Labetalol Overdose Successfully Treated With Amrinone and Alpha-Adrenergic Receptor Agonists*

Marin H. Kollef, M.D., F.C.C.P.

Circulatory collapse and obtundation occurred in a 37-year-old woman following an iatrogenic overdose of labetalol. Conventional therapy with glucagon and alpha-adrenergic receptor-stimulating agents was ineffective in raising the patient's cardiac output or improving her mental status despite increasing the arterial pressure. The administration of amrinone was temporally associated with significant increases in the cardiac output accompanied by improved mental status. This case suggests that amrinone may be effective adjunctive therapy for beta-adrenergic receptor blocker overdoses by reversing their negative inotropic effects.

(Chest 1994; 105: 626-27)

We present a patient who developed circulatory collapse and obtundation following the administration of labetalol. The addition of amrinone to more conventional therapies was associated with significant improvement in the patient's cardiac performance and was accompanied by improvement in her mental status.

CASE REPORT

A 37-year-old black woman presented to the emergency room with a 3-day history of dyspnea on exertion. Her past medical history was remarkable for long-standing hypertension that had necessitated two previous hospitalizations for hypertensive crises. Her prescribed medications included furosemide, clonidine, labetalol (400 mg twice daily), and nifedipine. The past medical history was notable for a cerebral aneurysm that had been surgically clipped 8 years earlier. The patient's medical records and reports from her family members suggested non-compliance with her antihypertensive regimen.

In the emergency room, the systolic blood pressure was 300 mm Hg with a diastolic pressure of 180 mm Hg. The patient was urgently transferred to the intensive care unit, where a nitroprusside infusion was begun and a radial artery catheter was placed for blood pressure monitoring. A chest radiograph demonstrated marked cardiomegaly. The electrocardiogram showed left ventricular hypertrophy with a sinus rhythm at 111 beats per minute. The blood pressure was brought down to 210/125 mm Hg with the intravenous nitroprusside infusion. An echocardiogram demonstrated marked left ventricular hypertrophy with some decrease in left ventricular function.

The day following hospital admission labetalol, 900 mg, was given by mouth. Over the next 2 h the blood pressure and heart rate progressively decreased despite discontinuation of the nitroprusside infusion. This was associated with progressive deterioration in the patient's mental status followed by a brief tonic-clonic seizure requiring tracheal intubation for airway protection. The blood pressure reached a nadir of 97/62 mm Hg, with the lowest heart rate being 56 beats per minute. Repeated intravenous boluses of normal saline solution were administered along with infusions of dopamine, phenylephrine, and glucagon. Ten hours following the administration of labetalol the blood pressure was 161/105 mm Hg, with a heart rate of 61 beats per minute associated with continued obtundation. A pulmonary artery catheter was inserted at this time.

The initial pulmonary artery catheter readings suggested depression of left ventricular function as manifested by a low cardiac index and elevated pulmonary capillary wedge pressure (Table 1). An infusion of amrinone was begun, which was associated with dose-related increments in the cardiac index corresponding with decreases in the pulmonary capillary wedge pressure despite the continued administration of intravenous fluids. These hemodynamic changes were temporally associated with significant improvements in the patient's mental status, which allowed her to be safely extubated 10 h after the beginning of the amrinone infusion. The remainder of the hospitalization was unremarkable, and the patient was left without new neurologic deficits.

**DISCUSSION**

Labetalol is a lipid soluble drug with combined alpha- and beta-adrenergic receptor blocking properties, which is used for the oral and intravenous treatment of hypertension.1 It has an elimination half-life of approximately 6 h, and the ratio of beta to alpha antagonism is 3:1 after oral administration and 6:9:1 after intravenous administration.2 Documented overdoses with labetalol appear to be uncommon.3 A recent study using transesophageal echocardiography in patients with postoperative hypertension suggests that the antihypertensive effects of labetalol are primarily due to its negative inotropic properties.4 In that study, decreases in blood pressure were associated with significant decreases in heart rate, cardiac index, and mixed venous oxygen saturation and a significant increase in the end-diastolic area of the left ventricle.

