Antagonism of Succinylcholine Paralysis in a Patient with Atypical Pseudocholinesterase

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Administration of succinylcholine (SCh) to patients with atypical pseudocholinesterase may be followed by prolonged paralysis. The advisability of attempting to antagonize this block when it is the desensitizing type is controversial.[1, 2] Paradoxically, anticholinesterase drugs may either antagonize or enhance a desensitizing neuromuscular block resulting from SCh.[1, 2] Consequently, Katz and Churchill-Davidson suggest that anticholinesterase agents should probably be avoided altogether in the management of patients with prolonged responses to SCh.[3]

The following is a case report of a patient with atypical pseudocholinesterase in whom prolonged SCh-induced neuromuscular blockades were successfully antagonized by neostigmine on two occasions. We also suggest clinical indications for the use of anticholinesterase drugs to antagonize prolonged neuromuscular blocks resulting from SCh.

REPORT OF A CASE

A 49-year-old Caucasian woman was admitted for insertion of a cardiac pacemaker for treatment of a complete atrioventricular block in March 1971. (In 1961 she had undergone a vaginal hysterectomy under general anesthesia; no muscle relaxants had been used.) No preanesthetic medication was given. After administration of diazepam, 7.5 mg iv, and thiopental, 75 mg iv, anesthesia was induced with halothane, nitrous oxide, and oxygen. The trachea was intubated after administration of SCh, 100 mg iv. Ventilation was controlled throughout the operation. During closure, the wound was irrigated with 300 ml of 0.1 per cent kanamycin in saline solution.

When spontaneous ventilation resumed at the end of the operation, the endotracheal tube was removed. The patient was breathing oxygen through a mask on the way to the recovery room. However, shallow ventilatory efforts and poorly-coordinated, jerky movements of the extremities suggested inadequate neuromuscular function. Force of thumb adduction was measured with a Grass (FT.03) force-displacement transducer and recorded with a polygraph.[4] The ulnar nerve was stimulated with a Grass S-44 stimulator at the wrist through 22-gauge thin-wall needles. A desensitizing neuromuscular blockade was suggested by the presence of posttetanic facilitation and an unsustained tetanus at 30 Hz (fig. 1). After administration of neostigmine, 1.0 mg, and atropine, 0.4 mg, iv, tetanus was sustained and posttetanic facilitation disappeared. Although not measured, tidal volume appeared to increase. The patient had no further difficulties in the postoperative period.

Two weeks later the patient was readmitted to the hospital for pacemaker failure and persistent atrioventricular block. Serum electrolytes were normal, as they had been during the previous admission. Operation for insertion of a new pacemaker was begun. After administration of thiopental, 150 mg iv, anesthesia was induced with fluroxene, nitrous oxide, and oxygen. About 3 minutes after administration of *d*-tubocurarine, 3 mg iv, SCh, 60 mg iv, was given to facilitate intubation of the trachea. Ventilation was controlled during the 90-minute operation. The wound was not irrigated with antibiotic solution. At the end of the operation, the patient's ventilation was shallow. The ulnar nerve was stimulated, but the force of thumb adduction was evaluated visually only. Tetanus was unsustained and posttetanic facilitation was present. After the administration of neostigmine, 1.5 mg iv, and atropine, 0.8 mg, tetanus was sustained, and posttetanic facilitation disappeared. The patient had an uneventful postoperative course following extubation in the intensive care unit.

During the following week, neuromuscular function was evaluated. The patient's dibucaine number was 25. Although the blood for determination of the dibucaine number had been drawn after the first anesthesia, we did not receive the result until after the second anesthesia. The electromyograph was normal. The proximal delay in nerve conduction was 7.2 mm/sec (normal <10 mm/sec); the distal delay was 2.8 mm/sec (normal <5 mm/sec); velocity of conduction was 59 mm/sec (normal range = 47 to 73 m/sec); amplitude of conduction was 14 μv. No fatigue or posttetanic facilitation was present.

DISCUSSION

This case report demonstrates the appearance of desensitizing neuromuscular blockade resulting from a single-bolus injection of SCh

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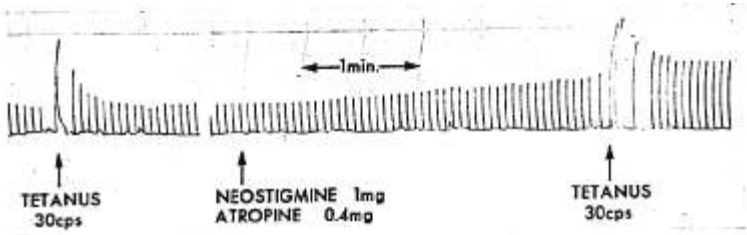

FIG. 1. Prior to administration of neostigmine and atropine, a desensitizing neuromuscular block was present, as evidenced by an unsustained tetanus and posttetanic facilitation. After administration of neostigmine and atropine, tetanus was sustained and posttetanic facilitation was attenuated. Twitch height also increased.

into a patient with atypical pseudocholinesterase (dibucaine number = 25). Although it may have contributed to the neuromuscular block in the first anesthesia, the antibiotic irrigating solution was not used in the second anesthesia. Successful antagonism of this patient's neuromuscular block by neostigmine may have eliminated the need for several hours of mechanical ventilation.

