

POTENTIATION OF SUCCINYLCHOLINE BY PROCAINE

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It is well known that intravenous procaine potentiates the curarizing effect of succinylcholine. This knowledge comes from experimental data obtained in animals and *in vitro*, and from the use of this combination in human anesthesia.¹

The work here reported was performed with the aim of further clarifying the interaction of these two drugs in humans.

The effect of different doses of succinylcholine was studied and a dose-response curve obtained; in addition, the effect of different doses of procaine in lengthening the time of apnea produced by succinylcholine was also recorded and analyzed.

METHOD

Four women, from the Psiquiatric Hospital were chosen, their ages being 19, 34, 43, and 66 years. Except for their chronic mental defect they were in good physical condition.

Two series of experiments were done with these 4 patients, always during the morning and in fasting condition.

The first of them consisted of intravenous administration of 2.6 mg./kg. of 2.5 per cent solution of thiopental followed immediately by 1.0 mg./kg. of succinylcholine. After this the length of respiratory paralysis was recorded as follows: the absolute absence of diaphragmatic contraction was considered the onset of apnea and the first evidence of contraction of the same muscle was taken as the end, this measure was obtained by observing tangentially the thorax and abdomen of the patient, this being done by one observer while another checked the observation by the control of the rebreathing bag.

This time recording was deemed satisfactory for the purpose of this experiment.

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After respiratory depression ensued and until breathing became normal again, the patients' lungs were manually ventilated. This manipulation was interrupted frequently to observe the diaphragmatic activity.

In successive days and always under the same conditions, these experiments were repeated, increasing the doses of succinylcholine in a ratio of 1.5, *i.e.*, 1.5, 2.25, and 3.37 mg./kg.

The second series was performed in a similar way and with the same patients, the difference lying in the fact that succinylcholine was kept constant at a dose of 1.0 mg./kg., followed immediately by procaine at doses ranging from 5.04 to 38.26 mg./kg., these quantities increasing in a ratio of 1.5.

Only 3 out of 4 patients were injected with 38.26 mg./kg. of procaine.

The timing of the respiratory paralysis was performed as in the previous experiment.

RESULTS

First Series. As it is shown in figure 1, any increase in the dosage of succinylcholine resulted in an increase in the time of respiratory paralysis, each successive dose prolonging this time approximately 50 seconds.

A linear regression was obtained plotting the time of apnea against the log dose ($F_{\text{slope}} = 5.3$, $0.05 > P > 0.01$).

Second Series. Figure 1 shows the results of this series.

Doses of procaine from 5.04 up to 11.34 mg./kg. induce constant lengthening of the time of apnea of approximately 78 seconds, while the doses from 11.34 to 38.26 mg./kg. bring about an increase in the duration of the respiratory paralysis parallel to the increase obtained by the succinylcholine dosage in the first series.

Statistically analyzed, the first part of the slope from 5.04 to 11.34 mg./kg. (fig. 1) is the estimation of a horizontal ($F_{\text{slope}} = 1.41$,

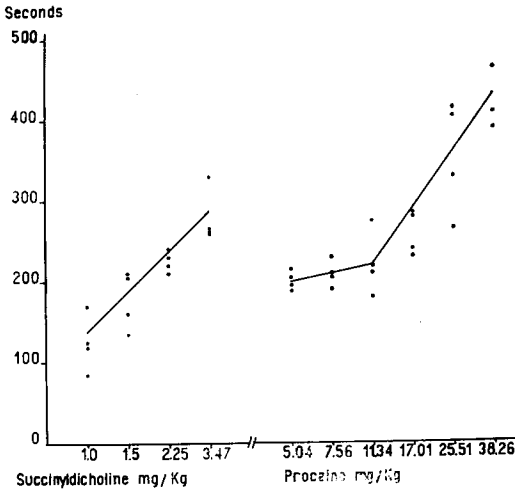


FIG. 1. *Left.* Dose response curve produced by succinylcholine. *Right.* Effect of 1.0 mg./kg. of succinylcholine and different doses of procaine. Observe the parallelism of dose response curve from 11.34 up to 38.26 mg./kg. of procaine with that of succinylcholine.

$P > 0.05$), while the second part from 11.34 to 38.26 mg./kg. is equal to the slope elicited by succinylcholine (fig. 1) ($F_{\text{parallelism}} = 1.99$, $P > 0.05$).

DISCUSSION

Procaine displaces succinylcholine from the cholinesterase system.¹ On the other hand, procaine alone is without curarizing effect,² in consequence procaine should act through succinylcholine itself. This hypothesis is amenable to experimental proof, and this has been the task of the present work.

