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UPPER LIP MUSCLES RESPONSE TO THE EFFECT OF ATRACURIUM, GALLAMINE OR PANCURONIUM WITH OR WITHOUT PRIOR TREATMENT WITH CHLORPROMAZINE

(With One Table and 6 Figures)

By

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(Received at 17/6/1990)

استجابة عضلات الشفة العليا لتأثير الأتراكيوريوم، الجلامين والبانكرونيوم
في وجود الكلوربرومازين أو بدونـــــــه

عبدالسلام الصـــــاوى

تم في هذا البحث تقييم الوظيفة العصبية العضلية عند اعطاء الاتراكيوريوم ، الجلامين والبانكرونيـــوم كل على حده وذلك باستخدام عضلات الشفة العليا في الكلاب المخدرة كذلك تمت دراسة تداخـــــــلات الكلوربرومازين مع هذه الإدوية كما تم تقدير وقت حلول المفعول،مدة المفعول ومعدل أفاقة العضلات مـــن هذه المرخيات . وقد تبين من هذه الدراسة أن تعاطي الكلوربرومازين مسبقا يؤدى الى اطالة النشـاط المرخي للاتراكيوريوم والجلامين والبانكرونيوم مع تقليل الجرعة اللازمة من كل منهم. لهذه النتائج أهمية تؤخذ فـــي الاعتبار عند اجراء عمليات التخدير.

SUMMARY

In the present study, the neuromuscular function following the administration of atracurium, gallamine, or pancuronium was evaluated using the upper lip muscles preparation of anaesthetised dogs. Moreover, the interactions of these drugs with chlorpromazine were investigated. The onset time, duration of action and recovery index of these muscle relaxants were measured.

The prior administration of chlorpromazine potentiated and prolonged the inhibitory effect of atracurium, gallamine or pancuronium with marked reduction of their doses. The importance of these findings in anaesthetic practice was refered to.

INTRODUCTION

In veterinary medicine the literature about the use of competitive neuromuscular blocking drugs is scantly although there is continuous need for them specially for diagnostic purposes in domestic animals, treatment of zoo animals and for capture of wild animals. Moreover, muscle relaxants are recommended in surgical interference in all animals. Furthermore, the great risk on using general anaesthesia specially in ruminant animals forces the veterinarian inject some expensive drugs like neuroleptics,

analgesics and tranquilizers like chlorpromazine which is widely used in veterinary practics for securing vicious animals and as a preanaesthetic medication.

Unfortunately, there is no available muscle relaxants in veterinary practice except xylazine which is used as a neuroleptic agent with central neuromuscular blocking activity (AZIZ, 1978).

The aim of the present study was to investigate:

1) The neuromuscular function following the i.v administration of some competitive neuromuscular blocking agents namely: atracurium, gallamine and pancuronium.

2) The effect of premedication with chlorpromzine on the dose and duration of action of the formentioned drugs on the neuromuscular transmission.

MATERIAL and METHODS

Atracurium besylate (Tracurium, Wellcome), Chlorpromazine (Neurazine, Misr), Gallamine Triethiodide (Flaxidel, Alex.) and Pancuronium bromide (Pavulon, Organon).

Experimental :

Anaesthesia in 12 mongrel mature healthy dogs of both sexes and weighing from 12-15 Kg.b.wt. was induced by thiopentone sodium (Biochemie) in an i.v dose of 10 mg/Kg b.wt. Anaesthesia was then maintained by pentobarbitone sodium (Abbot) in a dose of 25 mg/Kg b.wt. i.v. The trachea was cannulated and ventillation was controlled when required using AMBU apparatus consisting of a self inflating bag and non-rebreathing valve. The femoral or saphenous vein was cannulated for injection of drugs. Heparine (EL-Nil) 500 I.U/Kg b.wt. i.v was used as anticoagulant.

Four dogs were specified for each drug tretment. Firstly, the effect of each drug was evaluated alone then after 3 hours the animals were given chlorpromazine (2 mg/Kg. i.m.) and the effect of each drug was evaluated again. Dextrose- saline solution 5% was injected i.v. allover the experiments by drippling.

