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Title : CLINICAL STUDIES WITH ATRACURIUM: A NEW COMPETITIVE NEUROMUSCULAR BLOCKING AGENT

Authors : R. Hughes, Ph.D.,* J. P. Payne, M.B., F.F.A.R.C.S., D.A.**

Affiliation: **Research Department of Anaesthetics, Royal College of Surgeons of England and St. Peter's Hospitals, London and *The Wellcome Research Laboratories, Beckenham, Kent BR3 3BS, U.K.

Introduction. Atracurium is one of a new series of neuromuscular blocking agents whose properties may overcome the disadvantages of similar drugs used in anaesthetic practice.[1] In laboratory animals, it has been demonstrated that atracurium is a potent, competitive neuromuscular blocking agent with a wide separation between neuromuscular paralyzing doses and those producing inhibition of autonomic mechanisms.[2] This drug has now been evaluated in anaesthetized man.

Methods. Studies were carried out in 62 patients who had given their informed consent and were about to undergo routine urological surgery. The techniques employed have been described in detail elsewhere.[3] No premedication was given and anaesthesia was induced with 400-600 mg thiopentone I.V. and intubation was achieved during the administration of 2-4% halothane and after spraying the larynx with 4% lignocaine. The halothane was then withdrawn and anaesthesia was maintained with 60-66% nitrous oxide in oxygen using intermittent positive pressure ventilation. Supplements of thiopentone or fentanyl were given as required. Additionally, the practicality of intubation after atracurium was investigated during anaesthesia with nitrous oxide. Simultaneous recordings of the tetanic and single twitch contractions of the adductor pollicis muscles were obtained by stimulating each ulnar nerve supramaximally at the wrist every 12 sec., one with tetanic bursts of 50 Hz for 1 sec. and the other with single shocks. The arterial blood pressure and the electrocardiogram were recorded continuously.

Results. Intravenous doses of 0.3 mg/kg atracurium were sufficient to produce complete neuromuscular block of the tetanic response of the adductor pollicis muscle in 1.9 ± 0.1 min. The duration of maximum block was 15.5 ± 1.8 min. and when recovery had begun 34.9 ± 1.9 min. were required to reach 95% of the initial response. Values for a dose of 0.6 mg/kg were, onset 1.2 ± 0.1 min. duration 33.7 ± 3.0 min. and recovery 34.5 ± 4.4 min. Endotracheal intubation was achieved in 1 and 2 min. respectively after 0.6 and 0.3 mg/kg doses when the vocal cords were relaxed. Neuromuscular blockade was well antagonized by neostigmine and was enhanced during administration of 1% halothane. Comparative studies showed that recovery from neuromuscular blockade by atracurium was appreciably faster than that from known competitive agents. Doses of 0.2-0.6 mg/kg I.V. atracurium had no significant effect on arterial blood pressure or heart rate (Table 1).

Table 1

Neuromuscular and Cardiovascular Effects of Atracurium Measured at Time of Maximum Effect (Mean ± S.E.M.)

Dose mg/kg	Percentage of Control Values			
	Adductor Pollicis		Arterial Blood Pressure	Heart Rate
	Tetanus	Twitch		
0.2 n=10	0.6 ± 0.5	19 ± 3.5	99 ± 0.6	100 ± 0.7
0.3 n=9	0	2 ± 1.1	99 ± 0.6	99 ± 1.2
0.6 n=9	0	0	96 ± 1.7	103 ± 1.0

Atracurium provided good muscular relaxation for 15-30 min. when given in doses of 0.3-0.6 mg/kg initially depending on the duration of the surgical procedure. Incremental doses of 0.1 or 0.2 mg/kg produced relaxation for a further 15-30 min. as required. Reversal by neostigmine was not always necessary because of the rapid return of respiration.

Conclusions. Atracurium is a potent competitive neuromuscular blocking agent in anaesthetized man. Endotracheal intubation can be accomplished within 1-2 min. and paralysis is readily reversed by neostigmine. Recovery from neuromuscular blockade is quicker than that from known competitive agents. No cardiovascular effects occurred with atracurium at doses twice those required for full neuromuscular paralysis. The drug provided good relaxation during surgery.

References.

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3. Hughes R, Ingram GS, Payne JP: Br. J. Anaesth. 48:969-974, 1976