TITLE: DYNAMICS OF ATRACURIUM INFUSION

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Introduction: Atracurium besylate is a new, nondepolarizing muscle relaxant with a short duration of action, noncumulative properties, and few cardiovascular side effects.[1] This short duration of action and its spontaneous decomposition to inactive metabolites make it ideally suited for short surgical procedures, but would necessitate repeated bolus injections in those undergoing longer operations. The purpose of this study was to determine the infusion rate and concentration necessary for the induction and maintenance of relaxation during longer operations.

Methods: Twenty patients, 17 to 84 years of age, ASA status I and II, who were to undergo elective surgery, were studied. The study was approved by the Institutional Review Board and informed consent was obtained. Patients were premedicated one hour before surgery with oral diazepam 0.15 $mg \cdot kg^{-1}$. Anesthesia was induced with intravenous thiopental 3-5 $mg \cdot kg^{-1}$ and endotracheal intubation was facilitated with succinylcholine 1 $mg \cdot kg^{-1}$. Anesthesia was maintained with either enflurane or isoflurane in concentrations which resulted in an end-tidal concentration of 1.3 MAC, measured by a Perkin-Elmer mass spectrometer. Ventilation was controlled to maintain normal arterial blood gas tensions. Esophageal temperature was kept between 35 and 37° C. Supramaximal square wave pulses of 0.15 msec duration were delivered at 0.10 Hz to the ulnar nerve at the elbow through 30 gauge steel needle electrodes. The resultant force of thumb adduction was quantified with a grass FT-10 force displacement transducer and recorded on a polygraph. The thenar electromyogram (EMG) was acquired with surface electrodes, amplified, rectified, and integrated by an EMG processor and also displayed on the polygraph. Following the return of the control twitch height, atracurium was infused in a concentration of either 200 or 800 $\mu g \cdot ml^{-1}$ using an IMED volumetric infusion pump set at its maximal rate of 299 $ml \cdot hr^{-1}$ until the twitch height (EMG) was depressed by 80% from its control. The infusion rate was then changed to maintain 90% twitch depression for the duration of the operation. Ten minutes prior to the termination of surgery, the infusion was discontinued. The residual block was antagonized with edrophonium and glycopyrrolate at the conclusion of surgery.

Results: (See table) The time to achieve 90% twitch depression at a maximal infusion rate of 299 $ml \cdot hr^{-1}$ was significantly longer for patients receiving the less concentrated infusion, however, neither the infusion rate necessary to maintain 90% twitch depression in the steady state nor the average rate of infusion were concentration-dependent. Even though the infusion was continued almost until the end of the surgical procedure, its effect was readily antagonized with edrophonium.

Table

Atracurium Infusion Values for 1.3 MAC Enflurane or Isoflurane

Variables		
Concentration ($\mu g \cdot ml^{-1}$)	200	800
Time 90 (min)	8.45 ± 0.62	3.65 ± 0.49*
Maint Rate ($\mu g \cdot kg \cdot min^{-1}$)	2.34 ± 0.27	2.55 ± 0.48
Total Dose ($\mu g \cdot kg^{-1}$)	318.1 ± 42.1	461.6 ± 71.5
Avg Rate ($\mu g \cdot kg \cdot min^{-1}$)	4.20 ± 1.05	4.33 ± 0.88

*vs. 200 $\mu g \cdot ml^{-1}$ $p < 0.05$, Student t-test.

Time 90 = time to reach 90% twitch depression at an infusion rate of 299 $ml \cdot hr^{-1}$; Maint Rate = maintenance infusion rate for 90% twitch depression; Avg Rate = average rate of infusion for the entire duration.

Discussion: These data imply that with volatile anesthetics, neuromuscular block with atracurium can be efficiently induced and maintained using an IMED volumetric infusion pump. The ceiling infusion rate of the IMED pump used in this study prolonged induction time in the 200 $\mu g \cdot ml^{-1}$ group, undoubtedly by delaying the rate of rise of drug concentration in the effect compartment of these patients.[2] This was resolved in the study by increasing the concentration of the drug infusion, however, using an infusion pump with a higher ceiling infusion rate or employing a bolus loading dose would probably have been effective alternatives. Due to the expense of the drug, common sense dictates the employment of the less concentrated infusion unless a protracted surgical procedure is anticipated. Once 90% twitch depression was achieved, this desired degree of neuromuscular block was easily maintained at an infusion rate of approximately 2.5 $\mu g \cdot kg^{-1} \cdot min^{-1}$, independent of the drug concentration employed.

References:

1. Basta SJ, Ali HH, Savarese JJ, et al: Clinical pharmacology of atracurium besylate (BW33A): A new nondepolarizing muscle relaxant. Anesth Analg 61:723-729, 1982.

2. Weatherley BC, Williams SG, Neill EAM: Pharmacokinetics, pharmacodynamics and dose-response relationships of atracurium administered IV. Br J Anaesth 55:39S-45S, 1983.