A 30-year-old woman with no history of syncope or palpitations and normal preoperative serum electrolyte concentrations and a normal electrocardiogram had cardiac asystole while undergoing hysteroscopy under general anesthesia. After resuscitation, she received dopamine intravenously (25 μg per kilogram of body weight per minute) for hypotension. Although dopamine in this dose causes tachycardia,[1] her heart rate decreased from 118 to 80 beats per minute; after recovery, when the infusion was tapered by 5 μg per kilogram per minute every 15 minutes, the heart rate progressively accelerated from 77 to 95 beats per minute and mean arterial pressure decreased minimally from 70 to 65 mm Hg. We investigated this abnormal response after obtaining informed consent.

The patient had no orthostatic hypotension, had normal responses to carotid massage and the Valsalva maneuver, and had a normal corrected sinus-node recovery time (120 msec).[2] Echocardiography showed no heart disease. When she was given 25 μg of dopamine per kilogram per minute, her heart rate decreased from 115 to 100 beats per minute. Carotid massage then suppressed the sinoatrial node, and a transient atrioventricular nodal escape rhythm supervened. Sinus-node dysfunction was evident since junctional escape beats occurred before the sinus node recovered after overdrive suppression. When atropine (2 mg) was administered intravenously, the heart rate accelerated to 150 beats per minute and carotid massage caused no deceleration. The sinus-node recovery time decreased to basal levels (100 msec). During 60-degree head-up tilting, hypotension, bradycardia, and syncope developed after seven minutes (Fig. 1); these subsided when the patient returned to the horizontal position. When she was given isoproterenol (2 μg as an intravenous bolus dose) while supine, she had transient tachycardia and widening of pulse pressure — a normal response.[3] When the same dose was injected during head-up tilting, the effect was similar to that during tilting alone. However, 8 μg of isoproterenol with the patient in the supine position caused abrupt bradycardia, hypotension, and a transient atrioventricular nodal rhythm. Injection of 8 μg of isoproterenol after pretreatment with atropine caused hypotension but not bradycardia, whereas pretreatment with propranolol prevented both.

Beta-adrenergic stimulation, produced by both dopamine and isoproterenol,[3] probably triggered the vagally mediated bradycardia. As in spontaneous syncope, sudden loss of sympathetic vasomotor tone probably caused hypotension, since atropine did not prevent it but alpha-mediated vasoconstriction induced by dopamine did.[4] Using inotropic agents to treat patients with such conditions may pose problems. Dopamine in low doses (<10 μg per kilogram per minute), dobutamine, isoproterenol, and possibly digoxin (which is both inotropic and vagotonic)[5] may worsen circulatory failure by activating vasodepressor reflexes. Norepinephrine or dopamine in large doses may be preferred; their alpha-agonist activity will prevent hypotension.[5] Atropine may be added if bradycardia is troublesome.

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FAILURE OF PHYSOSTIGMINE IN TREATMENT OF ACUTE SEVERE INTRATHECAL BACLOFEN INTOXICATION

To the Editor: Intrathecal baclofen, supplied by implanted drug-delivery systems, has now been established as an effective treatment for spinal spasticity[1] and is currently being explored for its usefulness in treating supraspinal spasticity.[2] Overdosage is an inherent risk of this approach, with respiratory depression being of most concern in patients with this condition, as has been pointed out in letters to the Editor (Nov. 16 issue).[3,4] Intravenous physostigmine has been proposed as an "antidote,"[5,6] but our experience casts doubt on its value in cases of severe intrathecal baclofen overdose.

An accidental intrathecal bolus delivery of 10 mg of baclofen through a lumbar subarachnoid catheter occurred in a 16-year-old male patient with severe spastic tetraparesis after a head-and-brain injury, when the reservoir of an implanted pump (Cordis SECOR) was refilled. Fifty minutes later, the patient presented with somnolence; 80 minutes later he was comatose, and intubation and artificial ventilation became necessary. Treatment with intravenous physostigmine — 4 mg within 30 minutes, followed by 2 mg every 60 minutes, up to a total of 14 mg — was ineffective. In an attempt to remove some baclofen, 30 ml of cerebrospinal fluid was tapped and replaced. At 48 hours the patient started to breathe spontaneously, and he gradually improved, until on day 5 his neurologic condition had returned to base-line status.

In contrast to its reported effectiveness as an antidote for mild-to-moderate toxicity,[5,6] physostigmine was of no apparent value in the present case of severe poisoning; during profound respiratory depression and long-lasting coma,[7,8] the side effects of physostigmine, such as vomiting, hypersalivation, convulsions, and bradycardia, could seriously jeopardize intensive care efforts.[9] Thus, if a large bolus overdose has occurred, we suggest that a spinal tap be considered as soon as possible in order to reduce the intrathecal baclofen load; once the drug has had sufficient time to penetrate into the neural tissues, removing it by spinal tap is less effective, as our case shows. Depending on clinical judgment, the use of physostigmine remains an option.

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The above letter was referred to the authors of the article in question, who offer the following reply:

To the Editor: We agree that intravenous physostigmine is not likely to be of value after a massive overdose of intrathecal baclofen. The patient described by Saltuari and his colleagues received a dose more than two orders of magnitude higher than the test doses usually used in screening. In a series of experiments we performed in animals before using physostigmine in patients, moderate overdoses of baclofen in dogs (50 μg intracisternally) could be reversed, but not massive ones (200 μg or more). All the successful examples of reversal with physostigmine in patients with spasticity[1] (and two unreported cases) have occurred with boluses of 80 to 800 μg. Since we published our earlier observations, several physicians have com-