

SHORT COMMUNICATION :

EFFECTS OF NEUROMUSCULAR BLOCKING AGENTS ON ARTERIAL BLOOD PRESSURE IN THE RAT

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Summary: Gallamine triethiodide pancuronium bromide or d-tubocurarine was infused intravenously at different rates in urethane anaesthetized rats. When given in neuromuscular blocking doses, gallamine triethiodide produced significant hypotension if the rate of infusion exceeded 2 mg/min whereas neither pancuronium bromide nor d-tubocurarine produced a marked change in blood pressure in neuromuscular blocking doses.

Key words: neuromuscular rate of infusion hypotension blocking agents

INTRODUCTION

In the course of experiments on reflex effects of tooth pulp stimulation in rats, it was observed that the neuromuscular blocking agent gallamine triethiodide caused hypotension. It has been reported to have no effect on blood pressure in cats, dogs or rabbits even in very large doses (5) but it appears not to have been investigated in rats. The present experiments were therefore, carried out to compare the effects of some commonly used neuromuscular blocking agents in rats. A more detailed account of these experiments is available elsewhere (2).

MATERIALS AND METHODS

Rats weighing 350 - 375 g were anaesthetized with ethyl carbamate ('Urethane', B.D.H. chemicals, 0.8-1.0 g/kg body wt). Body temperature was maintained at 37°C and the animals were artificially ventilated at the rate of 60-65 cycles per min; the tidal volume was adjusted between 2.5 ml - 6 ml, to maintain an end-tidal CO₂% of 3.5-4. The sciatic nerve was stimulated once every 5 sec via silver wire electrodes using square wave pulses (0.05 ms, 5V). An electromyogram was recorded from the gastrocnemius muscle using insulated silver wire (0.03 mm diameter) implanted into the muscle. The integrated gastrocnemius e.m.g. and the iliac arterial blood pressure were recorded simultaneously on

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two channels of a pen recorder. The following neuromuscular blocking agents, diluted in Ringer's were infused intravenously at different rates.

Gallamine triethiodide (Flaxedil; May & Baker Ltd., Dagenham), pancuronium bromide ('Pavulon'; Organon Laboratories Ltd., Surrey) and d-tubocurarine chloride ('Tuberine'; Duncan, Flockhart & Co. Ltd., London).

RESULTS

Gallamine triethiodide :

When 10 *mg/kg* body weight (3), of gallamine triethiodide at a concentration of 40.0 *mg/ml* was infused intravenously over $\frac{1}{2}$ min, the blood pressure dropped steadily from its normal value of about 140/100 mm Hg and within a few min the animal died. With a more dilute solution (4.0 *mg/ml*) infused more slowly (0.4 *mg/min*), there was no detectable e.m.g. response for about 40 min till the total dose was about 21 *mg/kg* body weight and at this dose level the blood pressure was not markedly affected. Only when the total dose exceeded about 133.0 *mg/kg* body weight, did both diastolic and systolic pressures begin to fall steeply (Fig. 1). The results obtained with this and other intermediate

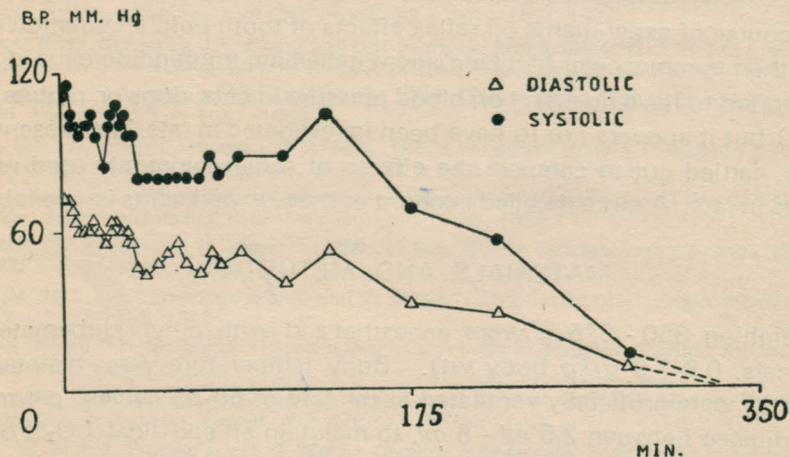


Fig. 1 : Effect of gallamine triethiodide on systolic (●—●) and diastolic (△—△) blood pressures when infused at 0.4 *mg/min*. The dashed line indicates the effect of the final lethal dose. Abscissa, time (min); ordinate, blood pressure (mm Hg)