The upper lip muscles preparation:

The preparation was adopted according to the method described by EL-SAWI et al. (1985). The dorsal buccal branch of the facial nerve was stimulated using a B. Braun nerve stimulator. Indirect muscle twitches were elicited by supramaximal single shocks of 1.5-6 volts applied every 10 seconds interval. Contractions were recorded on the somked drum of the kymograph.

The following parameters were studied according to MEISTELMAN et al. (1986).

Onset time:

The time from the end of injection till the maximum effect.

Duration of action:

The time from the end of injection to spontaneous recovery to 90% of the control value).

Recovery index:

The time required for recovery between 25% and 75% of the control value.

Statistical analysis: The obtained data were statistically analysed acording to Snedecor (1969). The obtained data wereexpressed as mean ± S.E.

RESULTS

The response of the upper lip muscles of anaesthetised dogs to the different competitive neuromuscular blocking drugs was recorded. The onset time, duration of action and recovery index of these drugs are shown in Table (1) and Figs. (1, 3 & 5).

Moreover, it was observed that atracurium (120 ug/Kg b.wt.i.v) induced apnoea which lasts 38.5 ± 4.1 minutes, meanwhile, gallamine (1.2 mg/Kg. b.wt. i.v) induced apnoea which lasts 36 ± 3.22 minutes. Apnoea induced by pancuronium (40 ug/Kg b.wt.i.v) lasts 35 ± 3.07 ninutes.

Table (1): Assessment of neuromuscular function following the administration of atracurium (120 ug/Kg. i.v), gallamine (1.2 mg/Kg. i.v) or pancuronium (40 ug/Kg. i.v) using the upper lip muscles of anaesthetised dogs. The mean time is in minutes ± S.E. Four trials for each drug were performed.

Parameter	Atracurium	Gallamine	Pancuronium
Onset time (min)	3.32 ± 0.79	1.3 ± 0.22	1.95 ± 0.42
Duration of action (min)	94 ± 8.62	17 ± 6,25	68 ± 6.7
Recover index (min)	33.73 ± 1.71	17.25 ± 2.23	29.15 ± 3.0

Interactions of chlorpromazine (2 mg/Kg. i.m) with muscle relaants:

Interaction with atracurium (n= 4):

It was found that atracurium (80 ug/Kg i.v) alone induced about 70 block of the indirectly elicited muscle twitches of the upper lip muscles of dogs, (Fig. 2,A). In the presence of chlorpromazine a dose of 40 ug of atracurium /Kg. i.v. induced about 75% block of the indirectly elicited muscle twitches (Fig. 2,B). Atracurium 50 ug/Kg i.v. induced very rapid neuromuscular blockade of the upper lip muscles of dogs premedicated with chlorpromazine.

Interaction with gallamine (n= 4):

Gallamine (0.9 mg/Kg i.v) alone induced about 70% block of the indirectly elicited muscle twitches with a mean duration of action of 56± 5.2 minutes. Dogs premedicated with chlorpromzine and administered gallamine (0.9 mg/Kg i.v) showed a mean duration of action of 80± 7.32 minutes (Fig. 4).

Interaction with pancuronium (n= 4):

Dogs administered pancuronium (20 ug/Kg i.v) showed 60-65% block of the indirectly elicited muscle twitches of the upper lip muscles with a mean duration of action of 32± 3.0 minutes. Pancuronium (20 ug/Kg i.v) induced rapid neuromuscular blockade of the upper lip muscles of dogs premedicated with chlorpromazine (Fig. 6) with a mean duration of action of 56± 5.2 minutes.

DISCUSSION

Anaesthesia in veterinary practice lack the use of proper competitive neuromuscular blocking drugs. Few reports about the use of gallamine or pancuronium are present. Moreover, there is no available data in veterinary anaesthesia about the use of atracurium in farm animals.

The present study revealed tht atracurium (120 ug/Kg i.v) is recommended for the production of neuromuscular block in the dog with onset time, duration of action and recovery index of 3.32±0.79, 94± 8.62 and 33.73±1.71 minutes respectively.

Also, the present study revealed that the onset time, duration of action and recovery index following gallamine (1.2 mg/Kg i.v) were 1.3±0.22, 74 ± 6.25 and 17.25± 2.23 minutes respectively. HALL (1974) mentioned that dogs administered gallamine (1 mg/Kg) showed complete relaxation within 2 minutes. Apnoea persists for 15-20 minutes.

