Title: POTENTIATION AND PROLONGATION OF VECURONIUM NEUROMUSCULAR BLOCK BY ADENOSINE TRIPHOSPHATE

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Introduction. Nitroglycerin has been demonstrated to cause a prolongation of neuromuscular block.[1] Adenosine triphosphate (ATP) has been used to induce clinical hypotension[2] and has the advantages over nitrogycerin and nitroprusside of not exhibiting tachyphylaxis. It also has the advantage that normotension rapidly returns following cessation of the intravenous (i.v.) infusion. The present study was undertaken to determine whether ATP has any effect on the neuromuscular block produced by the new medium-duration muscle relaxant, vecuronium.

Methods. Six adult cats of either sex were anesthetized with $\alpha$-chloralose (60 mg/kg) and pentobarbital sodium (5 mg/kg). The twitch tension of the indirectly stimulated tibialis-anterior muscle was recorded at a frequency of stimulation of 0.1 Hz. ATP was used at a concentration of 40 mg/ml (pH adjusted to 7.4 with NaOH) and was infused intravenously at a rate sufficient to lower the systemic arterial pressure to one of three levels; 100, 75 or 50 mmHg. Once the blood pressure was constant at one of these pressures, a single intravenous bolus dose of 25$\mu$g/kg of vecuronium was administered, and the following parameters were measured; percent decrease of twitch tension, time from injection to peak effect (onset), time from injection to 90% recovery (duration) and recovery rate (%/min) between 25% and 75% of control twitch tension. If the twitch tension did not decrease to 25% of control then the recovery rate (%/min) was measured from the maximum effect to 75% recovery. Results are presented as the mean $\pm$ S.E.M. Statistical comparisons were made using the Wilcoxon paired t-test.

Results. To achieve a decrease in systemic arterial pressure from the control (153 $\pm$ 10 mm Hg) to 100, 75 and 50, ATP infusion rates of 2.6 $\pm$ 0.7, 4.2 $\pm$ 0.5 and 9.0 $\pm$ 2.5 $mg \cdot kg^{-1} \cdot min^{-1}$ were required, respectively. The heart rate (197 $\pm$ 15 bts/min) did not change significantly throughout the experiment. During the infusions of ATP, which produced pressure of 75 and 50 mmHg, the intensity of the twitch depression produced by vecuronium was significantly increased (see table 1). Similarly, the duration of blockade of vecuronium was increased. In contrast, the onset time and recovery rate with vecuronium were not significantly ($p<0.05$) affected by ATP at the doses used. These results are summarized in Table 1.

Discussion. The results of the present study are similar to the findings observed with nitroglycerin and pancuronium,[2] that is, a prolongation of the duration of neuromuscular block. The fact that both the depth and the duration of the neuromuscular block are increased by the ATP with no effect on the rate of recovery indicate the effects of ATP are seemingly confined to a potentiation of block. The mechanism of this potentiation may be either pharmacokinetic or pharmacodynamic. Pharmacokinetically, ATP itself or its hypotensive action may affect the hepatic elimination of vecuronium or the redistribution to non-specific binding sites, however a change in the rate of recovery might be anticipated. ATP also increases the blood flow to skeletal muscle beds which may have an effect on the block produced by vecuronium. However, examination of these possible mechanisms does not reveal a straightforward mechanism to explain the interaction. Pharmacodynamically, the ATP may affect the interaction of vecuronium with the receptors of the neuromuscular junction or may affect the contractile process of the muscle itself. Unfortunately, the actual mechanism of action of ATP which results in a potentiation of the action of vecuronium cannot be determined from the results of the present study and further experimentation is neccessary. It is concluded that although ATP shares the ability of nitroglycerin to potentiate non-depolarizing neuromuscular block it has considerable advantages.

References

1. Glisson SN, El-Etr AA, Lim R: Potentation of pancuronium-induced neuromuscular blockade by intravenous infusion of nitroglycerin. Anesthesiology 51:47-49, 1979

2. Fukunaga AF, Ikeda K, Matsuda I: ATP-induced hypotensive anesthesia during surgery. Anesthesiology 57:A65, 1982

| | Mean Arterial Pressure | | |
|---|---|---|---|
| | 100 mmHg | 75 mmHg | 50 mmHg |
| % Block | 43 $\pm$ 8.3 | 75 $\pm$ 6 | 92 $\pm$ 3.7* |
| Onset (min) | 3.6 $\pm$ 0.2 | 4.0 $\pm$ 0.3 | 3.9 $\pm$ 0.4 |
| Duration (min) | 7.4 $\pm$ 0.8 | 10.5 $\pm$ 1.0 | 17.7 $\pm$ 3.1* |
| Rec. Rate (min) | 9.2 $\pm$ 1.3 | 12.0 $\pm$ 1.4 | 9.6 $\pm$ 2 |

Table 1. The effects of a lowered mean arterial pressure due to ATP on the response of the tibialis anterior muscle to 25 $\mu$g/kg of vecuronium. (*, $p < 0.05$, relative to 100 mmHg)