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Neuromuscular Blockade of Atracurium *Versus* Succinylcholine in a Patient with Complete Absence of Plasma Cholinesterase Activity

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Atracurium is an intermediate-acting nondepolarizing muscle relaxant that is rapidly eliminated by Hofmann elimination and ester hydrolysis, independent of the plasma cholinesterase.[1] The neuromuscular blockades of atracurium and succinylcholine were compared in a patient who lacks completely any plasma cholinesterase activity. The patient is probably homozygous for the silent gene ($E_1^sE_1^s$).[2]

REPORT OF A CASE

The patient was a 5-yr-old girl, 20-kg body weight, who manifested a markedly prolonged apnea (3 h) following succinylcholine 1 $mg \cdot kg^{-1}$ iv, when she was anesthetized for myelography. The apnea was secondary to neuromuscular blockade as documented by the absence of twitch response to ulnar nerve stimulation. The patient was scheduled 2 weeks later for laminectomy and excision of a spinal cord tumor. She was premedicated with im injections of pentobarbital 60 mg and atropine 0.5 mg. Anesthesia was induced with thiopental 5 $mg \cdot kg^{-1}$ iv followed by $N_2O:O_2$ supplemented by fentanyl 5 $\mu g \cdot kg^{-1}$ iv. Ventilation was controlled throughout the procedure.

The plasma cholinesterase activity was determined using propionylthiocholine as a substrate. The control value in our population is 4.1 ± 1.4 U/ml.[3] The plasma cholinesterase activity of the patient was zero, suggesting that the patient was homozygous for the silent gene ($E_1^sE_1^s$).

The ulnar nerve was stimulated supramaximally at the wrist every 20 s while displaying the resulting integrated electromyographic response. The monitor uses the train-of-four principle at a stimulus rate of 2 Hz and features an automatic search for the supramaximal current level.

Atracurium 0.25 $mg \cdot kg^{-1}$ was injected iv, while its neuromuscular blockade was recorded. Maximal neuromuscular blockade was achieved after 7 min, when tracheal intubation could be easily performed. The block was nondepolarizing in nature as evidenced by the marked decrease of the ratio of the fourth to the first evoked twitch response (T_4/T_1 ratio). Recovery of neuromuscular transmission to a train-of-four ratio of 75% was achieved after 18 min (fig. 1). One-fifth of the initial dose of atracurium (0.05 $mg \cdot kg^{-1}$) was then injected as an incremental dose. Maximal blockade was achieved in 4 min. Neuromuscular transmission was completely restored without reversal after an additional 25 min.

Ten minutes following complete recovery from atracurium blockade as evidenced by a 1.0 T_4/T_1 ratio, succinylcholine 0.5 $mg \cdot kg^{-1}$ was injected iv. Complete neuromuscular blockade was observed after 120 s.

Neuromuscular blockade continued for 60 min, to be followed by a gradual recovery of neuromuscular transmission. The total duration of succinylcholine blockade to 90–95% recovery was 120 min. The block during both the initial and recovery phases was depolarizing in nature as shown by the T_4/T_1 ratio, which ranged between 90–98% (fig. 2).

DISCUSSION

The rates of degradation of atracurium are not different whether the drug is incubated in normal plasma or in plasma obtained from genetically deficient homozygote patients with virtually no plasma cholinesterase activity.[1] This contrasts with succinylcholine, which is degraded extremely quickly in the normal samples, while degradation is dramatically slower in the samples with low cholinesterase activity.

