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Anesthesiology
65:525–528, 1986

Neuromuscular Blockade in a Patient with Stiff-baby Syndrome

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Stiff-baby syndrome (hyperekplexia) is a rare genetic syndrome characterized by marked muscle rigidity immediately after birth.[1–3] The muscle stiffness persists during early infancy but disappears gradually during the first few years of life. Because there are no reports of anesthesia for or the effect of neuromuscular blocking drugs on patients with stiff-baby syndrome, we describe the responses of a patient with stiff-baby syndrome to anesthesia, succinylcholine, and pancuronium.

REPORT OF A CASE

A 5-month-old, 6.3-kg boy with stiff-baby syndrome was admitted for repair of bilateral inguinal hernias. At birth he had been noted to be stiff and to startle easily. His father and paternal grandmother had had the same condition at birth. Both father and grandmother had had surgery and general anesthesia several times without any known complications, but the medical records had been destroyed by fire. A study of the infant was undertaken with the parents' informed consent.

Physical examination revealed a tense, stiff infant with a pinched, "worried" facial expression. His body, which was straight and rigid, did not sag when he was held supine and supported only by his occiput and his heels, or by a single hand under his waist (fig. 1). His arms and legs passively resisted movement and reflexes were hyperactive. The rest of the physical examination was remarkable only for bilateral inguinal hernias and an umbilical hernia. Although the infant had some choking associated with eating, there were no symptoms of gastroesophageal reflux. Preoperative hematocrit (Hct) was 31.5%, and urinalysis was within normal limits.

No preoperative medication was given. Anesthesia was induced and maintained by inhalation of halothane (1% end-tidal concentration according to mass spectroscopy) in N_2O (60%) and O_2 (40%). Atropine, 0.1 mg, was given as soon as an iv line was inserted. The trachea was

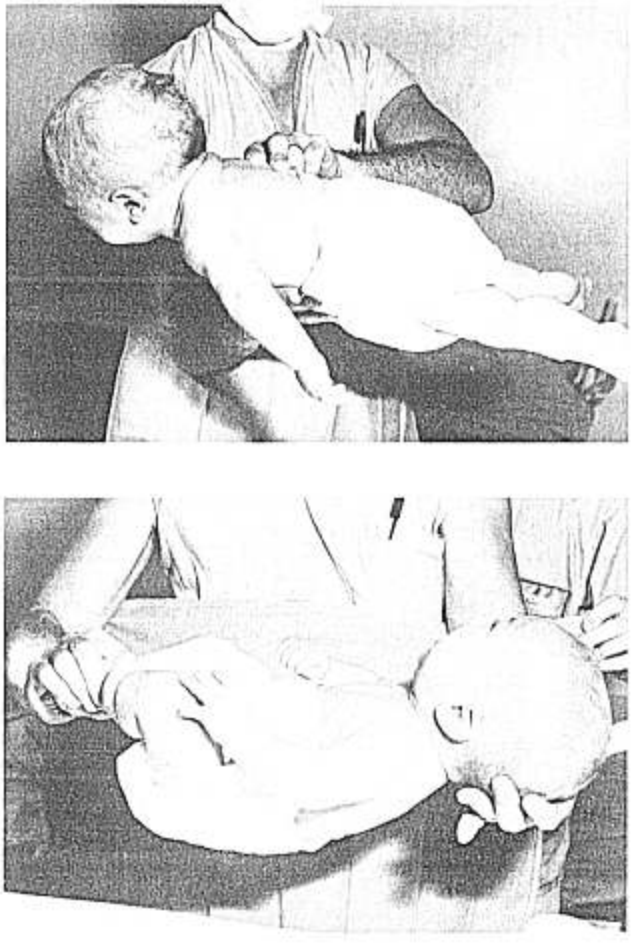

FIG. 1. The marked muscular rigidity of stiff-baby syndrome (hyperekplexia) in a 5-month-old boy.

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Received from the Department of Anesthesiology, University of Florida College of Medicine, Gainesville, Florida. Accepted for publication June 10, 1986.

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Key words: Anesthesia: pediatric. Muscle, skeletal: hyperekplexia. Neuromuscular relaxants: pancuronium; succinylcholine.

