Title: ATRACURIUM EFFECT ON MOTOR NERVE ENDINGS IN THE CAT

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Introduction.

Atracurium is a new non-depolarizing neuromuscular blocking agent of intermediate duration of action. It has been shown that d-tubocurarine and pancuronium in addition to their well known postjunctional effects have also prejunctional actions. [1,2] This study was undertaken to determine if atracurium has any prejunctional effects.

Methods.

The technique developed by Standaert [3] and Riker [4] was employed to study the effect of atracurium on the repetitive activity generated at the cat soleus motor nerve endings. This activity, known as stimulus-bound repetition or SBR, causes an obligatory potentiation of the indirectly evoked muscle contractile responses known as post-tetanic potentiation or PTP. [3] An *in vivo* soleus nerve-muscle preparation was made in cats anesthetized with alpha-chloralose. The isometric contractile responses of the soleus muscle were recorded on a Grass polygraph. A dorsal laminectomy was performed. Ventral roots L6, L7 and S1, which contain the motor axons of the soleus nerve, were identified and divided into filaments containing one to three axons. The soleus nerve was supramaximally stimulated at 0.4 Hz except when interrupted for 10 second tetanic trains of 400 Hz. After this high frequency conditioning, the rate of stimulation was returned to 0.4 Hz and SBR was recorded antidromically from the previously indentified soleus axons in the ventral root filaments. Thus, the motor nerve ending function was measured by determining the percentage of motor axons demonstrating SBR and by recording the obligatory PTP. The atracurium was administered intravenously in single doses ranging from 0.003 to 0.05 mg/kg.

Results.

Atracurium suppressed the SBR generated at the soleus motor nerve endings in a dose range from 0.005 to 0.035 mg/kg. These doses did not depress single impulse transmission. The threshold dose for SBR suppression was 0.005 mg/kg and at 0.035 mg/kg the SBR incidence was 91% suppressed. The obligatory PTP was correspondingly suppressed. The threshold dose required to abolish the PTP was 0.01 mg/kg and a dose of 0.05 mg/kg completely abolished the PTP. The dose of atracurium which completely suppressed PTP was also the threshold blocking dose (5%) for single impulse transmission.

Discussion.

Standaert [3] has clearly demonstrated that SBR originates in the cat soleus motor nerve endings. Thus, SBR signals a prejunctional event. The suppression of SBR by atracurium shows that this agent has a prejunctional site of action. Atracurium has two positive charged quaternary nitrogens. A charged molecule is much more likely to act at non-myelinated axonal sites, the motor nerve terminals and the nodes of Ranvier. Atracurium could act at one or both of these prejunctional sites. The doses of atracurium which suppressed SBR did not affect the single impulse transmission. Single impulse transmission is not affected until SBR and PTP are completely suppressed. The doses of atracurium which can block transmission exceed those needed to act at prejunctional sites. The present data demonstrate that atracurium has a prejunctional site of action. When the block of single impulse transmission commences, atracurium is acting at both prejunctional and postjunctional sites. Thus, the prejunctional effect of atracurium may contribute to the neuromuscular blocking effect of this agent.

References.

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