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# **A COMPARATIVE STUDY ON THE EFFECT OF SUCCINYL CHOLINE CHLORIDE WITH CHLORPROMAZINE IN DIFFERENT NEUROMUSCULAR PREPARATIONS** (With 2 Tables and 4 Figures)

By

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دراسة مقارنة على تأثير سكينيل كلوريد مع الكلوربرومازين  
 على التحفيزات العصبية العضلية المختلفة

عبد السلام الساوي

تم في هذا البحث دراسة تأثير سكينيل كلولين كلوريد وتداخله مع الكلوربرومازين وذلك بتسجيل الانقباضات العضلية الناشئة بالتنبيه العصبي للعضلة القصبية الأمامية وعضلات الشف العليا معا في آن واحد في الكلاب المخدرة وقد تم حساب وقت بدء المفعول ومعدل افاقة العضلات وقد وجد أن التعاطي المسبق للكلوربرومازين يطيل من النشاط المرخي للسكينيل كلولين ما يستلزم أنقاص جرعة. ومن ذلك يتخلص أن تأثير السكينيل كلولين في الكلاب المخدرة يختلف طبقا للتعاطي المسبق.

## **SUMMARY**

The action of succinyl choline chloride and its interaction with chlorpromazine was investigated by simultaneous recording of the indirectly elicited muscle twitches of the Tibialis anterior and the upper lip muscles of the anaesthetised dogs. The onset time, duration of action and recovery index were studied. The prior administration of chlorpromazine resulted in, prolongation of the neuromuscular blocking action of succinyl choline and reduced its relaxant dose.

It could be concluded that the effect of succinyl choline in anaesthetised dogs varied according to the premedication.

## **INTRODUCTION**

Succinyl choline has been used as a muscle relaxant in canine anaesthesia for many years. Its present role in veterinary anaesthesia has been reviewed by many authors.

There are considerable variations in the reports on the recommended dose and the duration of action of the drug in the dog.

HANNISON (1958) recommended a minimal dose of 0.07 mg/Kg of the drug which required a time of 8-9 minutes to restore completely the mechanical activity of the

gastrocnemius muscle which was produced by stimulation of the sciatic nerve. STEVENSON (1960) reported that the paralyzing dose of the drug lasted for 10-15 minutes but did not state the dose. TAVERNOR (1971) stated that a dose of 0.3 mg of succinyl choline/Kg produced paralysis for 5-10 minutes, whereas, SHORT (1974) recommended a dose of 0.3-0.5 mg/Kg but did not state the duration. HALL (1971) stated that a dose of 0.3 mg of succinyl choline/Kg produced a total paralysis of 15-20 minutes duration. JONES *et al.* (1978) reported that a dose of 0.3 mg/Kg of the drug is recommended for the production of the neuromuscular block in the dog. They added that the time to total recovery varied from 24-37 minutes with a mean time of 29 minutes.

In the light of these variable findings, it was of interest to investigate:

- (1) The dose and duration of action of succinyl choline in the dog.
- (2) The interaction of chlorpromazine with different doses of succinyl choline.

### MATERIAL and METHODS

Succinyl - bis-cholin chloride (Lysthenon Siccum, Chemie Linz, Austria). Chlorpromazine (Neurazine, Mistr).

#### Experimental :

Anaesthesia in 10 mongrel mature healthy dogs was induced by sodium thiopental (Biochemie) in a dose of 10 mg/Kg b.wt. i.v and maintained by pentobarbitone sodium (Abbot) in a dose of 25 mg/Kg b.wt. given slowly in the saphenous vein. The trachea was cannulated and ventilation was controlled when required using AMBU apparatus consisting of a self inflating bag and non-rebreathing valve. The saphenous vein was cannulated for injection of succinyl choline. Heparine (El-Nil) 500 I.U/Kg i.v was used as anticoagulant. Chlorpromazine was used as a preanaesthetic medication in a dose of 2 mg/Kg b.wt. i.m in four dogs.

Simultaneous recording of the responses of the Tibialis anterior (BROWN, 1938) and the upper lip muscles (EL-SAWI *et al.*, 1985) to succinyl choline was performed. The lateral popliteal nerve and the dorsal buccal branch of the facial nerve were electrically stimulated by supramaximal single shock of 1.5-6 volts applied every 10 seconds interval. Contractions were recorded on the smoked drum. The following parameters were studied according to MEISTELMAN (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 according to SNEDECOR (1969).



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## RESULTS

## 1) Effect of Succinyl Choline Chloride:

Succinyl choline chloride in an i.v dose of 0.1 mg/Kg b.wt. is recommended for the production of the neuromuscular block in the dog. The onset time, duration of action and recovery index are recorded in table (1). The results are expressed as mean  $\pm$  S.E.

