abdominal procedures and to allow the initiation of intermittent positive pressure ventilation (IPPV). Used as part of balanced anaesthesia they reduce the amount of general anaesthetic agent required (Hall and Weaver, 1954).

In order to administer a drug safely to patients, it is important that its pharmacological properties, its time course of action and the possible side-effects are known. The properties of rocuronium have been documented in the dog under experimental (Cason et al., 1990) and clinical conditions (Dugdale et al., 2002). In the present study, we compared the neuromuscular blocking properties of rocuronium at two different doses, administered as a single bolus to dogs, under clinical conditions (see Table 1).

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Table 1
Physical characteristics and anaesthetic protocols of two groups of dogs given different doses of rocuronium

IV rocuronium dose	0.3 mg/kg	0.6 mg/kg
Number of dogs	16	64
Age (years)	6.4 ± 4.1	5.2 ± 3.8
Weight (kg)	23.7 ± 13.1	22.7 ± 13.1
Lateral/dorsal recumbency	16/0	40/24
Stimulation side front/hind	0/16	33/31
Acepromazine/opioid (G1P)	3	37
Medetomidine/opioid (G2P)	6	16
Midazolam/opioid (G3P)	7	11
Isoflurane/fentanyl (G1M)	7	32
Propofol/fentanyl CRI (G2M)	9	32

G03 (0.3 mg/kg), G06 (0.6 mg/kg). Result expressed as the mean and standard deviation (SD).

2. Materials and methods

The study was designed as a prospective clinical study. Eighty dogs of different breeds undergoing a variety of surgical procedures under general anaesthesia were included. In all animals, muscle relaxation was part of the anaesthetic protocol. The dogs received only one bolus of rocuronium during anaesthesia and it was not antagonised so that the complete duration of action of the drug could be observed. The numbers and types of procedures carried out are summarised in Table 2.

The animals had a mean body weight of 22.1 ± 13 kg (mean ± SD) (range 2.6–50 kg) and a mean age of 5.6 ± 4.1 years (range 0.2–14.6). The dogs were classified as ASA[1] 1 (healthy, no systemic disease) to ASA 3 (mild systemic disease, moderate functional limitation) according to their history, clinical examination and the results of laboratory tests (Thurman et al., 1996).

Rocuronium (Esmeron, N.V. Organon) was administered at two different doses: 0.6 mg/kg (G06, $n = 64$) and 0.3 mg/kg (G03, $n = 16$) depending on the proposed duration of surgery.

Dogs were premedicated with different drugs and these were administered approximately 15 min before induction of anaesthesia. The drugs were mixed in a single syringe and administered as a bolus intravenously (IV). The choice of anaesthetic protocol depended on indication and ASA group and are given in Table 2. For premedication, the dogs in premedication group 1 (G1P) received 0.03 mg/kg acepromazine (Vanastress, Vana GmbH) and an opioid, either 0.4 mg/kg butorphanol (Butomidor, Richter Pharma) or 0.1 mg/kg methadone (Heptadon, Ebawe Pharma Gesmbh). In premedication group 2 (G2P), dogs received 0.01 mg/kg medetomidine (Domitor, Orion Corporation) and 0.1 mg/kg methadone. In premedication group 3 (G3P) they were given 0.3 mg/kg midazolam (Midazolam Mayrhofer Pharmazeutika) and 0.4 mg/kg butorphanol.

[1] American Society of Anesthesiologists.

Table 2
The numbers and types of procedures carried out

Procedures	Numbers of dogs
Cataract removal	33
Ophthalmic surgery	9
Osteosynthesis	10
Arthroscopy	2
Anterior cruciate ligament repair	5
Laparotomy	5
Laparoscopy	6
Soft tissue surgery	10

Anaesthesia was induced with propofol (2–6 mg/kg) (Propofol 1%, Fresenius) administered IV to allow tracheal intubation. The dogs were positioned in dorsal ($n = 22$) or lateral recumbency ($n = 58$) and connected to a circle system equipped with a pressure controlled mechanical ventilator (Ventilator 7800, Ohmeda). Anaesthesia was either maintained with isoflurane (Furane, Baxter) in 100% oxygen (group 1 maintenance = G1M) and supplemented with fentanyl 0.02–0.04 mg/kg/h (Fentanyl, Jansen-Cilag) or with total IV anaesthesia of propofol 10–14 mg/kg/h and fentanyl 0.02–0.04 mg/kg/h breathing 100% oxygen (group 2 maintenance = G2M). When spontaneous respiration ceased, IPPV was initiated and the dogs were ventilated at respiratory rate (RR) of 10–15 per min and a tidal volume (V_T) of 10 mL/kg. All dogs received a continuous intravenous infusion of lactated ringer's solution at a rate of 10 mL/kg/h (Ringer Lactat, Fresenius Kabi).

