Nifedipine: Use of an Oral Antihypertensive Agent in the Emergency Department Setting

Meyer P. Schwartz, MD, and A. Thomas Taylor, PharmD

Augusta and Athens, Georgia

Hypertensive emergencies and urgencies may pose grave risks to the patients. The causes of such episodes may vary, and therefore warrant potentially different therapies. With the introduction of new pharmacologic agents, the most appropriate drug to use in an emergency situation becomes the subject of debate. At the present time, nifedipine, a calcium channel blocker, appears to be the "standard of care" for acute hypertensive episodes. Nifedipine administered orally, sublingually, or rectally is gradually replacing clonidine, diazoxide, and hydralazine in a variety of clinical settings.

Case Report

D.H., a 44-year-old black woman, called emergency medical services when she began experiencing chest pain. The patient was a known hypertensive receiving oral nifedipine 10 mg three times daily. On initial evaluation by the paramedic team answering her call, the patient's blood pressure was 220/150 mm Hg, and her pulse was 92 beats per minute. Six minutes later, physician authorization was given to administer sublingual nifedipine 10 mg. Nine minutes after the nifedipine was given, her blood pressure was 200/120 mm Hg and her pulse was 80 beats per minute. After an additional 5 minutes, her blood pressure had dropped to 188/108 mm Hg, but her pulse remained at 80. Her chest pain continued.

On arrival at the emergency department, the patient's blood pressure was 159/111 mm Hg and her pulse was 64 (19 minutes after nifedipine). Thirty minutes after arrival in the emergency department, a sublingual nitroglycerine capsule was administered. The patient continued to suffer chest pain, and an additional sublingual nitroglycerine capsule was given 5 minutes later. Her chest pain continued. Five minutes later she was given intravenous morphine 4 mg, which provided relief of her symptoms. Her vital signs were taken again 1 hour and 16 minutes later; her blood pressure was 150/105 mm Hg, and her pulse was 62 beats per minute. The patient was admitted, and experienced an uneventful course with no evidence of myocardial infarction. She was sent home 3 days later. Her blood pressure at the time of discharge was 140/90 mm Hg. She was given prescriptions for captopril 6.25 mg twice daily and nifedipine 20 mg three times per day.

Comment

D.H.'s care demonstrates the confusion that may be caused by the ease of nifedipine administration. This patient complained of chest pain, which was eventually relieved by nitroglycerine and morphine. Both of these medicines reduce cardiac preload and may provide relief of chest pain as well as lower blood pressure.

Hypertension itself may cause angina. The acute rise in blood pressure increases afterload, which impairs left ventricular function. This impairment, in turn, increases myocardial oxygen demand and may decrease coronary blood flow and myocardial perfusion, leading to angina. This has led to the use of oral antihypertensive agents in the emergency department for the treatment of hypertensive emergencies, including those associated with myocardial infarction or angina.

Hypertensive emergencies are not defined by specific blood pressure values, but rather by end-organ damage reflected by hypertensive encephalopathy, renal compromise, or acute left ventricular dysfunction. Sodium nitroprusside is the most potent and most predictably effective of all antihypertensive agents used in the emergency department setting; it is the reference standard in treating...
hypertensive crisis. Its effects are virtually instantaneous, providing preload and afterload reduction according to dosage titration. It does not cross the blood-brain barrier. However, dilation of vessels is nonselective, affecting all systemic vascular beds. This may create a myocardial steal in patients with fixed coronary artery lesions. Nitroprusside has been shown to increase intracranial pressure twofold, making it undesirable in hypertensive encephalopathy or acute head trauma. It also requires that blood pressure be continuously monitored and has been associated with thiocyanate poisoning.

Nitroglycerine may be administered sublingually, or infused intravenously for a more rapid onset. Sustained effects may be carefully titrated intravenously and used for prolonged periods in patients with renal failure. In low doses it reduces preload, but as doses increase, afterload is also reduced. Another advantage includes coronary vasodilation.

