

Title: POTENTIATION OF PANCURONIUM AND SUCCINYLCHOLINE BY VERAPAMIL

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Introduction. The ability of verapamil to block the slow calcium ion influx into contractile and conductive myocardial cells and the consequent antiarrhythmic actions of the drug are well documented¹. In skeletal muscle, however, the role of a verapamil sensitive calcium ion influx has not been clearly defined. In addition to a possible action on calcium ion influx in skeletal muscle the drug has been shown to possess a local anesthetic action at high concentrations¹ and, like local anesthetics, to be able to release calcium from stores within skeletal muscle which may facilitate excitation-contraction coupling². The aim of the present study was to investigate the neuromuscular effects of verapamil particularly in view of its recent introduction into clinical practice in the USA.

Methods. Male New Zealand white rabbits were anesthetized with 1 to 1.3% halothane in oxygen and the twitch tension of the indirectly stimulated gastrocnemius muscle recorded at a frequency of nerve stimulation of 0.1 Hz. The effects of cumulative doses of verapamil alone (0.01 to 1.0 mg/kg) were studied either alone (n=6) or in the presence of 50% depression of the twitch tension produced by an i.v. infusion of either succinylcholine (n=6) or pancuronium (n=6). In some experiments the EMG of the gastrocnemius muscle was recorded in the presence of pancuronium. The ECG (lead II) was recorded to determine the P-R interval.

Results. Verapamil alone had no significant ($P > 0.05$) effect on twitch tension at any of the doses studied, however P-R interval was significantly ($P < 0.05$) increased in a dose-dependent manner from 71 ± 7 ms to a maximum of 118 ± 20 ms at 1.0 mg/kg; concomitantly the heart rate decreased from 271 ± 7 beats/min in control to a minimum of 209 ± 8 beats/min after 1.0 mg/kg and similarly the mean blood pressure decreased from 72 ± 3 torr to a minimum of 43 ± 4 torr. These values were not significantly ($P > 0.05$) different in the presence of a constant infusion of either succinylcholine (21 ± 5 μ g/kg/min), or pancuronium (0.6 ± 0.2 μ g/kg/min). However, the 50% depression of twitch tension produced by either succinylcholine or pancuronium was significantly ($P < 0.05$) increased by either 0.01 to 1.0 mg/kg or 0.1 to 1.0 mg/kg of verapamil respectively (fig.1). The depression of the EMG recorded in the presence of pancuronium paralleled the twitch depression produced by verapamil.

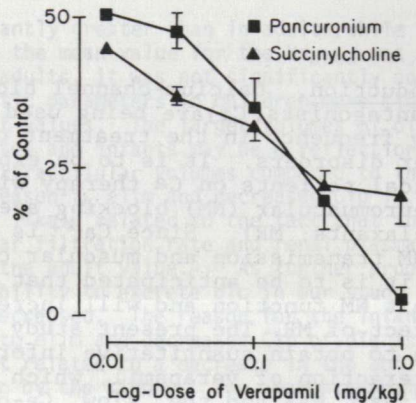


Figure 1. The effect of verapamil on the 50% twitch depression of the gastrocnemius muscle of the anesthetized rabbit produced by infusion of either succinylcholine or pancuronium.

Discussion. The present results indicate that verapamil potentiates the neuromuscular block produced by an infusion of either succinylcholine or pancuronium. This effect of verapamil was apparent at doses which produced significant changes in P-R interval, heart rate and blood pressure. The absence of any effect of verapamil alone on neuromuscular transmission indicates that the margin of safety of neuromuscular transmission must be reduced before the effect of verapamil becomes apparent. Since no increase in twitch tension was observed in response to verapamil it is unlikely that the drug is affecting intracellular calcium release. The fact that succinylcholine and pancuronium are both potentiated suggests a common action of verapamil at the neuromuscular junction, an action further supported by observation that in the presence of pancuronium verapamil depressed the amplitude of the EMG signal to the same extent as the twitch tension. It is concluded that the potentiation of the succinylcholine- and pancuronium-induced neuromuscular block by verapamil is due to either the known local anesthetic action of the drug or possibly the involvement of a verapamil sensitive calcium influx into skeletal muscle fibers.

References.

1. Singh BN, Ellrodt G, Peter CT: Verapamil: A review of its pharmacological properties and therapeutic use. *Drugs* 15:169-197, 1978
2. Bondi AY: Effects of verapamil on excitation-contraction coupling in frog sartorius muscle. *J Pharmacol Exp Ther* 205:49-57, 1978