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Treating Intraoperative Hypotension in a Patient on Long-term Tricyclic Antidepressants: A Case of Aborted Aortic Surgery

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HYPOTENSION may occur during treatment with tricyclic antidepressants (TCA).¹ Presently, recommendations conflict as to which sympathomimetic drugs should be administered to hypotensive patients receiving TCA therapy. Three standard anesthesiology textbooks suggest that to manage hypotension, administering sympathomimetics

that act indirectly, such as ephedrine, will exaggerate the pressor response¹⁻³ and instead recommend using a reduced phenylephrine dosage.^{1,3} Conversely, another standard reference⁴ warns of exaggerated blood pressure increases with direct-acting sympathomimetics, and the authors suggest avoiding them. None of these references differentiate between the management of hypotension in patients receiving acute TCA therapy and those receiving long-term therapy.

We present a patient who had received TCA therapy for 6 years and who experienced hypotension resistant to phenylephrine, ephedrine, and dopamine treatment after induction of general anesthesia; only a large dosage of potent direct-acting sympathomimetic norepinephrine was effective in increasing this patient's blood pressure.

Case Report

A 68-yr-old man (height, 167 cm; weight, 81 kg) was scheduled for repair of a thoracic aortic pseudoaneurysm. His medical history

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CASE REPORTS

was significant for hypertension managed with nifedipine and a 6-year history of depression that had been controlled with nortriptyline, 75 mg daily. The preoperative electrocardiogram (ECG) was unremarkable, and a dobutamine stress test revealed normal left ventricular size and function, no signs of myocardial ischemia, and a left ventricular ejection fraction of 65%. On the morning of surgery, the only medication he took was his usual 75-mg dose of nortriptyline.

The patient's preoperative blood pressure was 190/90 mmHg, and his heart rate was 95 beats/min. He was visibly anxious. Routine monitoring was begun; 1 mg of midazolam was given intravenously, and a thoracic epidural catheter was placed with the patient in the sitting position. During the catheter placement, the patient developed bradycardia (35 beats/min) with wide QRS complexes followed by an ECG pattern indicating left bundle branch block (the heart rate was 60 beats/min) lasting 10 min. This event was accompanied by a short period of hypotension during which his blood pressure was 80/45 mmHg. The blood pressure was elevated to 135/75 mmHg by placing the patient supine and administering 10 mg of ephedrine. A cardiologist was consulted, and he interpreted the ECG pattern as a ventricular escape rhythm probably caused by a vasovagal reaction that was followed by left bundle branch block. We did not administer any medications through the epidural catheter before the hypotensive event nor later during surgery.

Because the ECG changes and hypotension resolved relatively quickly and because the patient remained asymptomatic, the decision was made to proceed. Indwelling arterial and pulmonary artery catheters were placed, and general anesthesia was induced with sodium thiopental, 250 mg, and fentanyl, 250 mg. The blood pressure was 135/75 mmHg, and the heart rate was 85 beats/min. The endotracheal intubation was facilitated with pancuronium, and anesthesia was maintained with a mixture of isoflurane and nitrous oxide. Immediately after anesthetic induction, the patient's systolic blood pressure decreased to between 90 and 100 mmHg, and the heart rate decreased to between 60 and 70 beats/min. A dopamine infusion was started through the central venous catheter at $5 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ and increased to $10 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$. Ephedrine, phenylephrine, and fluids were given in attempt to elevate the blood pressure above 100/55 mmHg. Hydrocortisone, 100 mg, was administered. Although ephedrine, 50 mg, had been given, the heart rate remained at about 75 beats/min.

Surgery was initiated, and additional ephedrine and phenylephrine were administered to keep the systolic blood pressure above 100 mmHg. Ninety minutes after the start of surgery and after administering 6 l of crystalloid and colloid solutions and numerous intravenous boluses of phenylephrine and ephedrine, we increased the dopamine infusion to $20 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$. The cardiac output was 8.2 l/min; systemic vascular resistance was $575 \text{ dyn} \cdot \text{s} \cdot \text{cm}^{-5}$, and the pulmonary artery pressure was 32/22 mmHg; however, the systolic blood pressure remained between 80 and 90 mmHg. The anesthetic at the time was minimal (isoflurane, 0.2%). Transesophageal echocardiography revealed normal left ventricular function, absence of ventricular wall motion abnormalities, and good volume filling of the left ventricle. Only after an infusion of norepinephrine, $0.2 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$, was initiated did the blood pressure increase to 110/85 mmHg. Because of the need for major vasopressor support before the critical part of the procedure was initiated—cross-clamping of the thoracic aorta—the surgery was aborted.