In adults having normal plasma cholinesterase phenotype ($E_1^uE_1^u$), a bolus of succinylcholine 1.5 $mg \cdot kg^{-1}$ produces complete neuromuscular blockade for 6.2 ± 2.9 min, while atracurium 0.25 $mg \cdot kg^{-1}$ produces complete blockade for 27.7 ± 10.9 min.[4] In children, succinylcholine 0.5 $mg \cdot kg^{-1}$ produces a mean of 95% neuromuscular blockade; the mean time for 80% recovery is 4.8 min,[5] while atracurium 0.3–0.6 $mg \cdot kg^{-1}$ is followed by complete neuromuscular blockade for 15–30 min; complete recovery usually occurs within 40–60 min.[6]

Our patient lacks completely any cholinesterase activity, suggesting that she is most probably homozygous for the silent gene ($E_1^sE_1^s$), which is a quite rare gene (1:100,000).[2] The neuromuscular blockade following succinylcholine was markedly prolonged in our patient. In contrast, the response to atracurium was normal, supporting the belief that the duration of action of atracurium is independent of plasma cholinesterase activity.[4]

In summary, the neuromuscular blockade of atracurium was compared with that of succinylcholine in a patient homozygous for the silent gene ($E_1^sE_1^s$), who completely lacks plasma cholinesterase activity. The neuromuscular blockade of succinylcholine was markedly prolonged. In contrast, the blockade of atracurium was

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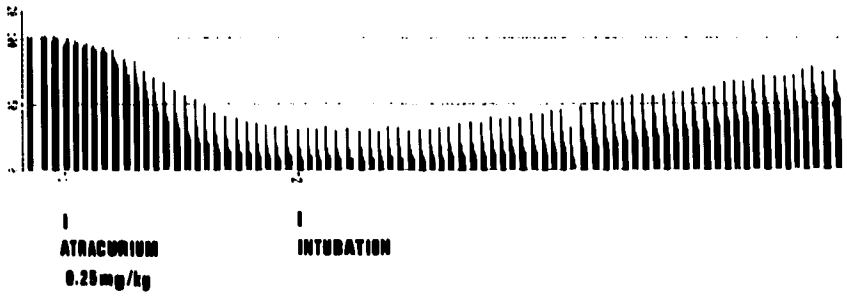

FIG. 1. Electromyographic (EMG) response following atracurium 0.25 mg · kg^{-1}. Seventy-five per cent neuromuscular blockade was achieved after 7 min, when the trachea was intubated.

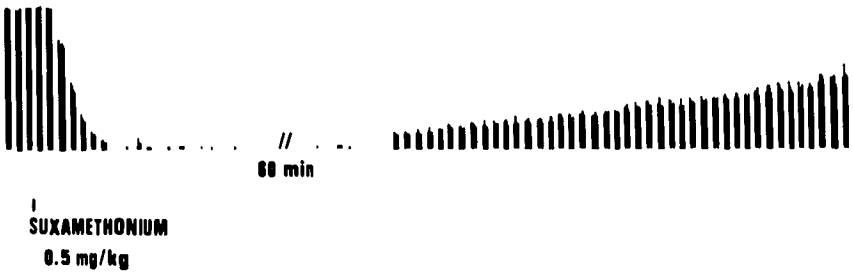

FIG. 2. EMG tracing showing the neuromuscular blockade achieved by succinylcholine 0.5 mg · kg^{-1}. Complete neuromuscular blockade was achieved within 120 s and lasted for 60 min, to be followed by a slow recovery. The blockade was depolarizing in nature during both the onset and recovery periods; the T_4/T_1 ratio ranged between 90–98%.

normal, suggesting that the elimination of atracurium is independent of the plasma cholinesterase activity.

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Mishaps with Patient-controlled Analgesia

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Improved methods for providing postoperative analgesia have led to renewed interest in patient-controlled analgesia (PCA).[1] With this system, the patient is allowed to self-administer small iv bolus doses of a narcotic analgesic using a special programmable infusion pump. Although experience with these devices has become widespread in the United States and abroad over the last 2 years, there have been no reported cases of respiratory arrest in patients receiving PCA therapy. We describe two cases in which healthy, postoperative patients experienced profound respiratory depression as a result of narcotic analgesic overdose secondary to operator errors.

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REPORT OF TWO CASES

Patient 1. A healthy 72-yr-old woman (76 kg) underwent a right total hip replacement under general anesthesia. Following an uneventful