## 2) Interaction between succinyl choline chloride and chlorpromazine:

Dogs premedicated with chlorpromazine (2 mg/Kg b.wt. i.m) and given succinyl choline (0.06 mg/Kg i.v) showed a significant increase in the duration of action and recovery index ( $P < 0.05$ ) than dogs given succinyl choline alone (0.1 mg/Kg). Compare tables (1 & 2) and Figs. (1 & 2).

**Table (1):** Assessment of neuromuscular function following the administration of succinyl choline alone (0.1 mg/Kg i.v) in dogs ( $n = 4$ ). The tibialis and the upper lip muscles are compared. Significance was made at 0.05 level.

Parameter	Tibialis anterior muscle	Upper lip muscles
	Mean $\pm$ S.E.	Mean $\pm$ S.E.
Onset time (seconds)	37.5 $\pm$ 2.5	36.3 $\pm$ 2.3
Duration of action (min).	26.3 $\pm$ 1.6	25.2 $\pm$ 1.2
Recovery index (minute)	6.3 $\pm$ 0.5	7.5 $\pm$ 0.6

**Table (2):** Assessment of neuromuscular function following the administration of succinyl choline (0.06 mg/Kg i.v) in dogs ( $n = 4$ ) premedicated with chlorpromazine (2 mg/Kg i.m). The tibialis and the upper lip muscles are compared.

Parameter	Tibialis anterior muscle	Upper lip muscles
	Mean $\pm$ S.E.	Mean $\pm$ S.E.
Onset time (seconds)	43.3 $\pm$ 6	70.2 $\pm$ 8.3
Duration of action (min.)	50 $\pm$ 3.1	43.5 $\pm$ 4.6
Recovery index (minute)	14.1 $\pm$ 2.2	14.6 $\pm$ 1.9

Dogs administered chlorpromazine (2 mg/Kg b.wt. i.m) and received succinyl choline showed  $ED_{50}$  of succinyl choline for the upper lip muscles was 35 ug/Kg b.wt. i.v. On the other hand, dogs without premedication with chlorpromazine showed  $ED_{50}$  of succinyl choline of 40 and 45 ug/Kg b.wt. for the tibialis and the upper lip muscles respectively (Figs. 3 & 4).

It was observed that premedication with chlorpromazine induced marked prolongation of the duration of  $ED_{50}$  of succinyl choline.

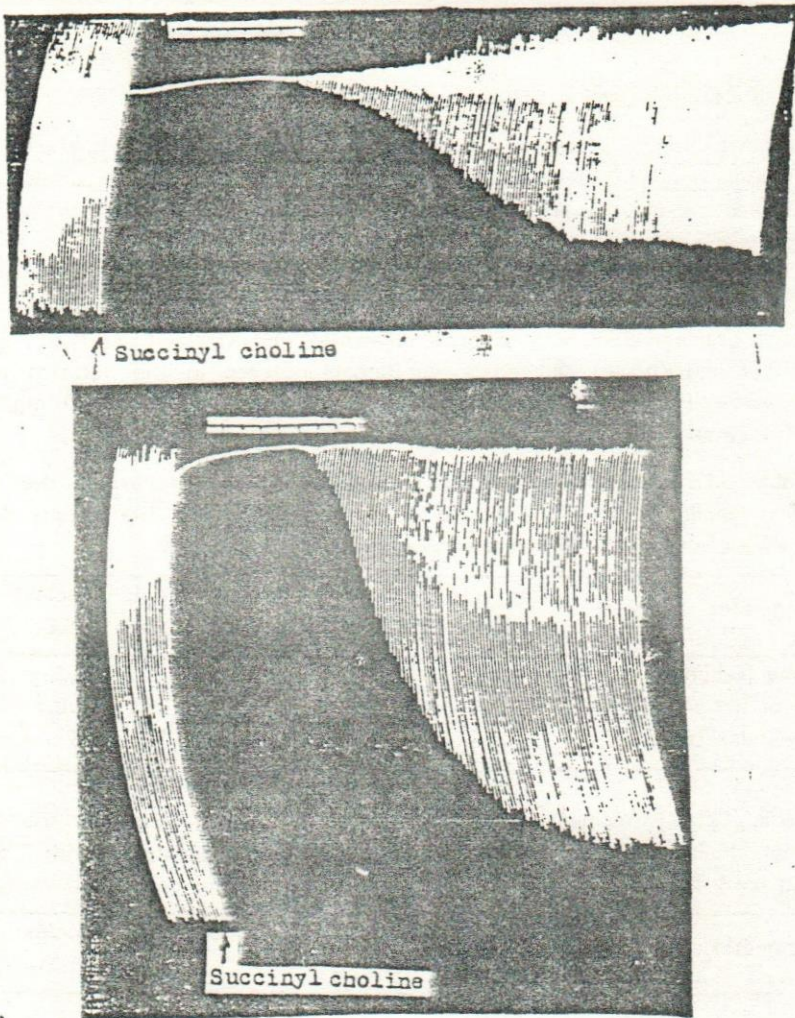


Fig. (1)