2.1. Neuromuscular monitoring

Neuromuscular function was assessed using an acceleromyograph (TOF-Guard, Organon Teknika). Depending on the surgical procedures and the body position, the ulnar nerve of the front limb or the peroneal nerve of the hindlimb was used for this monitoring. The electrical stimulation was in a train-of-four (TOF) mode at 2 Hz every 15 s with two needle electrodes placed subcutaneously over the nerve. The method of limb fixation and position of the electrodes was as described by Mosing and Auer (1999) and adapted for the hindlimb.

Electrical stimulation and corresponding responses were continuously recorded on a memory card for off-line analysis. Firstly, the electrical current needed for supramaximal stimulation (when the twitch height remained constant in spite of increasing electrical current) was determined. When responses were stable for 5–10 min, the baseline measurements were recorded and rocuronium was then administered as a rapid IV bolus injection.

The lag time (LT, time from end of injection to first depression of the first twitch = T1 of TOF) and onset time (OT, time from end of injection to total disappearance of all four twitch responses in case of total relaxation) were determined. If partial relaxation occurred, the first of three consecutive TOF stimulations with identical amplitude to the first twitch was defined as onset time (Viby-Mogensen et al., 1996). The time of 100% block (TonR, time from

onset in case of total relaxation with no detectable responses to TOF stimulation till return of the first twitch of TOF), the clinical duration of action $T1_{25}$ and T_{50} and T_{75} ($T1_{25,50,75}$, the time from end of injection until 25%, 50% and 75% recovery of the first twitch from baseline value) were determined.

The train-of-four ratio (TOFR) was calculated by dividing the fourth twitch height by the first twitch height. The times to reach a TOF-ratio of 0.7 (TOFR 0.7), 0.8 (TOFR 0.8) and 0.9 (TOFR 0.9) were then determined. The recovery time from neuromuscular block ($T1_{25–75}$, time of the first twitch height to increase from 25% to 75% of baseline values) was also calculated.

To investigate the influence of age and weight dogs, the dogs in G06 were divided into subgroups. Group weight classes (GW) were defined: GW1, 1–10 kg ($n = 19$); GW2, 10–30 kg ($n = 26$); GW3, >30 kg ($n = 19$). Groups of ages (GA) were also defined: GA1, 1–3 years ($n = 28$); GA2, 3–8 ($n = 18$); GA3, >8 ($n = 18$) years.

Heart rate (HR) was measured from an electrocardiogram (EKG HP M1001A, Hewlett Packard). Non-invasive arterial blood pressure (NIBP) was measured by an oscillometric method (NIBP HPM1008P, Hewlett Packard), using a cuff (HP pediatric blood pressure cuffs, Medical Production Group) around the distal part of the foreleg (width approximately 40% of the diameter of the leg). Respiratory rate (RR), end-tidal carbon dioxide ($FE'CO_2$) and isoflurane concentration (FE'ISO) were also monitored with a sidestream anaesthetic gas analyser (HP M1026A, Hewlett Packard). Core body temperature was measured with a temperature probe placed in the oesophagus (Hp Temp M1029A, Hewlett Packard). Numerical values and the time course of the monitored parameters were displayed on a screen (HP .CMS monitor, Hewlett Packard). Values were recorded manually at 5 min intervals on a standard anaesthetic record sheet. Changes immediately after drug administration were recorded as they occurred. Normally, surgery began within 2–10 ± 3.4 min after administration of rocuronium.