If the action of procaine is to actually prolong the paralysis induced by succinylcholine rather than by another unknown action of its own their dose response curves must be equal and this is actually the case (figure 1, from 11.34 to 38.26 mg./kg. of procaine and compare with the slope of succinylcholine).

The procaine dosage ranging from 5.04 to 11.34 mg./kg. induces a constant delay of the time of apnea, but no dose-response curve is obtained. This fact can be explained assuming that these two substances are distributed into three compartments, one readily accessible to both of these drugs (plasma) and

the other separated from the first. Succinylcholine is displaced by procaine from the cholinesterase system of the first compartment towards the third (neuromuscular junction), thus accounting for 78 seconds of constant delay, but the excess of procaine then passes to the second compartment and no additional succinylcholine is displaced until this second compartment is saturated when 11.34 mg./kg. of procaine is injected. From this dosage on, the second compartment is saturated and any increase of procaine releases a proportional quantity of succinylcholine, thus giving rise to the same response curve as the latter. For the sake of discussion, it is assumed that the second compartment contains no succinylcholine and the third one is not accessible to procaine (fig. 2).

A dose of 11.34 mg./kg. of procaine (plus 1.0 mg./kg. succinylcholine) would represent a threshold or the maximum capacity for the simultaneous hydrolysis of procaine and succinylcholine. The knowledge of this threshold would allow us to measure *in vivo* the capacity of hydrolysis of cholinesterase; in other words would give us an idea of the total quantity of cholinesterase available in a fixed moment, under the conditions of this experiment. The measure of this quantity might perhaps be employed as a functional hepatic test since cholinesterase seems intimately related to hepatic functions.³

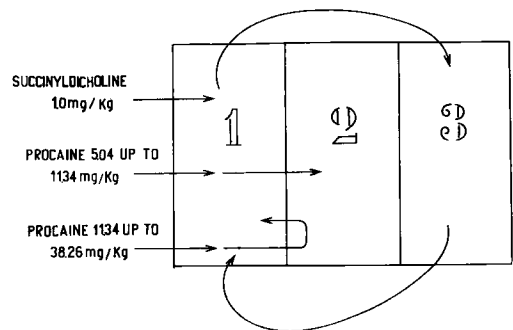


FIG. 2. Succinylcholine is displaced by procaine from compartment 1 (plasma) towards compartment 3 (neuromuscular junction), the excess coming back to compartment 1. Procaine enters first, compartment 1 and afterwards 2 until the latter is saturated and then returning back to compartment 1.

SUMMARY

The effect of procaine on the muscular paralysis due to succinylcholine was investigated.

Procaine in doses of 5.04 mg./kg. to 11.34 mg./kg. slightly lengthens the curarizing effect of 1.0 mg./kg. of succinylcholine, but doses over 11.34 mg./kg. give rise to a "dose-response" curve similar to that of succinylcholine. This effect is directly related to the increment of procaine doses.

The hypothesis suggested by these results is that three compartments are available for the hydrolysis of procaine and succinylcholine. Both drugs enter the first compartment while the other two compartments are accessible to only one of each drug. Procaine displaces succinylcholine from the first compartment, thus lengthening its curarizing effect.

The saturation of the second compartment measures the maximum capacity of hydrolysis of cholinesterase *in vivo*.

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DECAMETHONIUM Single motor units were isolated in the hind legs of rats and response to stimulation was recorded. Decamethonium administration resulted in decline of response amplitude, either gradual or in steps. There was increasing latency of response of sub-units. The evidence for this fractionation of the motor unit was the conversion of the initial single wave into a polyphasic wave of increased duration. This indicates that the initial effect of decamethonium is a curare-like or competitive block, with depolarization of the end-plate occurring later. (Locke, S.: *Fractionation of the Motor Unit: Response to Decamethonium, Electroenceph. Clin. Neurophysiol.* 13: 385 (June) 1961.)

BRONCHOSCOPY General anesthesia with Pentothal sodium, nitrous oxide and oxygen was used for 200 patients. Succinylcholine provided relaxation, and a 4 or 5 mm. Magill endotracheal tube was used in adults. (Rogers, F. A., and Erhardt, K. S.: *Bronchoscopy under General Anesthesia, J. Thor. Cardio. Surg.* 41: 817 (June) 1961.)

SODA LIME A significant amount of soda lime can be saved in the semiclosed system if the excess gas valve is located on the expiratory side. Arranging two canisters in tandem also increases economy. (Hennes, H. H., and Kreuzer, H.: *Saving of Soda Lime during Anesthesia with a Semiclosed System, Der Anaesthetist* 10: 181 (June) 1961.)