In summary, labor and delivery of an infant of a pregnant patient with PSS were successfully managed under epidural anesthesia. Careful preoperative assessment and a thorough understanding of the pathophysiologic interactions of scleroderma, pregnancy, and anesthesia are essential in formulating an anesthetic plan that will provide for all contingencies.

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Prolonged Neuromuscular Blockade Following Succinylcholine in a Patient Homozygous for the Silent Gene

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Prolonged apnea following administration of succinylcholine (SCh) to patients with abnormal cholinesterase (ChE) genes is well documented. However, no investigator has examined an increased sensitivity to SCh with documentation by peripheral nerve stimulation with the extremely rare genotype $E_1^sE_1^s$.[1] In the present study, we stimulated the ulnar nerve and examined the duration and the type of SCh-induced neuromuscular blockade in a patient diagnosed having the $E_1^sE_1^s$ genotype.

Report of a Case

A 44-year-old woman, weighing 60 kg, who was otherwise healthy, was admitted for removal of a rectal cancer. She had undergone cesarean section under spinal anesthesia at age 27 years without difficulty; there was no further surgical or anesthetic history.

In the preoperative examination, EKG, chest roentogenogram, lung function, and all laboratory values, except ChE activity, were within normal limits. Serum ChE activity, measured by the modified butyrylthiocholine method, was zero units (normal ranges 80–140 units). This method used butyrylcholine as substrate and dithiobisnitrobenzoic acid for coloration of thiocholine, a hydrolysis product of the substrate.[2] Coefficient of variation was 4%. Our study plan was approved by the Human Study Committee at the hospital. Premedication consisted of hydoxyzine 50 mg and atropine 0.5 mg im. Anesthesia was induced with droperidol 5 mg, fentanyl 0.05 mg and thiamylal 150 mg iv, and tracheal intubation was facilitated with SCh 1 mg/kg iv. Anesthesia was maintained with fentanyl and nitrous oxide. After the administration of SCh, supramaximal single twitch (0.4 Hz), tetanic (TS, 40 Hz for 5 sec), and train-of-four (TOF) stimulation were administered at 5-min intervals to the ulnar nerve at the wrist by means of steel needle (Ø 0.15 mm) electrodes. The resultant force of adduction of the thumb was measured using a force-displacement transducer and was recorded. The patient remained apneic, and the evoked responses could not be obtained until 45 min after SCh. The fade in the TOF and tetanic stimulation following SCh indicated significant phase II block. The TOF ratios obtained 50 and 105 min after SCh were 0.2 and 0.52, respectively (fig. 1). Spontaneous respiration reappeared about 150 min after SCh; thereafter, muscle paralysis was obtained by administration of pancuronium. After the end of surgery (390 min after SCh), residual paralysis was reversed effectively with neostigmine 1.0 mg and atropine 0.5 mg iv. After the reversal, the TOF ratio increased from 0.48–0.91 (fig. 1), and response to tetanic stimulation was sustained well.