2.2. Statistical analysis

Analysis of Variance (ANOVA) was used to determine the influence of the anaesthetic protocol, body position and stimulation site on the pharmacodynamic variables (LT, OT, $T1_{25}$, $T1_{50}$, $T1_{75}$, $T1_{25–75}$, TOFR 0.7, 0.8, 0.9). For normal variables an unpaired Student's *t* test was used to test for differences between GO3 and GO6. The Wilcoxon rank sum test was used for non-normally distributed parameters. Results were expressed as mean and standard deviation (SD) and differences were considered significant if $P < 0.05$.

3. Results

The results are shown in Table 3. There was no statistically significant difference between the two groups for age, body weight and of supramaximal stimulation current. Two dogs in G06 failed to show a response to the neuromuscular blocking agent after a single IV bolus of 0.6 mg/kg rocuronium and were excluded from the analysis.

Table 3
Pharmacodynamic parameters of two different dosages of rocuronium (Roc) in dogs (time in min, mean ± SD, range)

Parameter	0.3 mg/kg Roc	0.6 mg/kg Roc
LT	0.5 ± 0.3 (0.25–1)	0.4 ± 0.2 (0.3–1.3)
OT	2 ± 0.9 (0.7–3.5)	1.1 ± 0.6 (0.3–3)
$T1_{25}$	13.8 ± 5.5 (7–22.75)	22.3 ± 6.7 (10–46)
$T1_{50}$	16.1 ± 6.2 (8.3–26.3)	24.7 ± 7.3 (11.7–47.7)
$T1_{75}$	18.7 ± 7.6 (8.7–30.7)	27.7 ± 7.4 (14–48.7)
$T1_{25–75}$	5.2 ± 2.8 (1.3–10)	5.9 ± 2.4 (2–11)
$T1_{100}$	26.0 ± 7.7 (16.3–37.5)	31. 3 ± 6.7 (19.5–45.7)
TOFR 0.7	21.3 ± 6.8 (11.5–34.25)	29.8 ± 7.5 (17–48.5)
TOFR 0.8	22.1 ± 6.2 (12.5–31)	30.7 ± 7.1 (19–51)
TOFR 0.9	23.7 ± 6.6 (13.3–33)	31.9 ± 6.5 (17.5–46.7)
TonR	9.1 ± 4.9 (2.5–18.5)	16.9 ± 6.1 (7.5–33.7)
MA	42 ± 4 (40–51)	39 ± 12 (10–60)

LT, lag time; OT, onset time; $T1_{25}$, $T1_{50}$, $T1_{75}$, clinical duration; $T1_{25–75}$, recovery time; TOFR, train-of-four ration; TonR, time of no response; mA, milliAmpere.

LT was <1 min in both groups. OT was 2 ± 0.9 and 1.1 ± 0.6 min in G03 and G06, respectively. Total block occurred in all but ten dogs in G06 and two dogs in G03, in which the maximum block of T1 attained were 97% and 94%, respectively. These dogs showed a response to stimulation characterised by a barely visible first twitch of 3–6% of baseline value due to muscle stimulation, apparently due to a direct stimulation effect of the muscle rather than at the neuromuscular junction.

There was a significantly longer duration of action with 0.6 mg/kg compared to 0.3 mg/kg rocuronium. TonR was 9.1 ± 4.9–16.9 ± 6.1 min in G03 and G06, respectively. $T1_{25}$ was reached after 13.8 ± 5.5 min in G03 in comparison to 22.3 ± 6.7 min in G06. Recovery time $T1_{25–75}$ was similar in both groups. Total recovery to baseline values was achieved in 23.8 ± 6.6 min in G03 and 31.9 ± 6.5 min in G06 ($P < 0.05$).

Premedication, maintenance agents, body position and stimulation site had no significant influence on pharmacodynamic parameters in either G03 or G06 (Tables 4 and 5). Premedication with medetomidine (G2P) tended to produce a longer duration of action in comparison to the other premedication groups (G1P, G3P) but this was not significant in either G03 or G06.

Maintenance of anaesthesia with isoflurane (G1M) resulted in a tendency to a more rapid onset but longer duration of action of nearly 3 min in G03 and G06 when compared with the propofol group (G2M). Age and weight in G06 had no significant influence on the different measured pharmacodynamic parameters. Three dogs in G06 suffered from diabetes mellitus. They showed a shorter duration of action in all parameters in comparison with the results of the whole group even though they received isoflurane.

