Influence of diazepam on the effect of neuromuscular blocking agents

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There is much controversy in the literature about the effect of diazepam on the neuromuscular blockade produced by depolarizing and nondepolarizing skeletal muscle relaxants. Vergano, Zaccagna & others (1969) showed that pretreatment with gallamine or (+)-tubocurarine increased the transient blockade produced by diazepam in man as well as the frog sciatic nerve-gastrocnemius muscle preparation. Feldman & Crawley (1970) in their study on man reported that diazepam increased the magnitude and duration of the block by gallamine but reduced the block by succinylcholine. On the other hand, Dretchen, Ghoneim & Long (1971) observed that although diazepam had no effect on the recovery slope of the blockades produced by (+)-tubocurarine, gallamine and decamethonium, given intra-arterially as Valium, it reversed the myoneural blockade produced by both depolarizing and non-depolarizing blocking agents in the sciatic nerve-anterior tibialis muscle preparation of the dog. These workers also suggested that this property was due to the solvent system of the drug. Recently, Lorenzo Fernandez & Mediavilla Martinez (1973) reported that the commercially available solution of diazepam enhanced the recovery from the blockade caused by (+)-tubocurarine in the cat, but increased the recovery time of the succinylcholine blockade. In view of the above results, we have investigated the interaction of diazepam with depolarizing and non-depolarizing types of muscle relaxants.

The sciatic nerve-gastrocnemius muscle preparations were made in 10 dogs of either sex (7 to 12 kg) under sodium pentobarbitone anaesthesia (30 mg kg^{-1}, i.p.). The sciatic nerve was ligated and a shielded silver electrode was placed on the peripheral portion. The gastrocnemius muscle was freed and a thread was tied to the tendon and with the help of a pulley system twitch contractions were recorded on a smoked drum. The nerve was stimulated at the rate of 10 pulses min^{-1} with a duration of 2 ms at 8 to 12 V. The drugs were injected in femoral vein. Two series of experiments were performed with 5 dogs in each.

In the first series, after the twitch had stabilized, blockade was produced with a dose of 0·25 mg kg^{-1} of gallamine (Flaxedil) as control response. After 90 min, another identical blockade with the same dose of drug was produced, but at the beginning of the recovery from the maximum depression of the twitch height, a commercially available solution of diazepam (Calmpose) was injected in the dose of 2·5 mg kg^{-1}. In the second series an identical procedure was followed with succinylcholine (Scoline) as blocking agent instead of gallamine. The recovery time of blockades in control conditions and after diazepam was measured in both series of experiments.

The mean total recovery time of control twitch height after gallamine was 38·8 ± 2·6 min (± s.e.); after the injection of diazepam solution the mean value was 26·4 ± 2·2 min which was significantly shorter than the control ($P < 0.01$). The mean control recovery time in succinylcholine experiments was 13·5 ± 1·6 min and after diazepam it was 19·3 ± 1·4 min which was significantly longer than the control ($P < 0.05$).

These results show that diazepam in the commercially available solution significantly reversed the neuromuscular blockade produced by a non-depolarizing agent like gallamine but augmented the blockade caused by a depolarizing agent like succinylcholine. These data are in agreement with the observations of Lorenzo Fernandez & Mediavilla Martinez (1973) but are in disagreement with those of Feldberg & Crawley (1970) and are also in contrast to those of Dretchen, Ghoneim & Long (1971) in the sense that those authors observed an early recovery when the commercially available solution of diazepam was given during the blockade of a depolarizing agent, decamethonium. The solvent system of diazepam cannot account for this difference since both the commercially available drug and the solvent solution were found to produce similar effects on the blockade of depolarizing as well as non-depolarizing muscle relaxants in their study.

It appears that diazepam in commercially available solution and at high doses has an effect somewhat like neostigmine as it antagonized the neuromuscular blockade produced by gallamine and prolonged that produced by succinylcholine.

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