The patient was transferred to the intensive care unit with dopamine and norepinephrine infusions for hemodynamic support. The patient was weaned from both vasopressors soon after he arrived in

the unit. The anesthesiologist recommended discontinuing nortriptyline therapy, and the patient was rescheduled for surgery in 4 days. Because the patient had developed major depression and panic disorder after an aneurysm surgery (3 years previously), a psychiatrist also was consulted. He recommended continuing the nortriptyline therapy. Four h after receiving nortriptyline, when a nurse attempted to sit the patient up in bed, he collapsed with a blood pressure of 70/45 mmHg and a heart rate of 100 beats/min. The hypotension responded well to administration of fluids, phenylephrine, and placing the patient supine. Serum cortisol levels were normal. Nortriptyline was not given the morning of the subsequent surgery, and the thoracic aortic pseudoaneurysm was repaired without complications. During this surgery, the patient's blood pressure never exceeded 110/65 mmHg, and the heart rate did not exceed 80 beats/min.

Discussion

The side effects of TCA on blood pressure range from postural hypotension¹ to circulatory shock.⁵ Our patient experienced preoperative and postoperative orthostatic hypotension and severe intraoperative hypotension. In the differential diagnosis of the intraoperative hypotension, we considered several mechanisms. An insufficient endogenous steroid response to stress was excluded because the amount of hydrocortisone given during anesthesia should have been sufficient to prevent hypotension and because the subsequently determined serum cortisol levels were normal. Hypovolemia was ruled out. Further, the blood pressure did not increase with continuous intravenous fluid administration. Finally, the patient did not receive any medications through the epidural catheter before or after the event, and he did not take nifedipine on the day of surgery. He had no signs of an allergic drug reaction.

The recommendations for managing TCA-induced hypotension range from using only sympathomimetics that act indirectly⁴ to using only those that act directly.¹⁻³ Surprisingly, the duration of TCA therapy has not been considered in these discussions.¹⁻⁴ Although short-term TCA therapy may increase central and peripheral adrenergic tone, chronic treatment or acute TCA overdose may have the opposite effect on noradrenergic transmission and responsiveness.⁵ In addition, whereas short-term TCA therapy increases pressor responsiveness to direct-acting sympathomimetics,^{6,7} long-term treatment does not because compensatory mechanisms at the sympathetic nerve terminal may allow the initial hyperresponse to revert to normal.⁸ Teba *et al.*⁵ successfully used norepinephrine to manage circulatory shock caused by TCA overdose, whereas dopamine was ineffective. This situation is somewhat similar to ours.

Tricyclic antidepressants block norepinephrine reuptake at presynaptic catecholaminergic terminals and thus expose adrenergic receptors to high levels of nor-

epinephrine. As a result, adaptive down regulation of receptors may occur.⁹ In response to chronic treatment, receptor density and functional activity may be decreased.⁹ Szabo and Schultheiss¹⁰ determined that the relationship between sympathetic nerve activity and blood pressure was altered by desipramine in a manner indicating central inhibition of sympathetic activity. These physiologic changes may decrease responsiveness to catecholamines. We believe that this decreased response to catecholamines occurred in our patient. Even during the subsequent surgery, the hemodynamics in our patient were attenuated. We postulate that this attenuation may have happened because the period necessary to recover depressed adrenergic receptor function was longer than that required to eliminate the drug from the body. At the same time, discontinuing nortriptyline, even for only 24 h before surgery, may be beneficial because the plasma TCA concentration (achieved by a bolus injection followed by infusion) has a dose-dependent inhibitory effect on sympathetic nerve activity.¹⁰

Boakes *et al.*⁶ and Svedmyr⁷ studied the effects of direct-acting sympathomimetics and found an exaggerated blood pressure response that ranged from two to three times greater for phenylephrine, four to eight times greater for norepinephrine, and two to four times greater for epinephrine. Importantly, all these effects occurred after 4-7 days of TCA treatment, a situation which differs from that of our patient. We could not identify a study that tested the blood pressure response to sympathomimetics that act indirectly, but Svedmyr⁷ suggested that TCAs antagonize the effects of indirect sympathomimetics, which appears to be true in our patient, because administration of large dosages of ephedrine to our patient affected neither blood pressure nor heart rate.

We conclude that the less potent sympathomimetics

may not effectively manage hypotension in patients receiving long-term TCA therapy because in these patients, the adrenergic receptors are either desensitized or catecholamine stores are depleted. In these patients, potent, direct-acting sympathomimetics may be the only effective management for hypotension.

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