End-expired isoflurane concentration in GM1 at the time of rocuronium administration was 0.9 ± 0.3% and

Table 4
Influence of different protocols on pharmacodynamic parameter of rocuronium (0.3 mg/kg) IV

Protocol/parameter in min	LT	OT	TonR	$T1_{25}$	$T1_{50}$	$T1_{75}$	$T1_{25–75}$	TOFR 0.7	TOFR 0.9
Premedication									
G1P ($n = 3$)	0.5 ± 0.3	1.9 ± 1.1	7.4 ± 2.6	10.5 ± 2.4	12.5 ± 3.4	14.4 ± 3.6	4.45 ± 2.91	18.35 ± 4.39	21.31 ± 5.06
G2P ($n = 6$)	0.5 ± 0.4	2.8 ± 0.8	10.6 ± 7.1	21.5 ± 1.2	24.9 ± 1.2	30.4 ± 0.4	8.91 ± 1.46	29.37 ± 0.88	25.66 ± 2.96
G3P ($n = 7$)	0.6 ± 0.3	1.7 ± 0.6	9.8 ± 5.6	13.3 ± 5.6	15.3 ± 5.1	17.4 ± 6.8	4.25 ± 1.97	22.7 ± 6.46	25.75 ± 7.03
Maintenance									
G1M ($n = 7$)	0.5 ± 0.3	1.9 ± 0.9	8.9 ± 6.1	14.2 ± 6.5	16.2 ± 7.1	19.2 ± 8.9	4.75 ± 3.19	22.56 ± 7.71	26.32 ± 8.58
G2M ($n = 9$)	0.6 ± 0.2	2.1 ± 0.6	9.3 ± 3.1	13.2 ± 4.6	15.9 ± 5.4	18.1 ± 6.2	5.78 ± 2.43	21.25 ± 3.22	26.33 ± 7.27
Sum of $n = 16$	0.5 ± 0.3	2.0 ± 0.9	9.1 ± 4.9	13.8 ± 5.6	16.1 ± 6.2	18.7 ± 7.6	5.2 ± 2.84	21.34 ± 6.8	23.67 ± 6.55

LT, lag time; OT, onset time; $T1_{25}$, $T1_{50}$, $T1_{75}$, clinical duration; $T1_{25–75}$, recovery time; TOFR, train-of-four ration; TonR, time of no response; mA, milliAmpere.

Table 5
Influence of different protocols on pharmacodynamic parameter of rocuronium (0.6 mg/kg) IV

Protocol/ parameter in min	LT	OT	TonR	$T1_{25}$	$T1_{50}$	$T1_{75}$	$T1_{25–75}$	TOFR 0.7	TORF 0.9
Premedication									
G1P ($n = 37$)	0.34 ± 0.13	1.11 ± 0.68	16.77 ± 5.5	21.49 ± 5.37	23.99 ± 5.99	27.38 ± 6.48	6.05 ± 2.54	29.36 ± 7.63	31.33 ± 6.75
G2P ($n = 16$)	0.58 ± 0.34	1.2 ± 0.37	18.93 ± 5.37	23.81 ± 6.96	27.21 ± 9.26	30 ± 9.87	5.92 ± 1.9	31.66 ± 7.43	34.75 ± 6.24
G3P ($n = 8$)	0.47 ± 0.16	0.94 ± 0.39	15 ± 8.04	23.28 ± 11.01	26.25 ± 11.14	27.36 ± 10.22	5.64 ± 2.26	27.64 ± 7.39	32.71 ± 6.34
Maintenance									
G1M ($n = 30$)	0.37 ± 0.15	1 ± 0.43	18.77 ± 7.6	23.66 ± 7.59	26.06 ± 8.77	28.91 ± 8.28	5.84 ± 2.36	30.46 ± 8.75	29.98 ± 7.16
G2M ($n = 31$)	0.39 ± 0.27	1.21 ± 0.69	15.62 ± 4.6	20.87 ± 5.29	23.77 ± 6.06	26.82 ± 6.74	6.06 ± 2.45	29.02 ± 6.01	33.13 ± 6.02
Stimulation									
Hindlimb	0.41 ± 0.21	1.05 ± 0.47	16.33 ± 4.86	22.99 ± 7.88	25.28 ± 8.48	28.05 ± 8.26	5.68 ± 2.14	29.54 ± 8.75	30.19 ± 6.34
Forelimb	0.35 ± 0.15	1.17 ± 0.67	17.51 ± 7.26	21.65 ± 5.23	24.17 ± 5.95	27.33 ± 6.51	6.31 ± 2.67	29.96 ± 6.31	33.82 ± 6.41
Sum of $n = 61$	0.39 ± 0.2	1.1 ± 0.6	16.93 ± 6.1	22.33 ± 6.7	24.77 ± 7.3	27.71 ± 7.4	5.9 ± 2.4	29.76 ± 7.5	31.96 ± 6.5

