

Anesthetic Implications in Stiff-Person Syndrome

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Stiff-person syndrome (SPS) is a rare neurologic disease manifested by persistent muscle contractions causing marked rigidity in the affected individual (1). There are many case descriptions and clinical reviews in the neurologic literature, outlining a progression of knowledge from the early clinical description of SPS to advanced molecular biologic and immunologic studies implicating the γ -aminobutyric acid (GABA) receptor system (1–3). We report a case of prolonged hypotonicity after general anesthesia in a patient with SPS and discuss the possible anesthetic interactions.

Case Report

A 46-yr-old female presented to the operating room for repair of an intrathecal baclofen pump. Her diagnosis of SPS was based on clinical presentation and the presence of an autoantibody against the central nervous system enzyme glutamic acid decarboxylase (GAD). The syndrome began as muscle stiffness in her lower extremities and insidiously progressed to a state of constant stiffness resulting in permanent contractures of her lower extremities and moderate rigidity of her upper extremities. The patient's facial, cervical, and extraocular muscles were spared. When startled by a loud noise, the patient experienced a painful brisk spasm resulting in opisthotonic posturing. These acute exacerbations were treated with a 50-mg dose of diazepam administered intramuscular. Other pharmacologic therapies included intrathecal baclofen and 100 mg of diazepam orally per day. Past surgical history was significant for a 2-day history of prolonged postoperative weakness after the baclofen pump was inserted, and an overdose of baclofen was suggested as the cause. A review of the previous anesthetic record revealed that propofol and succinylcholine followed by desflurane was used for induction of anesthesia, tracheal intubation, and maintenance of anesthesia, respectively.

Anesthesia was induced with sufentanil 10 μ g, thiopental 375 mg (5.8 mg/kg), and vecuronium 8 mg (0.12 mg/kg) administered intravenously (IV). It was inferred from the slow and inadequate induction of anesthesia that the IV catheter had infiltrated subcutaneously although visual inspection was equivocal. A facial nerve train-of-four twitch monitor indicated an absence of all four twitches 10 min after induction of anesthesia. Inhalation anesthesia via a

mask with isoflurane allowed for an otherwise unremarkable tracheal intubation while another IV catheter was placed. Anesthesia was maintained with isoflurane and nitrous oxide for the duration of the procedure. Additional doses of muscle relaxant were not administered, and the patient regained all four twitches 60 min after the initial dose of vecuronium. Baclofen was not given intraoperatively due to the patient's previous experience with postoperative weakness. At the end of surgery, with all four twitches present, the neuromuscular block was antagonized with neostigmine 0.07 mg/kg and glycopyrrolate 0.02 mg/kg. Our preextubation clinical assessment revealed that she was responsive but weak—unable to lift her head for 5 s, raise an extremity, or grasp with either hand.

Upon arrival to the recovery room, the tracheally intubated patient had a respiratory rate of 12 breaths/min with a tidal volume of 300 mL and a normal arterial blood gas analysis. She would respond to yes and no questions by nodding her head. Due to her rare neuromuscular disorder, her neurologist was consulted for assistance with evaluation. His clinical examination, in addition to revealing muscle weakness in the presence of a vigorous response to ulnar nerve stimulation, also revealed a state of hypotonia unusual for this particular patient. The leg at the knee could be flexed 10–15° beyond its normally contracted state. The issue of subcutaneous infiltration of the thiopental was discussed, and barbiturate levels were drawn. The thiopental level 6 h after induction was reported as 10 μ g/mL.

The patient was transferred from the recovery room to the neurointensive care unit and her lungs were mechanically ventilated overnight. The next morning the patient's trachea was extubated. On postoperative Day 2, her strength had returned to baseline and the diazepam and baclofen were resumed.

Five months after surgery, the patient was again scheduled for repair of the baclofen pump. Induction of anesthesia was accomplished with 36 mg (0.55 mg/kg) of midazolam and halothane. The trachea was intubated without the use of a muscle relaxant, and neuromuscular block was avoided during the procedure. Anesthesia was maintained with isoflurane and nitrous oxide. At the time of extubation the patient responded appropriately to commands and did not display excessive rigidity or weakness.

Discussion

SPS (originally stiff-man syndrome) was first described by Moersch and Woltman in 1956 (4). Postulates of the pathophysiology involved in this disease began with psychiatric, metabolic, and myopathic etiologies, which have since been discarded (2). As more case reports were published, plausible theories

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included an inhibition of Renshaw interneurons or a dysfunction of γ -motor nerve fibers supplying muscle spindles (3). The isolation of autoantibodies to GAD in the cerebrospinal fluid of a single case report, followed by an extensive series, led to an autoimmune hypothesis of disease directed against GABA-ergic systems (5,6). Since GAD is an intracellular enzyme, autoantibodies may be a marker for systematic destruction of GABA-containing neurons. The resultant lack of inhibitory influence in various portions of the cerebral cortex, striatum, and basal ganglia then causes dysfunction in the γ -motor neuron system, continuous motor neuron activity, and clinical rigidity (7). Support for the autoimmune basis of SPS is shown by its association with other autoimmune diseases such as diabetes and thyroid dysfunction, as well as effective treatment with plasmapheresis and corticosteroid therapy (8-10). Thus, an autoimmune-mediated impairment of the normal inhibitory impulses generated by the central nervous system in SPS has supplanted previous theories (11).

Successful pharmacologic therapy for this disease has been directed at the enhancement of central GABA-ergic neurotransmission. The mainstay of therapy is a GABA-facilitating drug, diazepam, in doses ranging from 20 to 200 mg per day (12). Intrathecal baclofen was used in this case to augment diazepam therapy. It reduces spasticity by activating the GABA_B receptor in the dorsal horn of the spinal cord. Other medications have been studied and efficacy has been described with baclofen, clonazepam, and sodium valproate (13-15).

Although several case reports mention that the patient described underwent surgery with anesthesia, this is the first report of possible anesthetic interactions in SPS. Many drugs used during anesthetics (i.e., halothane, thiopental, propofol, and etomidate) have been implicated in their facilitatory effect upon the GABA system (16). Recent investigations into the antinociceptive properties of propofol and thiopental indicate that even small plasma concentrations of pentothal may modulate descending inhibitory influences through a GABA-mediated mechanism (17,18). Thus, the presence of these drugs may have an effect on the postoperative condition of the patient diagnosed with SPS. The serum barbiturate concentration reported for this patient 6 h after a possible subcutaneous infiltration is within the therapeutic range (although the patient was not excessively sedated) but higher than expected after a bolus dose (19). Computer-simulated pharmacokinetic analysis of thiopental redistribution indicated that the level of 10 $\mu\text{g}/\text{mL}$ could be achieved only with a very low volume of distribution and elimination rate constant (20).

The mechanism resulting in this patient's postoperative condition is unclear, although postoperative

weakness is most commonly the result of administration of an inappropriate amount of muscle relaxant. The uncomplicated anesthetic course seen upon return of the patient for a revision of the baclofen pump leads us to recommend avoidance or judicious use of non-depolarizing neuromuscular relaxants in patients with SPS. The question remains as to whether other anesthetics acting at the GABA receptor have an additive impact on anesthetic recovery, but the rarity of the syndrome makes direct investigation unlikely.

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