Fig. (1): Simultaneous recording of the responses of the upper lip muscles (upper tracing) and the tibialis muscle (lower tracing) to succinyl choline (0.1 mg/Kg i.v.) in pentobarbitone anaesthetised dog without chlorpromazine premedication. Indirect muscle twitches were elicited by 1.5-6 volts, applied at 10 seconds interval. Time interval : 1 minute.



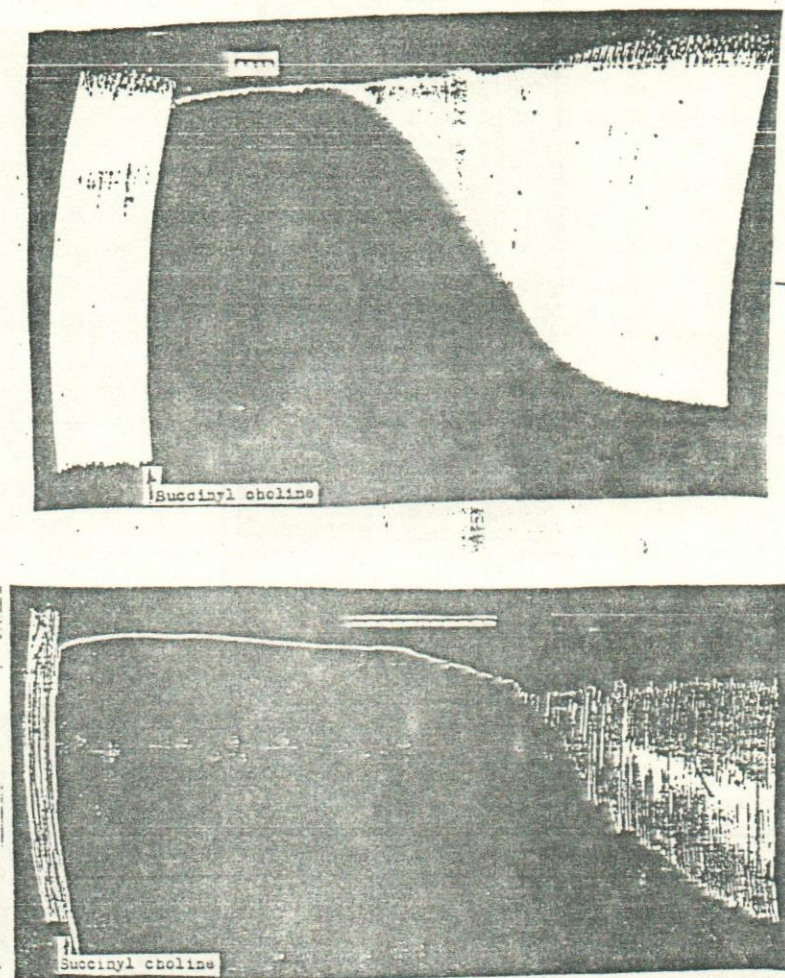


Fig. (2)

Fig. (2): Simultaneous recording of the responses of the upper lip muscles (upper tracing) and the tibialis muscle (lower tracing) to succinyl choline (0.06 mg/Kg i.v.) in pentobarbitone anaesthetised dog premedicated with chlorpromazine (2 mg/Kg i.m). Time interval : 1 mintue.

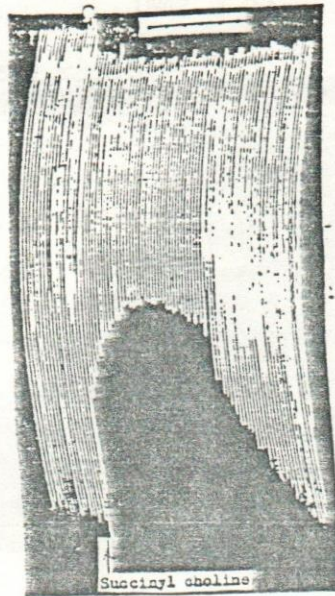


Fig. (3): The duration of  $ED_{50}$  of succinyl choline chloride (45 ug/Kg i.v.) in the upper lip muscles of anaesthetised dog without chlorpromazine premedication. Time interval : 1 minute.