LT, lag time; OT, onset time; $T1_{25}$, $T1_{50}$, $T1_{75}$, clinical duration; $T1_{25–75}$, recovery time; TOFR, train-of-four ration; TonR, time of no response; mA, milliAmpere.

maintained at a constant value between 0.9% and 1.3% during the observation period in both groups. Mean core body temperature was 37.2 ± 0.8 °C (38.4–36.3 °C) throughout the procedures in both groups. There were no marked changes in heart rate and arterial blood pressure immediately after drug administration and no major changes were observed throughout the procedures. No harmful side-effects such as bronchospasm, due to histamine release, bradycardia, dysrhythmias or life-threatening anaphylactic reaction occurred during the duration of action of rocuronium and the clinical assessment of the neuromuscular block was judged to be good to excellent in all cases.

4. Discussion

The results of this study indicate that both dosages of rocuronium (0.3 and 0.6 mg/kg) produced a 100% neuromuscular block in dogs with a mean time of duration of action of 23.7 ± 6.6 and 31.9 ± 6.5 min, respectively.

It is not clear why rocuronium failed to produce a neuromuscular block in two dogs as the injection was definitely IV. The same vial of the drug was used and an additional bolus from a new vial produced relaxation. Reduction of the activity of rocuronium caused by lack of refrigeration cannot be excluded.

These result are similar to those of Mosing (1998) and Dugdale et al. (2002) using 0.6 and 0.4 mg/kg, respectively. Cason et al. (1990), using similar dosages of rocuronium, demonstrated a longer duration of action ranging from 31 to 40 min. It must be accepted that in those studies different anaesthetic techniques and methods of neuromuscular monitoring were employed.

The majority of drugs routinely currently used in clinical veterinary anaesthesia may alter the time course of action of neuromuscular blocking drugs (Khuenl-Brady et al., 1992; Muir et al., 1989). There is little information concerning the influence of anaesthetic regimes on the pharmacodynamic effects of rocuronium in dogs (Jones, 1999). The different anaesthetic protocols used in the present study produced no significant influence on the duration of action of rocuronium although there was a tendency for prolongation of the duration of action when isoflurane and medetomidine were employed as part of the protocol.

Prolongation of the action of rocuronium during isoflurane anaesthesia has been reported in both man and dogs (Oris et al., 1993; Quill et al., 1991). In cats, halothane and enflurane produced a small increase in the time from

maximal block to 90% recovery with rocuronium (Muir et al., 1994). The volatile agents potentiated the intensity and duration of the block and this effect is more marked with ethers. This pharmacodynamic interaction (Cannon et al., 1987; Stansky et al., 1979) depends on several factors, including duration of anaesthesia, nature of the inhalational agent and its concentration. The effect is caused by a depressant action on the motor end-plate (Ngai, 1975) and depression of acetylcholine release from the motor nerve terminal (Hughes and Payne, 1979). The inhalational anaesthetic agent has to penetrate in the muscle compartment and the extent of interaction depends on the tissue concentration which is a function of the exposure time (Driessen et al., 1986). During procedures of long duration under inhalational anaesthesia a prolongation of action of rocuronium is probable and objective neuromuscular monitoring is recommended.