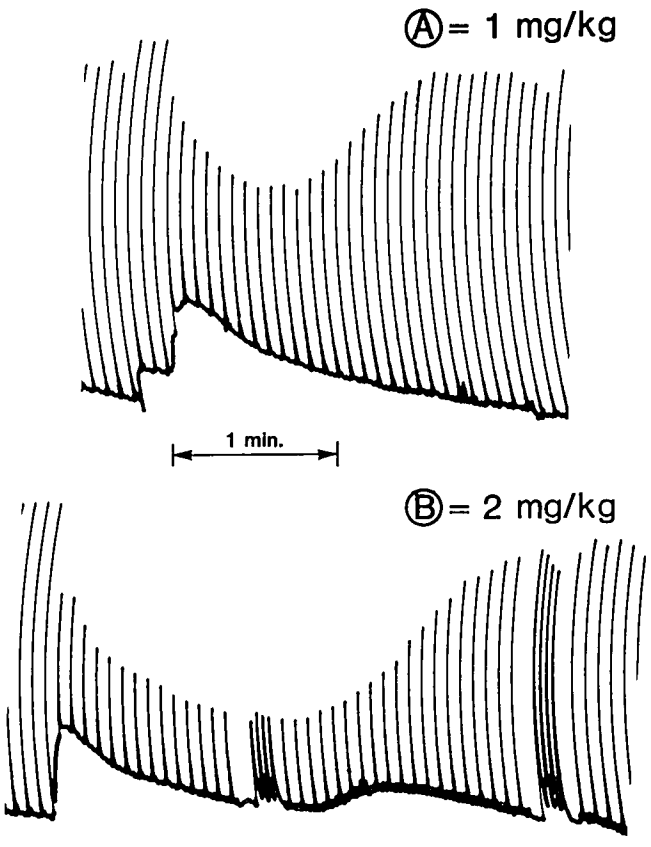

FIG. 2. The recorded twitch response to ulnar nerve stimulation in a patient with stiff-baby syndrome who received succinylcholine, 1 mg/kg (*A*) and 2 mg/kg (*B*). Notice the contracture response. Twelve twitches = 1 min.

intubated without paralysis. End-tidal CO_2 was kept at 30 ± 3 mmHg according to mass spectroscopy, which corresponded to a venous P_{CO_2} of 40 mmHg. Esophageal temperature ranged from 36.1 to 36.8° C. Hemoglobin oxygen saturation remained 97–99% as measured by pulse oximetry. The cardiac rate and rhythm were recorded continuously with an ECG (lead II).

Neuromuscular blockade was assessed by response of thumb adduction to supramaximal square wave stimuli (0.2-ms duration every 5 s) delivered to the ulnar nerve at the wrist *via* surface electrodes. The strength of the thumb response was measured with a Grass® FTO3 force displacement transducer[4] and recorded on a Grass® polygraph. When a consistent baseline twitch was achieved, succinylcholine, 1 mg/kg iv, was administered. Two and a half minutes after twitch height had returned to control height, a second dose of succinylcholine, 2 mg/kg, was administered; 10 min after complete recovery from the succinylcholine, pancuronium, 0.02 mg/kg followed by two doses of 0.005 mg/kg each, was administered to achieve 95–98% depression of twitch height. Serum samples were obtained before succinylcholine was administered for potassium and creatine kinase (CK) determination and 3, 5, and 12 min after injection for potassium and 12 h after the operation for CK.

The neuromuscular blockade was reversed with neostigmine, 0.06 mg/kg, and atropine, 0.02 mg/kg iv. The trachea was extubated when protective reflexes and normal respiration had returned. Twitch height and train-of-four response returned to baseline and tetanus was sustained for 5 s. Shortly after the procedure, while the patient was still sedated from anesthesia, electromyography was performed. Continuous muscle activity (consistent with stiff-baby syndrome) was demonstrated even though the patient appeared to be resting. Nerve conduction and action potentials were normal.

RESULTS

The infant had marked fasciculation in response to succinylcholine. Neither muscle rigidity nor masseter spasm was observed. The maximal depression of twitch height after succinylcholine, 1 mg/kg, was 51% within 1.5 min (fig. 2). Resting tone of the stimulated muscle increased during the onset of action of succinylcholine (fig. 2). Twitch height returned to 100% of control within 3.5 min. After the second dose, the maximal depression of twitch height was 74% within 3 min. Twitch height returned to 100% of control within 6.5 min. Train-of-four stimulation showed no evidence of phase II block, the train-of-four ratio being 0.92. Serum potassium levels were 3.7, 3.6, 3.9, and 3.6 mEq/l at 0, 3, 5, and 12 min, respectively, after the first dose of succinylcholine. Baseline CK was 334 iU/l (normal 5–180) but, 12 h after operation, increased to 3,260 iU/l. Pseudocholinesterase activity and dibucaine number in blood drawn before muscle relaxant was given were 5.6 U/ml (normal 3–8) and 79% (normal homozygotes 77–83%), respectively.