Moreover, the obtained results on the effect of pancuronium (40 ug/Kg i.v) revealed that the onset time, duration of action and recovery index were 1.95±0.42, 68±6.7 and 29.15±3.0 minutes respectively. These findings are in agreement to some extent with some reports in the field of veterinary anaesthesia. LUMB and JONES (1973) reported that during light ether anaesthesia a dose of 0.06 mg of pancuronium/ Kg. b.wt. induced complete paralysis, they did not report the duration. SAWYER (1982) mentioned that the onset of block following pancuronium (0.1 mg/Kg b.wt.) was within 60 seconds and the block lasting 30-60 minutes. WARREN (1983) mentioned that the dose of pancuronium forpreanaesthetic medication is 0.05-0.1 mg/Kg. b.wt.

If however minor disagreement in the extents of the neuromuscular funtion obtained by comparing the results in differnt works on this subject, it can be attributed to the concentration of the drugs and the anaesthetic technique used in every occasion.

On the other hand the present work revealed that premedication with chlorpromazine (2 mg/Kg. i.m) potentiated and prolonged the neuromuscular blocking activity of the studied drugs (Fig. 2, A&B, Fig. 4, Fig. 6) which necessitated reduction of their doses. Using other animals as cats, frogs and rats, it was found by other workers that chlorpromazine has a neuromuscular blocking effect on intact as well as isolated animal preparations (KOPERA and ARMITAGE, 1954 and SU & LEE, 1960). In addition, it has been reported by WISLICKI (1958) that chlorpromazine enhances the paralytic action of tubocurarine and its analogues. Also, EL-SAWI (1989) found that chlorpromazine

potentiated the neuromuscular blocking activity of vecuronium and reduced its dose necessary for production of neuromuscular block in the dogs.

It could be concluded that atracurium (120 ug/Kg i.v), gallamine (1.2 mg/Kg i.v) or pancuronium (40 ug/Kg i.v) is recommended for the production of the neuromuscular block in the dog. When using any of these drugs as muscle relaxant, care should be paid as regards whether the animal was given chlorpromazine before anaesthesia as a preanaesthetic or for securing, and the proper dose of the these drugs should be choosen as their neuromuscular blocking effect is largely potentiated by chlorpromazine

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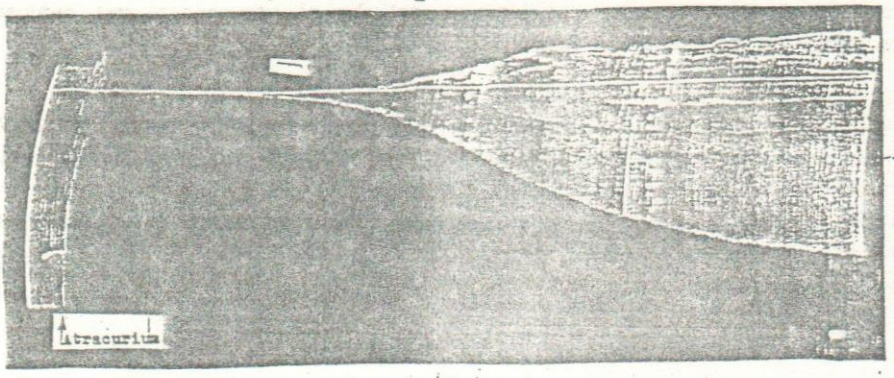

Fig. (1): The effect of atracurium besylate (120 ug/Kg b.wt. i.v) on the indirectly elicited muscle twitches of the upper lip muscles of anaesthetised dog. Indirect muscle twitches were elicited by electrical stimulation of 1.5-6 volts every 10 seconds interval. Time interval : 1 minute.