It is unlikely that propofol and midazolam significantly influence the neuromuscular blocking effects of rocuronium when given as a bolus prior to rocuronium administration (Khuenl-Brady et al., 1992). However, some of the dogs in this study were anaesthetised using propofol as a continuous rate infusion. There is little available information about the influence of injectable anaesthetic drugs on the action of neuromuscular blocking drugs in animals under clinical conditions (Jones, 1999). In the present study, medetomidine showed a tendency to prolong the duration of action of rocuronium. In one other clinical study the influence of medetomidine on the action of rocuronium was investigated in dogs. A prolongation of the neuromuscular blockade was found but this was not statistically significant (Kariman and Clutton, 2004). Ketamine potentiates the blocking effects and lengthens the recovery time for rocuronium in cats (Muir et al., 1994). In the present study the values of the time course of action of rocuronium with medetomidine were unaltered. The variability in response to rocuronium seems to be mainly based on patient-related factors and is independent of the anaesthetic protocol (Lambalk et al., 1991). It is essential to treat each one individually and to monitor the neuromuscular block.

In the study reported here no major changes in heart rate were observed at any time. This is in accord with the report of Mosing (1998). The lack of cardiovascular changes suggest that rocuronium is a safe agent in canine anaesthesia. The cardiovascular effects of neuromuscular blocking agents of an increase in heart rate are said to be due to cardiac muscarinic receptor block, increased noradrenaline release and blockade of its reuptake, nicotinic cholinoceptor blockade at the ganglia or histamine release. Cardiovascular effects following rocuronium administration occur with doses which are much higher than those required to produce neuromuscular block (Muir et al., 1989). There is no evidence of histamine release (Cason et al., 1990). Rocuronium has a mild vagolytic action and a slight but transient tachycardia is occasionally observed in humans (Khuenl-Brady et al., 1995). In dogs there was a significant increase in heart rate one min after IV administration of rocuronium at a dose of 0.6 mg/kg (Mosing, 1998).

In the present study age and weight had no significant influence on the pharmacodynamic parameters of rocuronium. This was as expected because the possible effects are thought to be far less than the variation between individual patients. In man, the onset time, duration of action and recovery time are prolonged in elderly patients and are also longer in infants than in children (Bevan et al., 1993; Matteo et al., 1993; Woelfel et al., 1992).

Neuromuscular monitoring is mandatory for the safe use of neuromuscular blocking agents. Electromyography or mechanomyography are considered scientific standards for monitoring the effects of a neuromuscular blocking agent under experimental conditions. Acceleromyography, as used in this study, is the recommended technique for clinical studies of neuromuscular blocking agents (Viby-Mogensen et al., 1996). It has been suggested that the accuracy of an accelerometer is similar to that of a mechanomyograph. A close correlation between these two measuring techniques has been demonstrated (Loan et al., 1995). Accerleromyography has advantages over tactile or visual evaluation, which are inadequate for precise evaluation of the TOF response. Studies in man have showed that visual evaluation of the TOF response correlates poorly with the true fade of TOF values (Eriksson, 2003).

When considering the wide range of duration of action under clinical conditions, especially in dogs with underlying disease, the time course of action can be significantly altered so that monitoring is essential to determine the optimal time for the administration of incremental doses and reversal of the block.

In this study two different peripheral nerve/muscle groups were monitored. Stimulation of the peroneal nerve in the hindlimb (Bowen, 1969) or the ulnar nerve in the forelimb with the recording of the movement of the paw have been described (Cullen et al., 1980). Others workers (Dugdale et al., 2002; Jones, 1999) have described a technique with stimulation of the facial nerve and recording of the movement of the nose. In the present study there was a tendency for a longer onset and recovery period when stimulation of the hindlimb nerve was performed. This is similar to findings in horses (Auer et al., 2002). The reasons for differences in response to rocuronium between the muscle groups are not clear. Differences in number and density of acetylcholine receptors (Martyn et al., 1992) or the in the constitution of the muscle fibre types (Jewell and Zaimis, 1953) have been demonstrated. Because different muscle groups have different sensitivities, results obtained for one muscle group cannot necessarily be extrapolated to others.

5. Conclusion

Rocuronium at a dose of 0.3 and 0.6 mg/kg produce a reliable neuromuscular block of 23–32 min duration, respectively. There was no significant influence produced by variations in anaesthetic protocols, age, weight and

nerve stimulation sites. The variability of the duration of action makes an objective monitoring of the block essential.

