Title : PREJUNCTIONAL NEUROMUSCULAR BLOCK IN VIVO

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Introduction. No previously described methods permit diagnosis of prejunctional neuromuscular block in the clinical setting, although many clinical neuromuscular conditions are thought to involve the motor nerve terminal. Investigation with beta-bungarotoxin, a model irreversible neuromuscular blocking venom which acts primarily by a prejunctional mechanism, has suggested a new electromyographic (EMG) method in vivo which may have clinical application by virtue of its noninvasiveness (personal observation). The present study examined whether this method will permit identification of a similar but reversible magnesium-type prejunctional neuromuscular block and differentiate it from hemicholinium-induced prejunctional block. It is well known that magnesium blocks by reducing the releasability and hemicholinium-3 by depleting the availability of transmitter from the motor nerve terminal.

Method. The neurally evoked compound EMG response of the tibialis anterior muscle was quantified in 12 anesthetized cats. The nerve was stimulated with square electric pulses of 0.1 ms duration and supramaximal voltage, via two electrodes 1 mm apart. After verifying that the compound EMG response to single nerve stimulus was single-peaked[1], twin stimuli of increasing inter-stimulus interval were applied to evoke the paired responses, R_1 and R_2. Both single and double stimuli were applied at control and again at appropriate levels of block. The relationship between the R_1 and the R_2 responses was quantified both in terms of refractoriness of neuromuscular transmission and in terms of the R_2/R_1 ratio. Neuromuscular block was produced by i.v. injection of either magnesium sulfate (Mg) or hemicholinium-3 (HC-3). In the case of HC-3, the nature of block required that the nerve-muscle preparation on the test side be stimulated continually at a high frequency (1 Hz) to produce the depletion. The identical nerve-muscle preparation on the contralateral side was stimulated at a low frequency (0.1 Hz) to verify the absence of block without depletion. Each cat served as its own control, $P<0.001$ by Students' t tests for paired values being considered significant.

Results. Mg-induced neuromuscular block consistently and markedly reduced the refractoriness of neuromuscular transmission and increased the R_2/R_1 ratio. (Fig. 1). The more profound the block, the more pronounced the effects became. At 75% block, the total ("absolute") refractory period (when R_2 just became discernable) was reduced from the control value of 1.8±0.2 (mean±SEM, N=6) ms

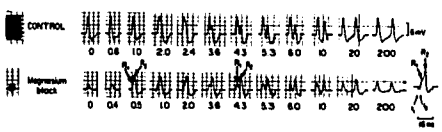

Fig.1. Numbers below each EMG indicate interstimulus time interval in ms.

to 0.5±0.1 ms; the partial ("relative") refractory period (when R_2 just equaled R_1) from 6.1±0.4 ms to 0.6±0.1 ms. Thus, twin stimuli 0.5 ms apart (0.4 ms in the example in Fig. 1) would evoke no discernable R_2 at all while twin stimuli only 0.1 ms further apart would evoke an R_2 already equaling or exceeding the corresponding R_1. The inverted relationship (i.e., $R_2<R_1$) which occurred during the block, was evident with any twin stimuli from 0.5 up to 100 ms apart. For example, twin stimuli 4.6±0.3 ms apart had an R_2/R_1 ratio of 0.75 at control, as opposed to 2.4±0.1 at 75% block. Calcium chloride 10 mg/kg i.v. reversed the block, as well as the inverted relationship between the paired responses. By contrast, HC-3 did not measurably alter the R_2/R_1 ratio in any cat.

Discussion. During prejunctional neuromuscular block produced by mechanism of reduced releasability of transmitter, not only successive endplate potentials will gain in amplitude ("facilitation") but also closely spaced endplate potentials may summate. If an endplate potential reaches threshold by either mechanism, facilitation or summation, the resultant action potential of the muscle cell will contribute only to R_2. Thus an increased R_2/R_1 ratio indicates dependence of part of the neuromuscular synapse population on facilitation or on summation of two endplate potentials to trigger one muscle action potential. By contrast, HC-3 does not affect releasability but rather reduces availability of transmitter. Hence, the relationship between R_1 and R_2 is not altered because the same fraction of available transmitter is released by either stimulus, during HC-3 block as during control. We conclude that double nerve stimuli may differentiate not only between pre- and postjunctional neuromuscular block but also between magnesium- and HC-3-type of prejunctional block.

References:

1. Lee C, de Silva AJC, Katz RL: Multi-peaking of the compound electromyographic response to single nerve stimulus: Its occurence and prevention in an experimental model. Br J Anaesth 50:459-462, 1978