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USE OF THE MUSCLE RELAXANT "VECURONIUM" BY DIFFERENT ADMINISTRATION TECHNIQUES IN DOGS

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ABSTRACT

Different administration techniques of the muscle relaxant vecuronium were studied on the anterior tibialis muscle preparation of thiopentone, α - chloralose anaesthetized dogs. The intubating dose, double intubating dose and the intubating dose after priming were studied . The time of injecting the top-up dose was chosen from our results to be at the maximal twitch depression of the priming dose . Our study demonstrated that, administration of the intubating dose (0.1 mg kg^{-1}) of vecuronium 5 minutes after priming doses (0.01 and 0.02 mg kg^{-1}) significantly reduced the onset time without altering the duration of action and recovery index . Likewise, the double intubating dose significantly decrease the onset time with a significant prolongation of the duration of action and recovery index . It could be concluded that, the priming appears to decrease the onset time rather than the duration of action and allowing rapid spontaneaus recovery. This is particularly important for the safety of patient's during intubation and in the immediate post-operative phase .

INTRODUCTION

Inspite of intensive research on muscle relaxant, it is still not possible to meet the well-known demands laid down by **Savarese and Kitz** [1] for the ideal fast onset, non-depolarizing and short or intermediate duration to replace suxamethonium. Anaesthetists still use suxamethonium in their daily clinical routines[2] even though they are very well aware of its hazardous and life- threatening side effects [3-5] .

If the anaesthetist wishes to replace suxamethonium in clinical practice, he must alter his administration technique , either by "priming" or by increasing the dosage of the agent used to obtain sooner onset of blockade .

The administration of doses 2-5 times greater causes short onset but at the same time lead to a marked increase in the duration of blockade [6,7].

The "priming principle" was introduced by **Foldes in 1984** [8,9] . This technique of giving initial small dose followed by a top up dose shorten the onset time . These are, however, difficult to compare since variables such as the priming dose and time interval are different .

The aim of this work was designed to study, the priming principle compared with the classical and doubling the intubating dose of the non-depolarizing neuromuscular blocker vecuronium, the recovery index was also determined spontaneously .

MATERIAL AND METHODS

A- Drugs :

1- Thiopental Sodium (Egyptian Int. Pharmaceutical Industries Co. A.R.E).
2- Alpha chloralose (Merck, Germany)
3- Vecuronium (Norcurone)® (Organon Teknika, Holland) each vial contains 10mg vecuronium .

B- Experimental Design :

Tibialis anterior muscle preparation was used for this study. Adult mangrel dogs of both sexes (10-15 kg), were anaesthetized with thiopentone sodium 10 mg Kg^{-1} and alpha -chloralose 100 mg kg^{-1} i.v.;.

Anaesthesia was maintained with a continuous infusion of alpha-chloralose 20 mg kg^{-1} every hour [10]. The trachea was cannulated and the lungs were ventillated mechanically .

It the right leg, the lateral popliteal nerve was freed from surrounding connective tissue and a pair of electrodes were applied and protected by cotton wool sooked with liquid paraffin . The tendons of the tibialis anterior muscle were freed, tied and passed across two pullies to the recording system [11] .

Supramaximal stimuli (0.1 Hz, 0.2 ms) was delivered from a stimulator every 15 seconds allover the experiment [12] and the evoked responses were recorded using T_3 isotonic transducer and 2 channal Oscillograph (BioScience, England).

Vecuronium was administred at the recommended intubating dose, the double intubating dose and the intubating dose after priming and the following parameters were determined [13] .

1- **Onset time :** Time from injection to maximum twitch depression .

2- **Clinical duration of action :** Time from injection to 10% twitch recovery.

3- **Recovery index :** The time between 25 and 75% twitch recovery . (during spontaneous recovery),

The maximal effect and the time course of the priming doses (0.01 and 0.02 μg kg^{-1}) were also studied.

The obtained results were statistically analysed using Student's "t" test [14] .

RESULTS

Following administration of the priming doses 0.01 and 0.02 μg Kg^{-1} vecuronium, a maximum % twitch depression of about 1.8 ± 0.4 and 10.5± 0.9 were observed within 3.2 ± 0.4 and 3.4 ± 0.2 minutes and remain for a duration of 6.8 ± 0.9 and 9.9 ± 0.7 minutes respectively (Table, 1).

Table (1) : Maximum twitch depression, onset time and duration to first appearance of twitch regression of the priming doses(0.01 and 0.02 μg kg^{-1}) vecuronium m ± S.E. (n =4)

Dose	Maximum twitch depression %	Onset time (min)	Duration first appearance of twitch regression (min)
0.01 μgkg^{-1}	1.8 ± 0.4	3.2 ± 0.4	6.8 ± 0.9
0.02 μgkg^{-1}	10.5 ± 0.9	3.4 ± 0.2	9.9 ± 0.7

The intubating dose (0.1 μg Kg^{-1}) induced 100% twitch depression in about 98.8 ± 3.7 seconds with a clinical duration (to 10% twitch recovery) of about 17.8 ± 1.5 minutes and recovery index 13.8 ± 3.0 minutes. On doubling the intubating dose (0.2 μg kg^{-1}), the onset time became 62.8 ± 3.6 seconds with a clinical duration of 37.0 ± 2.2 and recovery index 17.2 ± 2.6 minutes (Table 2).

