

Supine Hypertension During General Anesthesia in a Patient Taking Midodrine

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The diabetic patient is susceptible to a variety of complications affecting multiple organ systems, which can cause morbidity and lead to premature mortality. Autonomic dysfunction, as manifest by orthostatic hypotension (OH), can be one of the most debilitating of these because of its significant impact on the ability to perform activities of daily living (1–3). Midodrine, a selective α_1 -agonist, was approved by the Food and Drug Administration in 1996 to treat symptomatic OH. We describe a case of a diabetic patient being treated with midodrine who exhibited severe hypertension in the supine position during general anesthesia.

Case Report

A 34-yr-old, 56-kg woman with a 21-yr history of type I diabetes was admitted from the orthopedics clinic with an infected left below-knee amputation site. The patient's known complications related to her diabetes included proliferative retinopathy, proteinuria, and both autonomic and somatic neuropathy. At admission, her medications included NPH insulin 12 U in the morning and evening, midodrine 10 mg 3 times daily for symptomatic postural hypotension, lisinopril 5 mg daily for proteinuria, as well as venlafaxine, gabapentin, clonazepam, and oxycodone for chronic pain related to her somatic neuropathy. Laboratory values of note were serum concentrations of creatinine 0.9 mg/dL, albumin 1.5 g/dL, and hemoglobin A1C 12.4%. On the day of admission, the patient was nil per os including her usual medications for 6 h before going to the operating room (OR) for irrigation and debridement. Her initial blood pressure (BP) in the OR was 150/90 mm Hg with a heart rate of 90 bpm. Anesthesia was induced with 100 mg of propofol and 150 μ g of fentanyl IV. A laryngeal mask airway was inserted and anesthesia was maintained with isoflurane (0.6% to 1% expired concentration). Her BP ranged from 100 to 130/50 to 60 mm Hg with a heart rate of 90–100 bpm throughout the case. On postoperative day 4, the patient had an arterial BP of 220/128 mm Hg with a heart

rate of 120 bpm in the recumbent position. She denied chest pain or shortness of breath but complained of a "tingling" sensation in the left chest and arm. Her hypertension responded to treatment with labetalol 10 mg IV and nitropaste 1" given to treat possible myocardial ischemia. A subsequent electrocardiogram, however, showed no evidence of ischemia, and serial determinations of creatine phosphokinase and troponin T were negative. The internal medicine service was consulted for further management and recommended the midodrine dose be decreased to 5 mg each morning and noon. The following afternoon, 4 h after she had received a dose of midodrine, the patient returned to the OR for stump revision and primary closure of her left below-knee amputation. She received 10 mg of morphine and 2 mg of midazolam IV in the holding area. Her initial BP reading taken in the OR while she was supine with the head of the bed elevated 30° was 150/90 mm Hg with a heart rate of 80 bpm. Anesthesia was induced with 200 mg of propofol followed by 50 mg of rocuronium IV. In preparation for tracheal intubation, the OR table was flattened to a horizontal position and the patient was ventilated via a mask with sevoflurane (2% expired concentration) in 100% oxygen. Her next 3 BP readings in the supine position before laryngoscopy were in the range of 200/100–110 mm Hg. The sevoflurane concentration was increased, the trachea was intubated, and the bed was placed in reverse Trendelenburg position. Arterial BP then stabilized in the 110–120/50–60 mm Hg range for the remainder of the case. At the conclusion of surgery, the trachea was extubated and she recovered in the sitting position in the postanesthesia care unit where her BP remained in the range of 110–140/60–80 mm Hg.

Discussion

OH is defined as a reduction of systolic BP of at least 20 mm Hg within 3 minutes of standing, which may be either asymptomatic or symptomatic and severely disabling (4). When symptomatic, patients commonly present with complaints characteristic of cerebral hypoperfusion including lightheadedness, dizziness, blurred vision, cognitive impairment, and nausea. OH may arise from a variety of causes, both nonautonomic and autonomic (4,5).

There are a number of chronic medical conditions that may be classified as secondary autonomic causes

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of OH; of these, diabetes mellitus is the most significant (6). The pathophysiology of postural hypotension associated with diabetic autonomic neuropathy is poorly understood. Several mechanisms have been postulated, and each may be operative to a varying degree in any given patient (7). Of note, many diabetic patients with OH exhibit hypertension when supine (8). This is attributed partly to a lack of baroreflex control but also to hypersensitivity of partially denervated postsynaptic adrenoceptors to norepinephrine (9,10).

Midodrine, an α_1 -selective-adrenergic agonist, was approved by the Food and Drug Administration in 1996 for the treatment of severe symptomatic OH. Midodrine is a prodrug that is converted to the active compound desglymidodrine after oral administration. Plasma concentrations of the parent compound peak about 30 minutes after a dose whereas desglymidodrine plasma concentrations reach their peak at 1 to 2 hours. The elimination half-life for the active metabolite is three to four hours (11). Both the prodrug and its metabolite are excreted in the urine. The dosage is 2.5 to 10 mg 3 times a day. Desglymidodrine increases BP via an increase in peripheral vascular resistance. Although it has no direct effect on the heart, a reflex decrease in heart rate may be seen. In a double-blinded trial of 79 patients with neurogenic OH, midodrine was found to be superior to placebo, both in terms of increasing standing systolic BP as well as reducing lightheadedness (2). In a comparative trial, midodrine was more effective than ephedrine in eight patients with refractory OH attributed to autonomic failure (12). Midodrine therapy is generally well tolerated, with the most common side effects being piloerection, pruritus, and tingling of the scalp (2). Of greater concern however, is that supine hypertension (BP >180/110 mm Hg) has been reported in up to 25% of patients taking midodrine 3 times daily with an incidence as frequent as 75% in one study (1-3,12). Patients are advised to take their evening dose at least 4 hours before bedtime to minimize nocturnal supine hypertension (3,13). Furthermore, it has been suggested that supine hypertension can be attenuated by having the patient sleep with the head of the bed elevated to a 30° incline (12,13).

Although the possible etiologies of hypertension after the induction of general anesthesia are multiple, it was believed that the most likely cause in this particular patient was preexisting supine hypertension secondary to autonomic failure, midodrine effect, or both.

Any number of drugs may have been administered to decrease this patient's BP. We chose instead to control the airway and then simulate an upright position by placing the OR table in reverse Trendelenburg

because it is a known effective therapy for either exaggerated supine hypertension or midodrine effect, our working diagnoses in this patient. Second, it has the advantage of being quickly effective and, unlike most pharmacotherapy, readily reversible. By balancing bed position and anesthetic depth, the remainder of the case was uneventful.

In summary, diabetic patients with OH secondary to autonomic insufficiency may exhibit hypertension when supine. Midodrine, an α_1 -agonist used in the treatment of OH, may induce or exacerbate supine hypertension. Patients presenting for general anesthesia may be best advised to omit their midodrine on the day of surgery, particularly if a prolonged period of postoperative bed rest is anticipated. Clinicians should be aware of the potential for severe hypertension in patients taking midodrine, especially in a perioperative setting where other sympathomimetics may be administered.

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