References

Auer, U., Mosing, M., Uray, C., 2002. Comparison of the neuromuscular blocking effect of rocuronium on the M. levator nasolabialis and MM. extensorii of the limb in horses. In: Proceeding of the Association of Veterinary Anaesthetists Meeting, Crete, Greece, p. 76.

Bevan, D.R., Fiset, P., Balendran, P., Law-Min, J.C., Ratcliffe, A., Donati, F., 1993. Pharmacodynamic behaviour of rocuronium in the elderly. Canadian Journal of Anaesthesia 40, 127–132.

Bowen, J.M., 1969. Monitoring neuromuscular function in intact animals. American Journal of Veterinary Research 30, 857–859.

Cannon, J.F., Fahey, M.R., Castagnoli, K.P., 1987. Continuous infusion of vecuronium: the effect of anaesthetic agent. Anesthesiology 67, 503–506.

Cason, B., Baker, D.G., Hickey, R.F., Miller, R.D., Agoston, S., 1990. Cardiovascular and neuromuscular effects of three steroidal neuromuscular blocking drugs in dogs (ORG 9616, ORG 9426, ORG 9991). Anesthesia and Analgesia 70, 382–388.

Cullen, L.K., Jones, R.S., Snowdon, S.L., 1980. Neuromuscular activity in the intact dog – techniques for recording evoked mechanical responses. British Veterinary Journal 136, 154–159.

Driessen, J.J., Crul, J.F., Vree, T.B., Van Egmond, J., Booij, L.H., 1986. Benzodiazepines and neuromuscular blocking drugs in patients. Acta Anaesthesiology Scandinavia 30, 642–646.

Dugdale, A.H.A., Adams, W.A., Jones, R.S., 2002. The clinical use of the neuromuscular blocking agent rocuronium in dogs. Journal Veterinary Anaesthesia and Analgesia 29, 49–53.

Eriksson, L.I., 2003. Evidence-based practice and neuromuscular monitoring. Anesthesiology 98, 1037–1039.

Griffith, H.R., Johnson, G.E., 1942. The use of curare in general anaesthesia. Anesthesiology 3, 418–420.

Hall, L.W., 1952. A report on the clinical use of bis (beta-dimethylaminoethyl)-succinate bisethiodide (''Brevedil,E'' M and B2210) during anaesthesia in the dog. Veterinary Record 64, 491–493.

Hall, L., Weaver, B.M.Q., 1954. Some notes on balanced anaesthesia for the dog and cat. Veterinary Record 66, 289–293.

Hughes, R., Payne, J.P., 1979. Interaction of halothane with nondepolarising neuromuscular blocking drugs in man. British Journal of Clinical Pharmacology 7, 485–490.

Jewell, P.A., Zaimis, E.J., 1953. A differentiation between red and white muscle in the cat based on responses to neuromuscular blocking agents. Journal of Physiology 120, 47–48.

Jones, R.S., 1987. Observation on the neuromuscular blocking action of piecuronium in the dog. Research in Veterinary Science 43, 101–103.

Jones, R.S., 1992. Muscle relaxants in canine anaesthesia 1: history and the drugs. Journal of Small Animal Practice 33, 371–375.

Jones, R.S., 1999. Neuromuscular blockade. In: Gleed, R., Seymore, C. (Eds.), Manual of Small Animal Anaesthesia. BSAVA Publication, Cheltenham, pp. 109–118.

Jones, R.S., Clutton, R.E., 1984. Clinical observations on the use of the muscle relaxant atracurium in the dog. Journal of Small Animal Practice 25, 473–477.

Jones, R.S., Seymour, C.J., 1985. Clinical observation on the use of vecuronium as a muscle relaxant in the dog. Journal of Small Animal Practice 26, 213–218.

Kariman, A., Clutton, R.E., 2004. The effects of medetomidine on the action of vecuronium in anesthetised dogs. In: Proceedings of the Association of Veterinary Anaesthetists, Vienna, Austria, 67.

Khuenl-Brady, K.S., Agoston, S., Miller, R.D., 1992. Interaction of ORG 9426 and some of the clinically used intravenous anaesthetic agents in the cat. Acta Anaesthesiology Scandinavia 36, 260–263.

Khuenl-Brady, K.S., Sparr, H., Pühringer, F., 1995. Rocuronium bromide in the ICU: dose finding and pharmacokinetics. European Journal of Anaesthesiology 12, 79–80.