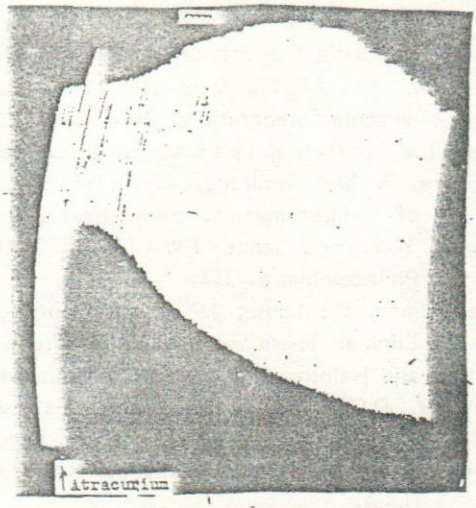

Fig. (2 B)

Fig. (2 A): The effect of atracurium (80 ug/Kg i.v) on the indirectly elicited muscle twitches of the upper lip muscles of anaesthetised dog. time interval : 1 minute.

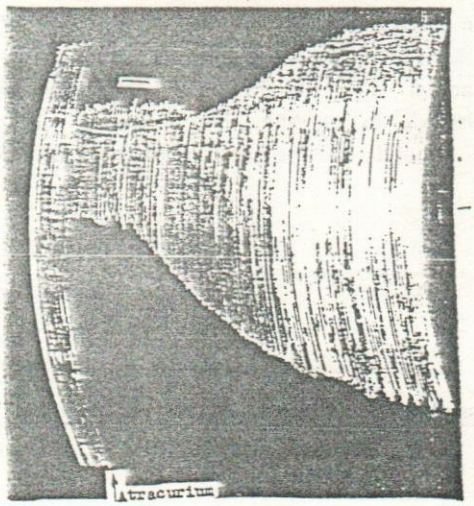

Fig. (2 B)

Fig. (2 B): The effect of atracurium (40 ug/Kg i.v) on the indirectly elicited muscle twitches of the upper lip muscles in the presence of promazine. Time interval : 1 minute.

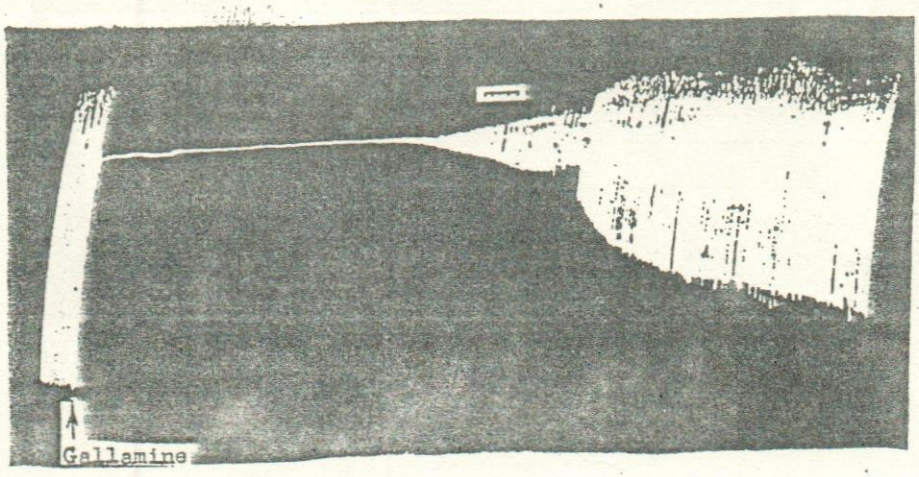

Fig. (3): The effect of gallamine (1.2 mg/Kg b.wt. i.v) on the indirectly elicited muscle twitches of the upper lip muscles of anaesthetised dog. Time interval : 1 minute.