Other reports suggest that attempts to antagonize this type of neuromuscular block with neostigmine may have resulted in neuromuscular block more profound in both magnitude and duration.[1-3] How can we predict successful antagonism of a desensitizing neuromuscular block? Cissen *et al.* place importance on the presence of SCh in the plasma.[5] In the absence of circulating SCh, anticholinesterase drugs will antagonize a desensitizing block induced by SCh. However, if SCh is still circulating in the plasma, anticholinesterase drugs will either not affect or actually enhance the SCh-induced desensitizing block. Since no simple method for determining the SCh level in plasma exists, they suggest that anticholinesterase drugs be avoided altogether in the management of patients with prolonged responses to SCh.

We suggest that attempts to antagonize prolonged SCh-induced blocks may be appropriate in well-defined circumstances. Although we were successful in antagonizing two desensitizing neuromuscular blockades, the initial administration of neostigmine may have prolonged the block. In retrospect, to avoid this possibility we suggest the use of edrophonium as a diagnostic drug. If tetanus becomes unequivocally sustained, posttetanic facilitation disappears, and tidal volume, vital capacity, or inspiratory force increases for at least 3–5 minutes following administration of edrophonium, it is reasonable to expect complete and prolonged antagonism of the SCh blockade by neostigmine.[1]

Apparently, antagonism of a desensitizing neuromuscular block should not be attempted when the patient is apneic.[1] A review of the reported cases with low dibucaine numbers suggests that attempts to reverse SCh desensitizing blocks before evidence of spontaneous muscle activity was present have resulted in more profound and prolonged neuromuscular blocks. Perhaps this indicates a high level of SCh in the plasma. However, in those cases in which spontaneous muscle activity had begun to appear, there usually was an immediate and lasting antagonism of the neuromuscular block when an anticholinesterase was given.[1] In both episodes in this case, our patient showed evidence of spontaneous muscle activity.

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Two Rare Mixed Heterozygotes for the Fluoride Variant and Silent Cholinesterases

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Serum cholinesterase (acylcholine acyl-hydrolase, EC 3.1.1.8) breaks down the muscle relaxant, succinylcholine. The usual (E_1^u), dibucaine variant (E_1^a), fluoride variant (E_1^f), and silent (E_1^s) genes function as alleles at the E_1 locus and control the type of cholinesterase present. Kalow and Staron [1] have described the dibucaine variant gene; Harris and Whittaker,[2] the fluoride variant gene; Liddell *et al.*,[3] the silent gene. Individuals with the E_1^a, E_1^f, and E_1^s genes are at risk when exposed to succinylcholine.

Whittaker [4] made the first identification of the mixed heterozygote for the fluoride variant and the silent cholinesterases (genotype $E_1^fE_1^s$) in the course of a family study. Simpson [5] made the second identification of this rare genotype in a 40-year-old Caucasian woman who had 20 minutes' apnea after 30 mg of succinylcholine. The present family study was made because the propositus was markedly sensitive to succinylcholine.

METHODS

The propositus was a 4-year-old Caucasian boy. He received 40 mg of succinylcholine intramuscularly at 9:35 AM and was apneic until 11:45 AM. Respiratory assistance was needed until 12:15 PM, at which time respiration reverted to normal. Sera were collected from the patient and members of his family and stored at −20 C until needed.

Serum cholinesterase activities were measured by hydrolysis of benzoylcholine in 0.067 M phosphate buffer at *p*H 7.4 and 25 C according to the method of Kalow and Lindsay.[6] Dibucaine numbers were determined by the method of Kalow and Genest,[7] and fluoride numbers by the method of Harris and Whittaker.[2] Sernylan and Ro 2-0683 numbers were determined in exactly the same way as dibucaine numbers except that 5×10^{-5} M Sernylan (Parke, Davis) or one hour's preincubation with 1×10^{-3} M Ro 2-0683 (Hoffmann-LaRoche) were substituted for 1×10^{-5} M dibucaine (Nupercaine, Ciba) in the test system. Sernylan (phencyclidine hydrochloride), Ro 2-0683, and dibucaine are described chemically as: Sernylan, 1-(1-phenylcyclohexyl) piperidine monohydrochloride; Ro 2-0683, the dimethyl carbamate of (2-hydroxy-5-phenylbenzyl) trimethyl ammonium bromide; dibucaine, 2-butoxy-n-(2-diethylaminoethyl) cinchoninamide hydrochloride.† All determinations were made in triplicate.

RESULTS AND DISCUSSION

Table 1 gives the results of the family study. Serum cholinesterase activities are expressed as μmol of benzoylcholine hydrolyzed per min per ml of serum. Dibucaine, fluoride, Ro 2-0683, and Sernylan numbers refer to percentage inhibition of benzoylcholine hydrolysis in the presence of the inhibitor.

On the basis of the inhibition studies, the mother was genotype $E_1^uE_1^a$; the propositus could be $E_1^aE_1^a$ or $E_1^aE_1^s$; the paternal grand-

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