(B)

(A)

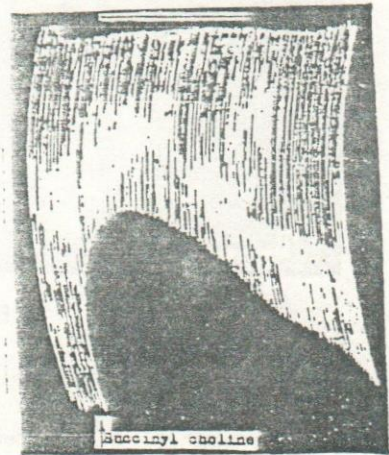
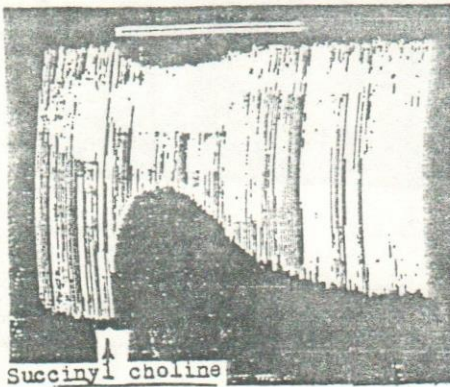


Fig. (4): The duration of  $ED_{50}$  of succinyl choline chloride in anaesthetised dog premedicated with chlorpromazine.

(A) Response of the upper lip muscles to succinyl choline (35 ug/Kg).

(B) Response of the Tibialis muscle to succinyl choline (30 ug/Kg). Time interval : 1 minute.



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**DISCUSSION**

It is evident from the present study that succinyl choline chloride in a dose of 0.1 mg/Kg. b.wt. i.v is normally recommended for the production of neuromuscular block in the dog, although there are a number of variable reports in the literature. A mean time of 26 minutes was required for 90% recovery of the muscle activity for the tibialis and the upper lip muscles.

Variations in the dose and duration of action of succinyl choline in dogs could be attributed to many factors. Among those suggested are: the role of plasma cholinesterase, the anaesthetic and/or premedication and the type of skeletal muscle and nerve used. STOWE (1955) mentioned that the duration of action of succinyl choline varies widely depending on the species and the inherent plasma cholinesterase level. BOWMAN (1980) mentioned that abnormality of plasma cholinesterase may modify the potency and duration of the drug. He added that diminished activity of the enzyme may arise from the use of drugs such as chlorpromazine, a finding which was also reported by LUMB and JONES (1973).

The present work demonstrates the role played by premedication using chlorpromazine. By comparing the induced neuromuscular blockade by succinyl choline alone (0.1 mg/Kg) and succinyl choline (0.06 mg/Kg) with chlorpromazine (Tables 1 & 2) it can be observed that chlorpromazine significantly increased the duration and recovery index of the drug. Also, a marked reduction in the  $ED_{50}$  of succinyl choline and prolongation of its duration were induced by prior premedication with chlorpromazine. This means that chlorpromazine prolongs and potentiates the action of succinyl choline. In the same direction, using other animals as cats, frogs and rats, it was found by other workers that chlorpromazine has a neuromuscular blocking effect using intact as well as isolated skeletal muscle preparations (KOPERA & ARMITAGE, 1954 and SU & LEE, 1960).

The obtained results revealed that the  $ED_{50}$  of succinyl choline alone was 40 and 45 ug/Kg for the tibialis and the upper lip muscles respectively. These findings are compatible with those reported by HANNSON (1956). He mentioned that succinyl choline iodide (0.045-0.060 mg/Kg) induced 50% relaxation in dogs. The chloride salt of succinyl choline is 1.5 times as potent as the iodide (LUMB and JONES, 1973).

Furthermore, differences in sensitivity of some skeletal muscles of the same animal to muscle relaxants were reported by JEWELL and ZAIMIS (1954); BONTA and GOORISSON (1968); ZAIMIS (1976) and EL-SAWI (1987). Accordingly, the gastrocnemius muscle sciatic nerve of dogs used by HANNSON (1958) showed a duration of action of succinyl choline of 8-9 minutes. HONES *et al.* (1978) used the evoked electrical and mechanical response to stimulation of the ulnar nerve of dogs premedicated with acepromazine. They reported a mean time of 29 minutes for complete recovery. The present work recorded a mean time of 26 minutes for 90% recovery of tibialis and the upper lip muscles.



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