Lambalk, L.M., De Wit, A.P., Wierda, J.M., Hennis, P.J., Agoston, S., 1991. Dose-response relationship and time course of action of Org 9426. A new muscle relaxant of intermediate duration evaluated under various anaesthetic techniques. Anaesthesia 46, 907–911.

Loan, P.B., Elliott, P., Mirakhur, R.K., Bunting, H.F., Bhanumurthy, S., McMurray, T.J., 1995. Comparison of the haemodynamic effects of mivacurium and atracurium during fentanyl anaesthesia. British Journal of Anaesthesia 74, 330–332.

Martyn, J.A., White, D.A., Gronert, G.A., Jaffe, R.S., Ward, J.M., 1992. Up- and down tregulation of skeletal muscle acethylcholine receptors. Effect on neuromuscular blockers. Anesthesiology 78, 822–843.

Matteo, R.S., Ornstein, E., Schwartz, A.E., Ostapkovich, N., Stone, J.G., 1993. Pharmacokinetics and pharmacodynamics of rocuronium (Org 9426) in elderly surgical patients. Anesthesia and Analgesia 77, 1193–1197.

Mosing, M., 1998. Eine klinische Studie über das Muskelrelaxans Rocuroniumbromid (Esmeron®) beim Hund. Thesis, Doctor Thesis, Veterinary Medicine University Vienna, Vienna.

Mosing, M., Auer, U., 1999. Anwendung des Muskelrelaxans Rocuroniumbromid (Esmeron®) beim Hund. Tierärztliche. Praxis 27, 389–395.

Muir, A.W., Houston, J., Green, K.L., Marshall, R.J., Bowman, W.C., Marshall, I.G., 1989. Effects of a new neuromuscular blocking agent (Org 9426) in anaesthetized cats and pigs and in isolated nerve-muscle preparations. British Journal of Anaesthesia 63, 400–410.

Muir, A.W., Anderson, K.A., Pow, E., 1994. Interaction between rocuronium bromide and some drugs used during anaesthesia. European Journal of Anaesthesiology (Supplement 9), 93–98.

Ngai, S.A.H., 1975. Action of general anaesthetics in producing muscle relaxation: interaction of anaesthetics with relaxants. In: Katz, R.L. (Ed.), Muscle Relaxants. American Elsevier, New York, pp. 279–297.

Oris, B., Crul, J.F., Vandermeersch, E., Van Aken, H., Van Egmond, J., Sabbe, M.B., 1993. Muscle paralysis by rocuronium during halothane, enflurane, isoflurane, and total intravenous anesthesia. Anesthesia and Analgesia 77, 570–573.

Pickett, D., 1951. Curare in canine surgery. Journal of American Veterinary Medicine Association 119, 346–353.

Quill, T.J., Begin, M., Glass, P.S., Ginsberg, B., Gorback, M.S., 1991. Clinical responses to ORG 9426 during isoflurane anesthesia. Anesthesia and Analgesia 72, 203–206.

Stansky, D.R., Ham, J., Miller, R.D., 1979. Pharmacokinetics and pharmacodynamics of d-tubocurarine during nitrous oxide-narcotic and halothane anaesthesia in man. Anesthesiology 51, 235–241.

Thurman, J.C., Tranquilli, W.j., Benson, G.J., 1996. Consideration for general anaesthesia. In: Thurman, J.C., Tranquilli, W.j., Benson, G.J. (Eds.), Lumb and Jones Veterinary Anesthesia, third ed. Wiliams & Wilkins, Baltimore, pp. 5–34.

Viby-Mogensen, J., Engbaek, J., Eriksson, L.I., Gramstad, L., Jensen, E., Jensen, F.S., Koscielniak-Nielsen, Z., Skovgaard, L.T., Ostergaard, D., 1996. Good clinical research practice (GCRP) in pharmacodynamic studies of neuromuscular blocking agents. Acta Anaesthesiology Scandinavia 40, 59–74.

Woelfel, S.K., Brandom, B.W., Cook, D.R., Sarner, J.B., 1992. Effects of bolus administration of ORG-9426 in children during nitrous oxide-halothane anesthesia. Anesthesiology 76, 939–942.