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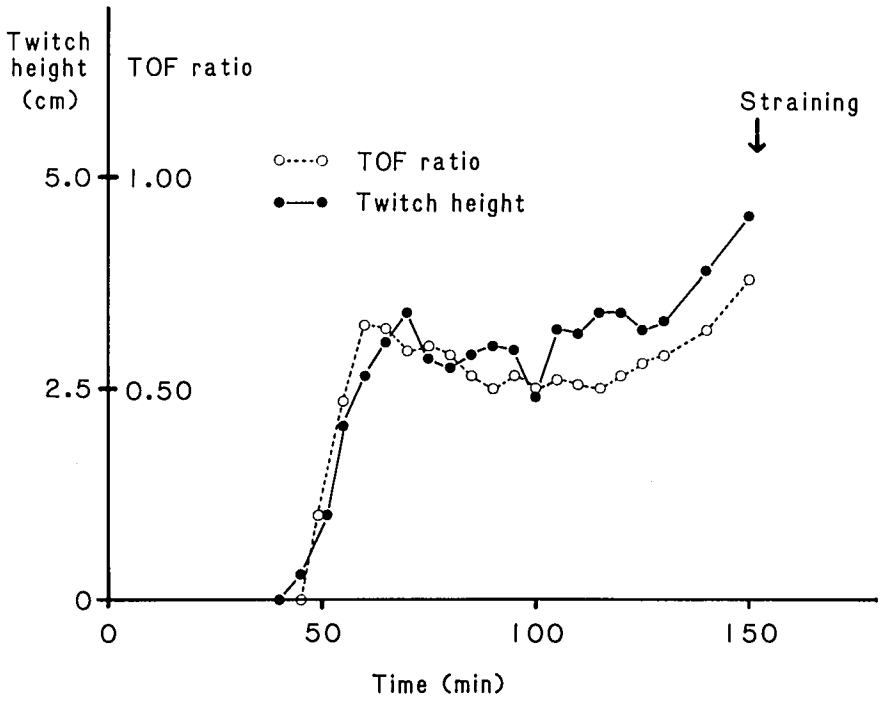

FIG. 1. Time course of spontaneous recovery of the TOF ratio and the first twitch height in the TOF stimulation after SCh 1 mg/kg iv in patient genotyped as $E_1^sE_1^s$.

During the surgical procedure, vital signs were stable, and recovery from operation and anesthesia were uneventful. The trachea was extubated after the confirmation that the TOF ratio was above 0.91, and that the tidal volume, inspiratory force, and grip strength were totally adequate. Analysis of arterial blood gases and serum electrolyte concentrations were within normal limits.

DISCUSSION

The important factors observed in our case are that the sensitivity to SCh was increased markedly and that the ChE activity essentially was zero. The genotypes whose sensitivity to SCh are increased markedly are $E_1^aE_1^a$, $E_1^sE_1^s$, and $E_1^aE_1^s$,[3] and among them, the ChE activity is zero only in the genotype $E_1^sE_1^s$.[4] Accordingly, then our case could be genotyped as homozygous for the silent gene ($E_1^sE_1^s$).

After either the overdosage of SCh to patients with normal enzyme or after the usual doses to patients with an abnormal enzyme, the neuromuscular blockade would be a mixed type, showing both the phase I and phase II type of blocks simultaneously.[5,6] In our case, the fact that the block was antagonized completely with neostigmine suggests that the phase I block was negligible at this time.

Our study revealed that the type and duration of neuromuscular blockade after SCh 1 mg/kg iv in $E_1^sE_1^s$ were quite similar to those observed in $E_1^aE_1^a$.[7] When the response to nerve stimulation reappeared after the injection of SCh, the block already was phase II. Also, the time course of spontaneous recovery of the neuromuscular blockade could be divided into four phases; the time for each phase was quite similar to that reported in $E_1^aE_1^a$ (fig. 1).[7] The total time necessary for recovery of the TOF ratio to 0.7 was 140–150 min in this study (fig. 1), while it was 137–152 min in patients with $E_1^aE_1^a$.[7] Finally, the block was the mixed type at almost similar times after SCh administration in both genotypes. These similarities in the type and duration of neuromuscular blockade after SCh between $E_1^sE_1^s$ and $E_1^aE_1^a$ might result from the equally and prominently depressed enzymatic hydrolysis of SCh in both genotypes. Although the atypical enzyme increases its activity with rising plasma concentrations of SCh, its action is negligible at the concentrations obtained after usual doses of SCh.[8] Conversely, in $E_1^sE_1^s$ no ChE activity exists to hydrolyze SCh, or, even if it does exist, the activity is extremely low.