After total doses of 0.02 mg/kg, 0.025 mg/kg, and 0.03 mg/kg of pancuronium, the twitch height was depressed by 70, 88, and 98%, respectively. The single twitch response spontaneously returned from 2 to 50% of control within 46 min. Recovery of the single twitch response from 50 to 95% of control occurred within 3 min after reversal with neostigmine, 0.06 mg/kg, and atropine, 0.02 mg/kg.

During the procedure, monitoring of heart rate, temperature, end-tidal CO_2, and central venous gas tensions did not reveal evidence of malignant hyperthermia.

DISCUSSION

The stiff-baby syndrome appears to be transmitted in a genetically dominant fashion with variable penetrance.[1–3] Similarities between stiff-baby syndrome and hyperexplexia (also hyperekplexia), or "startle disease,"[3,5] are remarkable and they may be the same disease.[3] Electromyography demonstrates continuous muscle activity with only rare periods of quiescence. Action potentials and nerve conduction studies are normal. Histologic examination of muscle has not been reported. Clinical presentation includes an exaggerated startle response to sudden noises or movement that may persist into adulthood. Indeed, affected adults, when startled, may stiffen and fall; unable to stop or break their fall, they may suffer severe injuries. Choking, vomiting, and difficulty in swal-

lowing are also common in infancy and may be fatal.[2] The motor development of these infants is delayed but intelligence is normal.

The response to succinylcholine of the infant presented in this report is abnormal (fig. 3). In a study of infants receiving halothane anesthesia (unmeasured concentration), succinylcholine, 1.0 mg/kg, produced a maximal twitch depression of 83.3 ± 12.0% (mean ± SD) of control.[6] At this same dose, the twitch depression in our patient was only 51%, a degree of depression nearly 3 SD less than the reported mean. A dose of 2.0 mg/kg of succinylcholine would be expected to produce approximately 95% twitch depression in normal infants,[7] far more than the 74% twitch depression observed in our patient (fig. 3). The time to full recovery of twitch height was within the normal range.[6]

In denervated muscle, serum potassium peaks 3–5 min after succinylcholine administration for at least 15 min.[8] In our patient, serum potassium increased only 0.2 mEq/l 5 min after succinylcholine was given, which is consistent with data for the average person.[9]

The resistance to succinylcholine is difficult to explain. The succinylcholine we used was potent, as evidenced by 100% twitch depression after a dose of 1.0 mg/kg in the next patient, an 18-month-old infant. Other possible causes include: 1) decreased blood flow to muscle; 2) another plasma factor that metabolized succinylcholine; or 3) an abnormal neuromuscular junction; although no data support any of these explanations. Resistance to depolarizing muscle relaxants has also been reported in myasthenia gravis[10,11] and neurofibromatosis,[12] but again, the cause was not clear.

During the onset of action of succinylcholine, a substantial increase of the resting tension of muscle of our patient manifested as an increase of twitch height to 25% of baseline (fig. 2). This pattern may be normal in infants‡ but is considered abnormal in adults. Its significance in our patient is unknown because masseter spasm did not occur.

Whether the elevated baseline CK level in our patient is common in patients with stiff-baby syndrome is unknown because CK values have not been reported in the literature. After halothane and succinylcholine anesthesia in normal children, CK has increased as high as 30 times the normal or baseline level.[13,14]

In our patient the magnitude of twitch depression after incremental doses of pancuronium and the recovery time are similar to values reported from studies in which pancuronium was administered after succinylcholine to adult patients receiving halothane.[15,16] Similar studies with infants have not been performed. The time from injection

‡ Cook DR: Personal communication, 1985.