doses are summarized in Table I. When gallamine (1 *mg/kg*) was repeatedly injected, the first few doses were more effective than later doses in causing a drop in blood pressure (Fig.2).

Pancuronium bromide :

Pancuronium bromide (0.2 mg/ml) administered at a rate of 20 $\mu\text{g}/\text{min}$ at a total dose of 0.67 mg/kg body weight, produced a neuromuscular block which lasted for a period of less than 10 min. This dose produced no significant change in blood pressure.

TABLE I : Doses of gallamine triethiodide producing hypotension and neuromuscular paralysis at different rates of intravenous infusion.

Rate of infusion (mg/min)	Dosage which produced marked hypotension (mg/kg body wt.)	Dosage necessary to produce complete paralysis (mg/kg body wt.)
8.0	died	died
2.0	2.5	8.0
1.0	32.0	9.0
0.8	67.0	13.5
0.4	133.0	21.3

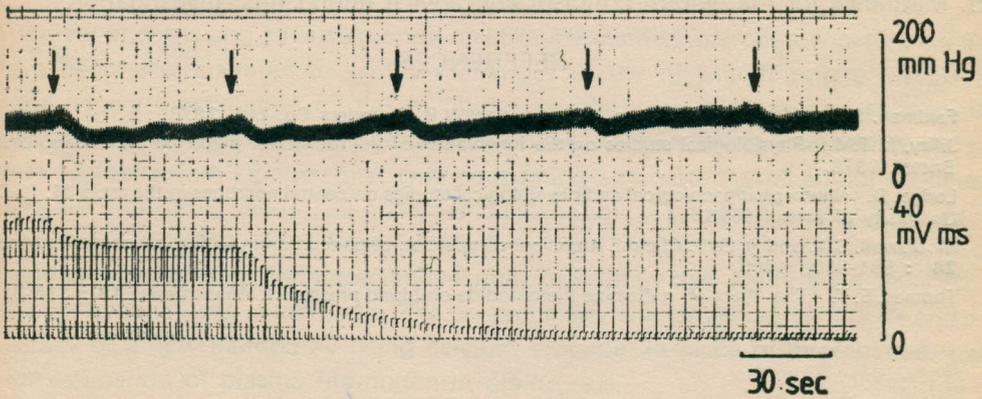


Fig. 2 : Effects on the blood pressure and gastrocnemius e.m.g. of five 1 mg doses of gallamine triethiodide.

d-Tubocurarine :

d-Tubocurarine (0.04 mg/ml) infused at the rate of 4 $\mu\text{g}/\text{min}$ produced neuromuscular paralysis at a total dose of 0.068 mg/kg body weight; the effect lasted for 1½ hr. There was no significant change in blood pressure with this dose. Even when the dose was increased four or five fold, there was no marked effect on the blood pressure.

DISCUSSION

In cats, dogs, and rabbits, even very large doses of gallamine produce no effect on blood pressure (5). In the present study with rats however, gallamine produced marked hypotension when it was infused at the rate of 2 mg/min or more. With lower infusion rates (1 mg/min or less), neuromuscular block occurred prior to the onset of severe hypotension but these rates of infusion called for the administration of gallamine over a period of about 10 min or more.

Pancuronium bromide produced no marked effect on blood pressure in doses which block the neuromuscular junction; this is in agreement with results in other animals (4). The drug produced neuromuscular blockade of very short duration.

Hypotension has been reported, with d-tubocurarine in various animals and in man. Cats and dogs show very marked hypotension associated with histamine release (1) and this has been shown to occur in man too (5). However, in the present study on rats, d-tubocurarine produced no marked change in blood pressure.

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