Onset time was highly significantly decreased to 73.3 ± 4.2 and 65.0 ± 3.9 seconds after injection of the intubating dose 5 minutes following priming with 0.01 and 0.02 μg kg^{-1} vecuronium respectively. A nonsignificant increase in the clinical duration (18.5 ± 2.3 and 20.2 ± 2.6 min) and recovery index (13.3 ± 2.4 and 14.8 ± 2.9 min) were observed after priming with the previous techniques (Table 2).

DISCUSSION

Vecuronium is a monoquaternary analogue of pancuronium that unlike its analogue lacks vagolytic effects or substantial dependence on renal function for its clearance from plasma [15]. When short onset time was required, anaesthetists must increase the dose of the drug or follow the priming principle .

It has been long no answer for imporant questions regarding priming; which dosage are involved and what is the optimal time interval for administration?

The doses of priming were selected using the straight lines for the log dose response plots of vecuronium [16,17]. Thus, we suggested that the priming dose must produce a twitch depression not too more than 10%. The time of injection after priming was determined according to our results depending on the maximum twitch depression and its duration. It was found that 5 minutes was sufficient after priming with vecuronium in doses of 0.01 and 0.02 μg kg^{-1}.

Our results indicated that the onset time was significantly decreased in dogs receiving the double intubating dose and the intubating dose after priming with vecuronium . The results agrees with that previously reported [18]. He reported that the onset of blockade is more rapid with priming, and for increasing doses[6,7].

Likewise, the duration of clinical relaxation was highly significantly increased with the double intubating dose of vecuronium, while a nonsignificant increase in the clinical duration after priming with the previous selected two doses was noticed . Increasing doses associated with increased clinical duration was also reported [6,7] .

Recovery from neuromuscular blockade is just as important as onset. Our data represents a nonsignificant difference in the recovery index between dogs received the intubaling dose of vecuronium alone or after priming with 0.01 and 0.02 μg kg^{-1}.

On the other hand, a significant increase in recovery index in dogs administred the double intubating dose of vecuroniumwas obtained .

It could be concluded that, the priming appears to affect the onset time rather than the duration of action, resulting in decreased onset time and allow rapid spontaneous recovery. This is particularly important for the patient's safety during intubation and in the immediate post-operative phase .

Table (2) : Onset time, duration of clinical relaxation and spontaneous recovery index of vecuronium by different administration techniques. m ± S.E. (n =4)

Administration techniques	Onset time (Seconds)	Duration to 10% recovery (min)	Recovery index (25-75%) (min)
-Intubating dose 0.1 μg kg^{-1}	98.8 ± 3.7	17.8 ± 2.5	13.8 ± 1.5
- Double intubating dose	62.8 ± 3.6**	37.0 ± 2.2**	17.2 ± 1.8*
-Intubating dose after priming with 0.01 μg kg^{-1} #	73.3 ± 4.2**	18.5 ± 2.3	13.3 ± 1.8
- Intubating dose after priming with 0.02 μg kg^{-1} #	65.0 ± 3.9**	20.2 ± 2.5*	14.8 ± 2.0

Injection was started 5 mine after priming. * $P < 0.05$ ** $P < 0.01$ (t test).

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إستخدام مرخى العضلات الفيكيورونيوم بتقنيات تجريع مختلفه فى الكلاب

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لقد تمت دراسة إعطاء الفيكيورونيوم على عضلة القصبة الامامية للكلاب المخدرة بالثيوبنتال والالفاكلورالوز . وقد تم اعطاء الجرعة المقررة لتركيب الانبوبة الحنجرية وضعفها وقد اعطيت ايضا الجرعة المقررة لتركيب الانبوبة بعد كل من الجرعتين التحضيريتين ٠,١ و ٠,٢ ميكروجرام /كجم . وقد تم تحديد وقت اعطاء الجرعة المقرره لتركيب الانبوبه من النتائج بحيث تكون فى وقت الحد الاقصى لتأثير الجرعة التحضيرية .

أوضحت النتائج أن اعطاء الجرعة المقرره من الفيكيورونيوم لتركيب الانبوبه بعد الجرعات التحضيريه يحدث اختزال معنوى فى مدة حدوث التأثير الاكلينيكى مع عدم حدوث تأثير معنوى على مدة ابقاء التأثير الأكلينيكى أو مؤشر الافاقه من التأثير مقارنه بأعطاء الجرعة المقررة لتركيب الانبوبة بدون جرعات تحضيرية بينما احدثت الجرعة المضاعفة من الفيكيورونيوم اختزال معنوى فى مدة حدوث التأثير مع زيادة معنوية فى مدة ابقاء التأثير الاكلينيكى ومؤشر الافاقة .

ومن النتائج يستخلص أن الجرعة التحضيرية من الفيكيورونيوم تسبب انخفاض فى مدة حدوث التأثير ولاتؤثر على مدة أبقاء التأثير الاكلينيكى ومؤشر الافاقة وأن هذا له أهمية فى الامان اثناء وضع الانبوبة الحنجرية وعودة العضلات الى طبيعتها بعد العمليات الجراحية .