Effect of Dibutyryl Cyclic AMP on Neuromuscular Transmission in Myasthenia Gravis

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The effect of dibutyryl 3',5'-cyclic monophosphate (D-cAMP) on the neuromuscular transmission was studied in a patient with myasthenia gravis during anesthesia. D-cAMP caused a slight increase in single twitch tension, and an initial transient decrease in tension which resulted from the trains of 2 Hz stimuli disappeared after D-cAMP. The finding of the present study suggests that D-cAMP has an anti-fatigue effect in patients with myasthenia gravis.

dibutyryl cyclic AMP; neuromuscular transmission; myasthenia gravis

Epinephrine is well known to improve neuromuscular transmission by facilitating the release of acetylcholine from the motor nerve terminals. It has been suggested that epinephrine stimulates the formation of adenosine 3',5'-cyclic monophosphate (cAMP) by activating adenyl cyclase and the nucleotide thus augments the release of acetylcholine at the nerve terminals (Breckenridge and Malschinski 1967). Furthermore, xanthines, the inhibitors of cAMP hydrolysis, have been reported to increase the tension of intercostal muscle in myasthenic patients (Jacobs et al. 1973). Based on these findings, the effect of dibutyryl adenosine 3',5'-cyclic monophosphate (D-cAMP) on twitch response elicited by peripheral nerve stimulation was studied during anesthesia in a patient with myasthenia gravis undergoing thymectomy.

The patient was a 31-year-old male. The first symptom of his illness appeared 6 years ago as a generalized muscular weakness. The medical treatment with 10 mg of ambenonium three times a day started six months ago. Before the operation, he was premedicated with meperidine and atropine one hr prior to the induction of anesthesia. Ambenonium 10 mg was also given as a regular morning dose. Anesthesia was induced with sodium thiamylal and maintained with nitrous-oxide oxygen and halothane (0.5-1.5%).

During anesthesia the median nerve was stimulated indirectly at the elbow using a Nihon Kohden SEN-1101 stimulator with supramaximal square-wave stimuli of 0.2 msec duration through the subcutaneous needle electrodes. Trains of stimuli of 2 Hz were also delivered for 10 sec. The resultant tension due to adduction of the middle finger was recorded using a force-displacement transducer attached to a recorder (Nihon Kohden multipurpose polygraph).

When a steady twitch response was obtained, an initial transient decrease followed by facilitation in tension was observed by the trains of stimuli (Fig. 1, upper trace). Such a change in tension did not occur in normal subjects. Around 10 min after the intravenous administration of 300 mg of D-cAMP, an increase in single twitch tension by 23% to the control and an initial transient decrease in tension which resulted from the trains of 2
Hz stimuli disappeared (Fig. 1, middle trace). An increase in single twitch tension sustained 20 min after the administration of D-cAMP, but an initial transient decrease became noted again (Fig. 1, middle and lower traces).

Goldberg and Singer (1969) reported that D-cAMP increases the amplitude of end plate potential in the isolated rat diaphragm. The present study demonstrated that D-cAMP caused a slight increase in twitch tension and an "anti-fatigue" effect in a patient with myasthenia gravis, probably owing to its certain effect on the motor nerve terminals. The augmentation of twitch tension, however, may also reflect the effect of D-cAMP on postsynaptic events and muscle blood flow. Further clinical studies are necessary to evaluate the efficacy of D-cAMP in the treatment of myasthenia gravis including the mechanism of its action.

References