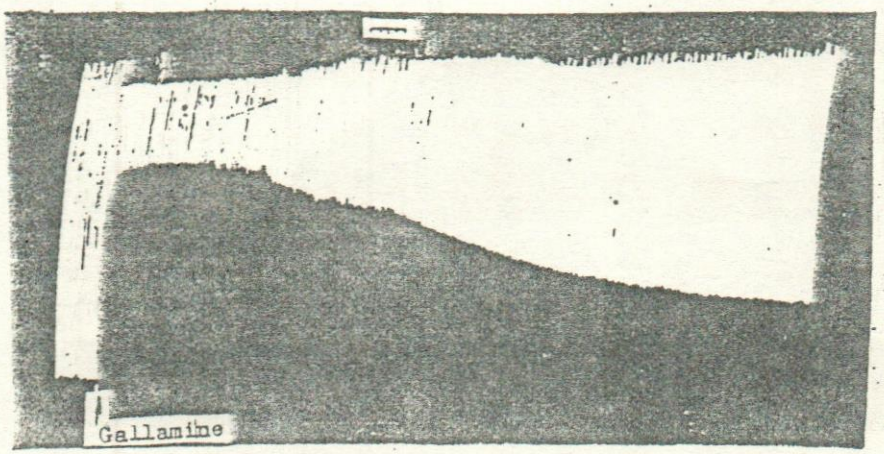

Fig. (4): The effect of glalamine (0.9 mg/Kg b.wt. i.v) on the indirectly elicited muscle twitches of the upper lip muscles of anaesthetised dog (in the presence of chlorpromazine 2 mg/Kg b.wt. i.m). Time interval : 1 minute.

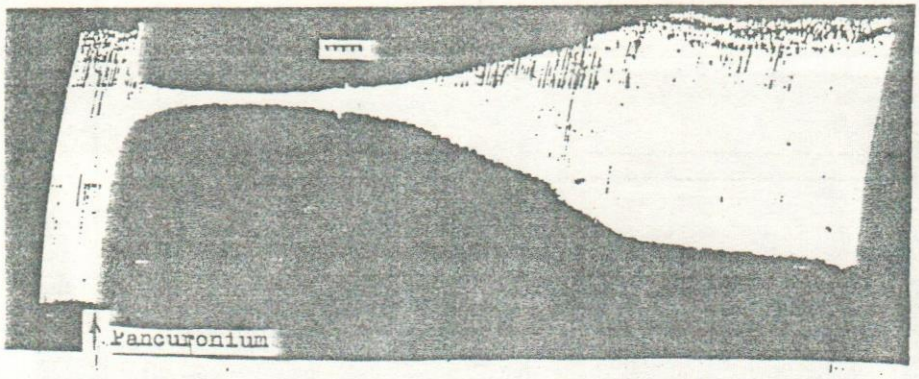

Fig. (5): The effect of pancuronium (35 ug/Kg b.wt. i.v) on the indirectly elicited muscle twitches of the upper lip muscles of anaesthetised dog. Time interval : 1 minute.

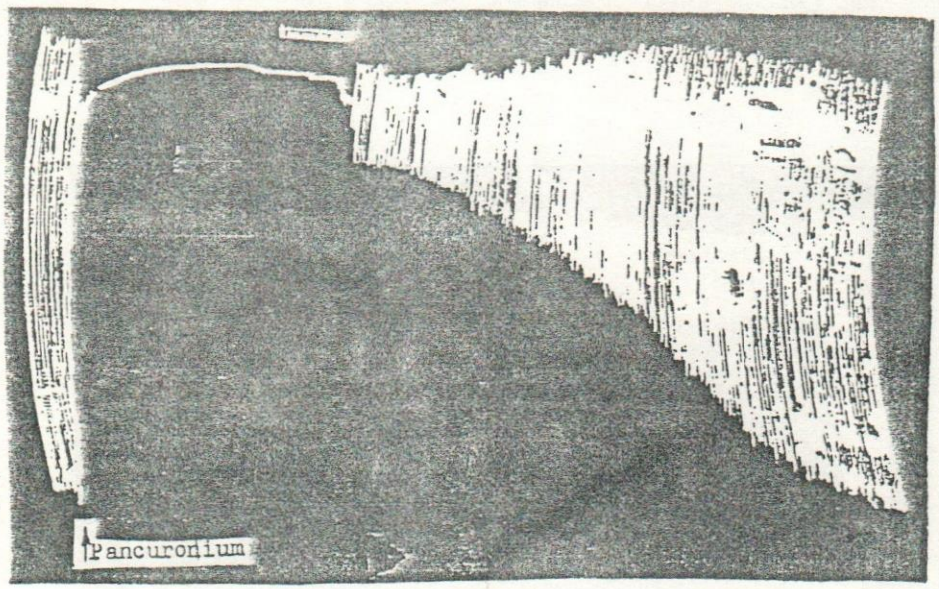

Fig. (6): The effect of pancuronium (20 ug/Kg. b.wt. i.v) on the indirectly elicited muscle twitches of the upper lip muscles of anaesthetised dog (in the presence of chlorpromazine (2 mg/Kg b.wt. i.m). Time intrval : 1 minute.