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 Title : NEUROMUSCULAR BLOCK WITH NEOMYCIN AND (+)-TUBOCURARINE
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Introduction. Neuromuscular block by antibiotics is a significant clinical problem, particularly the synergism between certain antibiotics and neuromuscular blocking agents^{1,2}. Neomycin has been shown to be synergistic in potency with (+)-tubocurarine both *in vitro*² and *in vivo*¹ using twitch tension as an index of neuromuscular block. However the diagnostic characteristics of the neuromuscular block due to neomycin and (+)-tubocurarine together have not been more fully elucidated. The present study examined the characteristics of an equiactive mixture of neomycin and (+)-tubocurarine on tetanic tension and train-of-four, in addition to twitch tension, in the anesthetized cat.

Methods. The sciatic nerve-tibialis anterior muscle preparation of fifteen anesthetized cats was used to determine neuromuscular block at a stimulation frequency of 0.1 Hz. Cumulative dose-response curves to either i.v. (+)-tubocurarine (n=5), neomycin (n=5) or an equiactive mixture (n=5) were constructed. At 50% recovery a response to train-of-four (T4) nerve stimulation (2 Hz) was elicited. At 90 to 100% recovery a further administration of the antagonist under study was made to repeat a 50% block of twitch tension at which time a 10 s tetanic stimulus (50 Hz) was applied, followed by 10 s rest and a single stimulus to give the post-tetanic facilitation. Subsequent posttetanic exhaustion, if any, was taken as the minimum height of the twitch tension after the tetanus compared to immediately before the tetanus. Results are presented as the mean \pm SEM of five observations.

Results. The characteristics of the neuromuscular block produced by (+)-tubocurarine alone and neomycin alone are shown in table 1.

	(+)-TUBOCURARINE	NEOMYCIN
ED50	0.2 \pm 0.02 mg/kg	22 \pm 4 mg/kg
Recov time (25-75%)	9 \pm 1 min	6 \pm 2 min
T4 fade	-73 \pm 7%	-3 \pm 2%
% Δ of tetanic tension	-57 \pm 24%	-18 \pm 8%
Posttetanic facilitation	+254 \pm 24%	+268 \pm 38%
Twitch/tetanus ratio	0.25 \pm 0.05	0.17 \pm 0.02
Posttetanic exhaustion	0%	100%

TABLE 1. Comparison of the neuromuscular blocking characteristics of (+)-tubocurarine and neomycin.

The characteristics of block of an equiactive mixture of (+)-tubocurarine and neomycin are shown in table 2.

	Observed	Expected
ED50	0.52 \pm 0.1 ml/kg	1 ml/kg*
Recov time (25-75%)	6 \pm 2 min	7.5 min
T4 fade	-43 \pm 9%	-38%
% Δ of tetanic tension	-12 \pm 22%	-38%
Posttetanic facilitation	+396 \pm 84%	+261%
Twitch/tetanus ratio	0.16 \pm 0.04	0.21
Posttetanic exhaustion	-68 \pm 13%	-50%

TABLE 2. Comparison of the neuromuscular blocking characteristics of an equiactive mixture of (+)-tubocurarine and neomycin (*1 ml/kg contains 0.5 of the ED50 of (+)-tubocurarine and 0.5 of the ED50 of neomycin). The expected results were calculated from table 1.

Discussion. The results of the present study clearly show that an equiactive mixture of (+)-tubocurarine and neomycin results in a neuromuscular block which has the characteristics which would be expected when the parameters of the block produced by the individual drugs are averaged, apart from a slightly greater posttetanic facilitation and the expected synergism¹. The posttetanic exhaustion which is characteristic of neomycin-induced neuromuscular block is still apparent during the neuromuscular block produced by the mixture. This phenomenon could be used as an indication that the neuromuscular block is at least partially due to the antibiotic. The synergism observed in the present study is most likely due to the predominantly pre-junctional action of neomycin and the predominantly postjunctional action of (+)-tubocurarine as proposed by previous workers². It is concluded that although there is marked synergism in potency between neomycin and (+)-tubocurarine, the characteristics of tetanus and train-of-four elicited during neuromuscular block produced by a mixture of the two drugs demonstrate a straightforward combined action.

References.

1. Stanley V F, Giesecke A H, Jenkins M T: Neomycin-curare neuromuscular block and reversal in cats. *Anesthesiology* 31:228-232, 1969
2. Burkett L, Bikhazi G B, Thomas K C, Rosenthal D A, Wirta M G, Foldes F F: Mutual potentiation of the neuromuscular effects of antibiotics and relaxants. *Anesth Analg (Cleve)* 58:107-115, 1979