

Title: The efficacy of atracurium by continuous infusion

Authors: Margaret A. Gargarian, M.D., Salvatore J. Basta, M.D., John J Savarese, M.D., Hassan H. Ali, M.D., N. Sunder, M.D, Ralph Scott, M.D., Michael Gionfriddo, B.A., A. Gail Batson, B.S.

Affiliation: Department of Anesthesia, Harvard Medical School at Massachusetts General Hospital, Boston, MA and Medical Department, Burroughs Wellcome Company, Research Triangle Park, NC

Introduction: Atracurium (Atc) is an intermediate duration, nondepolarizing relaxant; shown to be non-cumulative following successive bolus doses. To avoid frequent intermittent boluses, Atc by infusion seems to be a feasible clinical technique. The purpose of this study is to evaluate the efficacy of Atc via continuous infusion, by asking the following questions: (a) what is a reasonable infusion rate for good muscle relaxation? (b) do long infusions exhibit cumulative properties? (c) are final recovery rates comparable after infusions and intermittent boluses? (d) can infusions be readily antagonized?

Methods: Thirty-seven adult ASA I-II surgical patients aged 19-59 gave institutionally approved informed consent. Preoperative medication included morphine (0.1 mg/kg) i.m., and diazepam (0.05-0.20 mg/kg) p.o. an hour before induction. Baseline neuromuscular function was established using evoked single twitch responses (0.15 Hz) of the ulnar nerve-adductor pollicis system. Anesthesia was induced with thiopental (4-5 mg/kg) i.v., and N₂O/O₂ (50:50) by mask. Thirty seconds following the thiopental injection, each patient received an intravenous dose of Atc 0.5 mg/kg. Following endotracheal intubation, ventilation was controlled with N₂O/O₂ 4:2 (L/min) and I.V. narcotics were administered to provide satisfactory general anesthesia. Patients recovered to 5% of control twitch height, at which time the Atc infusion was started at 10 µg/kg/min. The infusion rate was adjusted to maintain 90-99% twitch suppression. Duration of infusion was measured from the initial 0.5 mg/kg Atc injection to termination of infusion. Twenty-three patients recovered spontaneously from neuromuscular blockade. Fourteen patients were reversed with neostigmine (0.06 mg/kg) and atropine (0.03 mg/kg). In the spontaneous recovery group (n=23), measurements were taken of: (a) recovery from 5-95% of control twitch height; (b) recovery from 25-75% of control twitch height and (c) infusion rate at steady state (constant 90-99% twitch suppression). This group was further divided into long infusion (>120 min: n=12) vs. short infusion (<120 min: n=11). Results were compared with student's t-test for uncorrelated data or by analysis of variance. Changes were considered significant when p<0.05. Results are expressed as mean ± standard error.

Results and Discussion: For all patients (n=37), a mean infusion rate of 8.4±0.3 µg/kg/min maintained 90-99% twitch suppression with a range of 4.8-12.0 µg/kg/min.

The recovery rates between continuous infusion vs bolus patients³ are not significantly different as shown in Table 1.

Table 1

Atracurium dose (mg/kg)	n	Recovery (min)	
		5-95%*	25-75%*
0.2	-	27.4±5.2	11.2±0.7
0.3	18	27.1±1.7	11.1±0.8
0.4	13	28.2±2.2	11.9±1.0
0.5	13	28.8±2.5	11.5±1.1
continuous infusion (58.2-415.7 min)	23	26.6±1.3	10.9±0.7

* 0.4<p<0.5

Table 2 shows the length of atracurium infusion had no significant bearing on either infusion or recovery rates.

Table 2*

Mean Infusion Length (min)	n	Recovery (min)		Steady state infusion rate (µg/kg/min)
		5-95%	25-75%	
93.2±6. (58.2-117.5)	11	25.1	9.8	8.6
198.4±27.7 (121.2-415.7)	12	28.5	11.9	7.2

p>1 p>1 p>.05
*Standard errors omitted for purposes of space

Six patients reversed at similar depth of block (87.0±0.2% twitch suppression) showed a mean reversal-95% recovery time of 10.6 min; reversal data for bolused patients at 75.5±5.2% twitch suppression showed a mean reversal-95% recovery time of 7.3 min (via T₄).⁴ There was no statistical or clinical difference between the two groups.

Conclusion: Atc by continuous infusion produces excellent muscle relaxation at a mean infusion rate of 8.4 µg/kg/min. The recovery rates from neuromuscular blockade do not differ between continuous infusion and bolus administration. The length of the Atc infusion does not influence either infusion or recovery rates, thereby, supporting the drug's lack of cumulative properties. Antagonism following discontinuation of infusion is easily accomplished. It appears that Atc by continuous infusion is an effective method of providing excellent muscle relaxation for surgical patients.

References:

1. Payne JP, Hughes R: Br J Anaesth 53:45, 1981.
2. Flynn PJ, Hughes R, Walton, Jothlingam S: Br J Anaesth 55:135S, 1983.
3. Personal communication, John J. Savarese, M.D.
4. Basta SJ, Ali HH, Savarese JJ, et al: Anesth Analg 61:723-9, 1982.