Diazoxide resembles the thiazide diuretics without diuretic effect. It is a potent arteriolar smooth muscle relaxant. In large boluses, precipitous uncontrolled reduction in blood pressure may result within 3 to 5 minutes, which is sustained for as long as 24 hours. This hypotension may be associated with tachycardia and increased cardiac work as well as angina, myocardial infarction, and stroke. Hyperglycemia, potentiation of warfarin effect, hyperuricemia, and fluid retention may also result.

The injectable agents have important side effects and require intensive monitoring. This has led to a search for oral medications such as the calcium channel blocker nifedipine.

None of the currently available calcium channel blockers has been approved by the US Food and Drug Administration for the treatment of hypertensive emergencies or urgencies. Nifedipine, the most vasoactive, inhibits the penetration of extracellular calcium through cell membranes and the influx of calcium ions from the sarcoplasmic reticulum into the cell plasma where adenine triphosphatase is located. This uncouples excitation-contraction, reduces the contractile activity of the heart, and vasodilates coronary and systemic vessels.

Nifedipine was first used in hypertensive emergencies in the 1970s in Japan, because medications such as diazoxide and sodium nitroprusside were unavailable. Original studies showed that nifedipine (1) decreased left ventricular systolic and diastolic pressure; (2) decreased mean arterial pressure; (3) decreased total peripheral and coronary vascular resistance; (4) increased coronary blood flow; (5) increased cardiac index; (6) increased (reflex) heart rate; and (7) elevated plasma renin activity. The earliest double-blind studies conducted in the early 1980s showed that nifedipine safely reduced blood pressure.

Nifedipine is usually given sublingually; however, it may be given orally. When given sublingually, the capsule is usually pierced and the contents expressed into the buccal cavity. Logic would imply that this route is quicker at lowering blood pressure, but experiments do not support this belief. Following sublingual administration, maximal antihypertensive effects occur within 30 to 60 minutes. These effects are usually achieved earlier in oral routes. Studies have implied that absorption across the buccal mucosa is poor, and the effects occur only after active absorption by the stomach. Even faster drop in blood pressure may be achieved by a bite-and-swallow technique.

Nifedipine administration, however, may not be benign. Commonly reported side effects of nifedipine have included facial flushing, burning paresthesias, headaches, and ventricular premature beats. Much more severe complications have also occurred. Two cases of severe hypotension resulting in cerebral ischemia have been reported. The hypotensive effect of nifedipine is inversely proportional to the patient’s pretreatment level of hypertension; the drug exerts a greater effect in severe hypertension than in mild hypertension. Usually the patient’s blood pressure lowers to baseline. Nifedipine has been linked to complete heart block, with ventricular standstill occurring in one patient. More recently, a report of three myocardial ischemic events secondary to nifedipine administration were acknowledged. In addition, nifedipine may increase serum quinidine and digoxin concentrations. One unsuccessful suicide attempt with nifedipine 900 mg has been reported. In cases of overdose, hypotension and bradycardia were the predominant hemodynamic effects of the drug. Although nifedipine has few specific contraindications, it may not be the first-line choice. When time is of the essence, as is the case in true hypertensive emergencies, nifedipine may act too slowly. These emergencies include intracranial hemorrhage, hypertensive encephalopathy, dissecting aortic aneurysm, eclampsia, pheochromocytoma, and acute catecholamine states such as occur in “crack” cocaine overdose. Nitroprusside is still the recommended first choice for each, except for eclampsia and acute catecholamine states. These conditions can best be managed by hydralazine and labetalol, respectively.

In conditions of hypertensive urgencies, the case of administration and observation of nifedipine, coupled with low side effect and contraindication profiles, make it an outstanding emergency department medication. Nifedipine can then be used when patients are begun on an
oral antihypertensive regimen outside of the emergency department.

To our knowledge, there has been only one study that examined cost considerations in this area, and that one compared only nifedipine and nitroprusside.24 Even when drug preparation and administration costs were excluded, nitroprusside was significantly more expensive because of its requirement for hospitalization and intensive monitoring.

In conclusion, it is our belief that not only is the choice of antihypertensive medication selected in the acute care setting critical, but its placement in therapy should be appropriate for the patient's overall management.

References