In summary, we found that the patient homozygous for the silent gene remained totally apneic for at least 30 min after SCh and that the TOF ratio was depressed to the value of 0.76 even 150 min after SCh. The mixed phase I and II block was evident 105 min after SCh. The time course of spontaneous recovery of the neuromuscular blockade observed in the present study was quite similar to those reported in $E_1^aE_1^a$.[7]

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Clonidine Withdrawal Complicated by Amitriptyline Therapy

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Withdrawal from clonidine characterized by rebound hypertension and tachycardia is a recognized, but infrequent, complication of therapy with this drug. The withdrawal syndrome may be exacerbated by other drug therapy, particularly beta adrenergic receptor blockers.[1–3] We recently encountered a patient who had a lengthy period of rebound hypertension, tachycardia, and anxiety after sudden cessation of clonidine and amitriptyline therapy.

REPORT OF A CASE

A 73-year-old woman was admitted after a 12-hr illness consisting of nausea, vomiting, and abdominal pain. Her medications included digoxin 0.25 mg and furosemide 40 mg every day, amitriptyline 25 mg four times a day, and clonidine 0.1 mg twice a day. Her arterial blood pressure was 156/80 mmHg and heart rate was 96 beats·min.$^{-1}$ Eight hours after admission, an exploratory laparotomy and resection of 2 feet of necrotic jejunum was performed. Because of insufficient ulnar circulation to both hands, arterial blood pressure was measured indirectly either by blood pressure cuff and stethoscope or an oscillometric monitor (Dinamap®). The patient was given an enflurane and nitrous oxide anesthesia, supplemented by small doses of morphine. Muscle relaxation was induced by pancuronium. At the beginning of the procedure, the arterial blood pressure was 170/90 mmHg and heart rate was 100 beats·min^{-1} but during the anesthetic, arterial blood pressure was as high as 220/120 mmHg, with a heart rate of 120 beats·min^{-1}; arterial blood pressure was controlled by increasing the concentration of enflurane. Because she had not taken any of her regular medications for approximately 24 hr, she was given 500 mg of alpha methyldopa iv during surgery. On the first postoperative day, arterial blood pressure ranged from 170/120–240/150 mmHg, with heart rate of 100–135 beats·min^{-1}. Alpha methyldopa 250 mg was given iv every 6 hours and nitroprusside for sudden increases in arterial blood pressure. Despite adequate analgesia and diazepam administration, she complained of extreme anxiety. On the second postoperative day, the dose of alpha methyldopa was increased to 500 mg q 6 hr; nitroprusside was used briefly. Because tachycardia was a prominent part of her syndrome, she also was given propranolol 1 mg IV q 6 hrs. On that day arterial blood pressures were as high as 220/70 mmHg and heart rates 95–105 bpm. On the third postoperative day her arterial blood pressure was 210/90 mmHg at 0800. Alpha methyldopa and propranolol were continued. Two hours later, arterial blood pressure was 170/90 mmHg and the propranolol was decreased to 0.5 mg q 6 hrs. By that evening, arterial blood pressure was 140/80 mmHg and the propranolol was discontinued. On the following day, arterial blood pressure ranged from 160/70 to 120/70 mmHg and the alpha methyldopa was decreased to 250 mg q 6 hrs. Her blood pressure has remained well controlled since on 250 mg of alpha methyldopa four times a day.

DISCUSSION

Clonidine is a central alpha agonist and blocks sympathetic outflow from the central nervous system.[4] Upon cessation of therapy, catecholamine levels in blood and urine have been found to increase by more than 100%.[5,6] This increase in catecholamines is felt to be responsible for the symptoms of agitation, anxiety, insomnia, headache, nausea, tremor, and palpitations, and in some patients may lead to a severe "rebound" hypertension. Such a withdrawal can begin as soon as 8 hours or up to 36 hours after the last dose and last 72–96 hours.

Other drug therapy can add to the withdrawal phenomenon. Simultaneous withdrawal of beta adrenergic blocker or withdrawal of clonidine without discontinuance of a beta blocker may result in an unopposed alpha adrenergic crisis.[1,2] In our case, the therapy with amitriptyline may have contributed to and prolonged

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