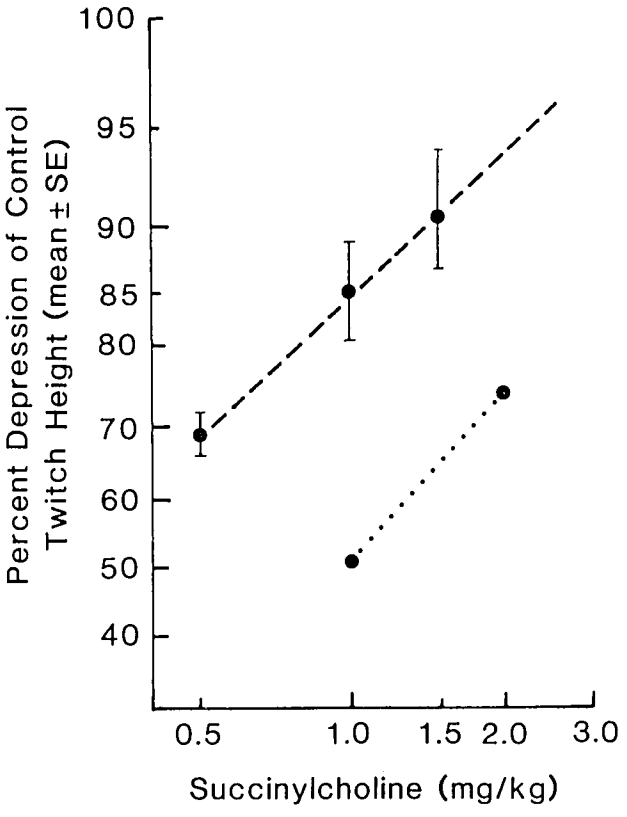

FIG. 3. Dose–response curve in normal infants (*dashed line*) who received succinylcholine during halothane anesthesia compared with the dose–response curve of the infant with stiff-baby syndrome (*dotted line*). Modified and reproduced with permission of the American Society of Anesthesiologists from Cook DR: Muscle relaxants in children, 1984 ASA Refresher Courses. Edited by Hershey SG. Philadelphia, JB Lippincott, 1984, p 50).

of neostigmine or atropine to complete reversal of neuromuscular blockade in our patient was consistent with that in infants anesthetized with halothane.[17]

In summary, stiff-baby syndrome (hyperekplexia) may be associated with a markedly abnormal resistance to succinylcholine but a normal response to pancuronium and neostigmine. As with any myopathy, we suggest that with hyperekplexia, the muscle response to peripheral nerve stimulation be monitored during muscle relaxation.

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Anesthesiology
65:528–531, 1986

Evaluation of Esmolol in Controlling Increases in Heart Rate and Blood Pressure during Endotracheal Intubation in Patients Undergoing Carotid Endarterectomy

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Endotracheal intubation can produce cardiovascular stress, which is of concern in patients with coronary artery disease.[1] Beta-adrenergic receptor blockers can blunt the tachycardia and hypertension associated with surgical stresses.[2–4]

We examined the effect of esmolol on hemodynamics during endotracheal intubation in patients with carotid artery disease. Esmolol (methyl 3-4-[2-hydroxy-3-(isopropylamino) propoxy-phenyl] propionate hydrochloride) is a water-soluble, cardioselective beta-adrenergic blocker of rapid onset and ultrashort duration of action with a half-life of 9 min.[3] It is an ester and is rapidly metabolized by esterases in the blood to a free acid metabolite that has a beta-adrenergic blocking potency that is 1/1,600 of esmolol and methanol.

METHODS

The study was a randomized, double-blind, placebo-controlled multicenter trial. With institutional review board approval and written patient consent, 74 patients undergoing elective carotid endarterectomy were included. Exclusion criteria are shown in table 1. Twelve patients were eliminated from data analysis because of significant deviations from the protocol. After a 5-min preinfusion period, an infusion of esmolol or placebo was administered for 12 min (500 $\mu g \cdot kg^{-1} \cdot min^{-1}$ for 4 min, then 300 $\mu g \cdot kg^{-1} \cdot min^{-1}$ for 8 min) by calibrated infusion pump. Infusion rates for both esmolol and placebo were identical and calculated by weight.

Arterial blood pressure (BP) determinations were made from direct arterial tracings and intraoperative ECG tracings from a V5 lead. Heart rate was counted from the electrocardiogram.

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Key words: Blood pressure: hypertension. Heart: dysrhythmias; tachycardia. Sympathetic nervous system: esmolol.