Neuromuscular Blocking Properties of Lincomycin

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The intravenous injection of lincomycin (12.5, 25, and 50 mg./Kg.) into rabbits produced a dose-related neuromuscular blockade. This blockade was not reversed by the injection of neostigmine methylsulfate.

PREVIOUS investigators have reported that certain antibiotics possess neuromuscular blocking properties. Among these are neomycin (1), streptomycin (2), paromomycin (3), colistin (4), kanamycin, dihydrostreptomycin, and polymixin B (5). Thus, it was of interest to evaluate a new antibiotic, lincomycin, with respect to its potential as a neuromuscular blocking agent.

METHODS

Dutch rabbits weighing 0.6 to 1.9 Kg. were anesthetized with sodium phenobarbital (200 mg./Kg. i.v.), and bipolar silver electrodes were placed on the peripheral end of the sectioned sciatic nerve. The nerve was stimulated once per second for 0.2 sec. with monophasic square wave pulses of 0.5 msec. duration at a frequency of 250 pulses per second and of supramaximal voltage. A model S-4 Grass stimulator was used in all experiments. Semi-isometric contractions were recorded using a Grass force transducer and a Gilson or Offner recorder.

All drugs were administered by slow injection into a marginal ear vein. Lincomycin injection[1] was diluted with isotonic sodium chloride solution so that each dose was given in a volume of 1 ml. The vehicle of the commercial product (containing 0.9% benzyl alcohol) was found to have no effect on the preparation.

In the dose-response study, each animal received all three doses (12.5, 25, and 50 mg./Kg.) of lincomycin according to a Latin square design. The contractions were allowed to return to control level before the administration of the next dose. An analysis of variance (6) was performed, and the per cent-log dose regression line was computed according to the method described by Finney (7).

In addition, the effects of neostigmine methyl sulfate on the neuromuscular blockade produced by lincomycin were evaluated.

RESULTS

Neuromuscular blockade was produced by lincomycin throughout the dosage range studied. The per cent-log dose regression line is shown in Fig. 1. In the analysis of variance, a significant difference between animals was found ($p < 0.05$). This would suggest that there is a considerable difference between animals in their sensitivity to the neuromuscular blocking properties of this agent. However, the analysis demonstrated that there was no significant effect ($p > 0.1$) due to the order in which the doses were given. Thus the prior administration of a blocking dose of lincomycin had no effect on the response of the next dose of the drug, after return of the contractions to control levels.

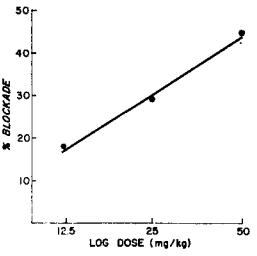

Fig. 1.—Plot of per cent blockade *vs.* dose (log scale). Three animals were used in a Latin square design. Slope of line = 45.6.

In an attempt to reverse the neuromuscular blockade produced by lincomycin, neostigmine methyl sulfate (25 and 50 mcg./Kg.) was administered at the peak of the response to lincomycin. The pattern of recovery to lincomycin did not appear to be altered by the neostigmine.

DISCUSSION

Data presented in this paper indicate that the administration of lincomycin in sufficient doses in rabbits can result in neuromuscular blockade. The character of this blockade is similar to that reported by Adamson *et al.* (4) for colistin sulfate, in that it apparently is not reversed by neostigmine. This is in contrast to the blockade produced by neomycin, streptomycin, dihydrostreptomycin, or paromomycin which is reversed by neostigmine (1–3, 5).

No reports of adverse clinical effects resulting from the neuromuscular blocking properties of lincomycin have, to our knowledge, been reported. However, it is conceivable that lincomycin could produce undesirable effects under circumstances such as overdosage or in the presence of other drugs which are additive with or enhance its neuromuscular blocking action.

Received July 23, 1965, from the Department of Pharmacology, College of Medicine, University of Iowa, Iowa City.

Accepted for publication September 14, 1965.

This investigation was supported in part by grants FI-GM-25075 and FI-GM-25081 from the National Institute of General Medical Sciences, U. S. Public Health Service, Bethesda, Md.

Added in proof: Since this paper was submitted for publication, it has been reported that 100 mg./Kg. of lincomycin does not produce neuromuscular blockade. [Adamson, R. H., and Dixon, R. L., *J. Pharm. Sci.*, **54**, 1226(1965).] The difference between their results and ours probably lies in the stimulus parameters which were used. Using the stimulus parameters that were described by these investigators (*i.e.*, pulse train every 5 sec. rather than once per second), we also found that lincomycin had no consistent effect on the contractions.

[1] Marketed as Lincocin by The Upjohn Co., Kalamazoo, Mich.

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