The hemodynamic derangements that occurred in this patient were thought to result from the iatrogenic overdose of labetalol. The temporal association between the administration of labetalol and the hypotension suggests a causal relationship. The presence of marked left ventricular hypertrophy may have predisposed to the development of toxicity from the negative inotropic effects of labetalol. The observed hemody-

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</table>

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Table 1—Hemodynamic Measurements After Administration of Amrinone*

*SVR = systemic vascular resistance; FCWP = pulmonary capillary wedge pressure.
†Four hours after discontinuation of amrinone infusion.

Successfully Treated Labetalol Overdose (Marin H. Kollef)
namic response (Table 1) in this case suggests that both the beta- and alpha-adrenergic receptor blocking properties of labetalol are important in mediating its hemodynamic effects following an overdose. Our patient's hypotension responded to the administration of alpha-adrenergic receptor agonists and glucagon. Improvement in cardiac function and mental status was temporally associated with the administration of amrinone, although the dose of phenylephrine was also decreased during this time period.

Current recommendations for the treatment of beta-adrenergic receptor blocker overdoses associated with hemodynamic instability include the administration of glucagon, epinephrine, atropine, and dopamine; external or transvenous cardiac pacing; and the use of an intra-aortic balloon pump in patients refractory to medical therapy.2,3 Glucagon has been advocated by some authors as being the treatment of choice for beta-adrenergic receptor blocker toxicity,2 due to its ability to activate the adenyl cyclase system independently of the beta-adrenergic receptor.3 The enthusiasm for glucagon has been tempered because of its toxicity (emesis, hyperglycemia, hypocalcemia), lack of availability, and cost, as well as the potential toxicity resulting from its diluent, which contains phenol.3,4 Unlike other beta-adrenergic receptor blockers, the alpha-adrenergic receptor blocking properties of labetalol add to its complexity in terms of the hemodynamic effects produced by this drug.

Pulmonary artery catheterization provided important management data in our patient, which resulted in the administration of amrinone. Improved cardiac performance temporally associated with an improved mental status following the administration of amrinone suggests a beneficial effect from its use. To our knowledge this is the first documented case describing the use of amrinone for the treatment of beta-adrenergic receptor blocker toxicity. Amrinone is a positive inotropic agent with intrinsic vasodilator activity, which, like glucagon, can increase intracellular cyclic adenosine monophosphate (c-AMP) independent of the beta-adrenergic receptor. Amrinone is thought to directly inhibit c-AMP phosphodiesterase activity, although other actions may coexist.5 In a recent animal study,6 amrinone was shown to be equivalent to glucagon in reversing depressed myocardial function produced by propranolol, although it appeared to have less chronotropic activity.

In summary, this case illustrates the potential complexity of the resultant hemodynamic responses produced by labetalol toxicity. Our experience suggests that the administration of amrinone, guided by appropriate hemodynamic data, may be an effective therapeutic adjunct for the treatment of beta-adrenergic receptor blocker toxicity due to labetalol.

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REFERENCES
8 Molenson HC, Caracceo TR, Laundano J. Glucagon for propranolol overdose. JAMA 1986; 255:2025-26

Bilateral Pneumothorax After Percutaneous Transthoracic Needle Biopsy*

Evidence for Incomplete Pleural Fusion

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Although the pleural cavities are anatomically separate in humans, we describe bilateral pneumothoraces that occurred after percutaneous needle biopsy of the lung. In some individuals, there may be communication between the pleural spaces; it is important for those performing interventional procedures to be aware of this uncommon anatomic variant.

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CT = computed tomography

The pleural cavities in humans are usually anatomically separate.1 Bilateral spontaneous synchronous pneumothoraces have been described in association with underlying pulmonary conditions such as bullous emphysema, cystic fibrosis, eosinophilic granuloma, Marfan's syndrome, endometriosis, and Pneumocystis carinii pneumonia, as well as situations in which both pleural cavities were violated by trauma or a single surgical or interventional procedure.2 Recently, communication between the pleural spaces was described in patients after sternotomy.3 We report bilateral pneumothoraces after percutaneous lung biopsy in a patient without any of these predisposing factors. To our knowledge, this has not been previously described.