Considerations in Drug Therapy

Effective Treatment of Severe Hypertension

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The effective treatment of hypertension is associated with decreased mortality and morbidity from many diseases including stroke, congestive heart failure, and renal failure.[1] In the vast majority of cases, the treatment of hypertension is most effectively accomplished in the outpatient setting. The main goal of treating hypertension is to lower the patient's blood pressure to the target level described by the Sixth Report of the Joint National Committee on the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC VI).[2] In most patients, this target is 140/90 mm Hg but, in selected other populations, the goal may be as low as 125/75 mm Hg. For most patients, this will require one or more antihypertensive medications; selection of medications that a patient can tolerate for years is key in maintaining patient compliance.

In a small number of circumstances, however, rapid and predictable lowering of blood pressure is needed. This must be accomplished in the hospital, most effectively with IV medications (Table), with close hemodynamic monitoring, and intense nursing care. These hypertensive emergencies include situations where there is evidence of ongoing target organ damage, such as intracerebral hemorrhage, acute aortic dissection, eclampsia, and pheochromocytoma crisis.[3] Hypertension after coronary artery bypass surgery or during acute myocardial infarction also constitutes a hypertensive emergency, as do many other situations in which target organ damage is evident.

Autoregulatory mechanisms provide some organ protection during extreme blood pressure elevation and, for this reason, it is important to decrease blood pressure by no more than 25% or to a level of 160/110 mm Hg, over a period of minutes to hours, depending on the specific clinical situation. If blood pressure is decreased more aggressively, target organ ischemia can result. Subsequent sodium and fluid retention may necessitate diuretic use later in the treatment of the hypertensive emergency to maintain blood pressure control.[4]

There are many other situations that constitute hypertensive urgencies that, while concerning, do not require immediate intervention as in the case of hypertensive emergencies. These situations require prompt lowering of blood pressure, usually within 24 hours with the use of oral agents. Some examples of hypertensive urgencies are accelerated hypertension (a blood pressure of 250/150 mm Hg, for example, in an asymptomatic person with no evidence of target organ damage can usually be treated as an urgency rather than an emergency), rebound hypertension after drug withdrawal, postoperative hypertension, and acute glomerulonephritis.[5]

DRUG THERAPY FOR HYPERTENSIVE EMERGENCIES

Once the diagnosis of hypertensive emergency has been made, the most commonly used IV drug for treatment is sodium nitroprusside. This drug has a nearly immediate onset of action and a short half life. It acts by causing relaxation of vascular smooth muscle, resulting in dilatation of peripheral arteries and veins. For these reasons, the patient's blood pressure can be precisely titrated to the desired level.[6] Administration requires an IV infusion pump and an arterial line for continuous measurement of blood pressure. The usual dose is 0.25–10 μg per kg per minute, with the maximal dose to be used for only very short periods of time (<10 minutes). At rates of infusion >2 μg per kg per minute, cyanide is generated faster than most patients can eliminate it. This production is initially buffered by serum methemoglobin which is normally present in the body. However, the system can be exhausted by the

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TABLE. IV MEDICATIONS FOR HYPERTENSIVE EMERGENCIES

Drug	Usual Dosage	Advantages	Concerns
Sodium Nitroprusside	• 0.25–10 ug/kg/min Maximal dose for up to 10 minutes	• Nearly immediate onset of action • Short half life • Enables precise titration to desired blood pressure level	•Cyanide toxicity •Thiocyanate Toxicity •Requires IV infusion pump and arterial line •Can cause hypotension
Labetalol	• 20 mg IV slow injection, with subsequent increasing doses of 40 mg and 80 mg to a total of 300 mg • Alternatively, 2 mg/min continuous infusion	• Potential for easy conversion to oral form • No concern for cyanide or thiocyanate monitoring or toxicity • Easy to administer	•Can rarely cause hypotension or heart block •Blood pressure control cannot be precisely titrated
Fenoldopam	• 0.03–1.6 ug/kg/min	• No concern for cyanide or thiocyanate monitoring or toxicity • Can be used in patients with renal insufficiency or potential of renal dysfunction (immunosuppressed, diabetics, or after iodinated contrast agents)	•Requires IV infusion and may require arterial line •Expensive

cyanide production from about 500 μg per kg of nitroprusside, the amount administered in 50 minutes at a rate of 10 μg per kg per minute.[7] For this reason, therapy with nitroprusside at the maximum dose for >10 minutes is not recommended. Therapy with nitroprusside carries the risk of cyanide toxicity which can result in venous hyperoxemia, acidosis, mental status changes, and death. At some centers, sodium nitroprusside is administered concomitantly with sodium thiosulfate, minimizing the possibility of cyanide toxicity by providing sufficient substrate to aid the conversion of cyanide to thiocyanate. Thiocyanate is excreted by the kidneys, is mildly neurotoxic, and can cause confusion at high levels. Thiocyanate levels of >60 mg/L are mildly neurotoxic, and can become life threatening at levels of about 200 mg/L. Thiocyanate levels can be determined in most hospital laboratories within a reasonable time period and should be monitored in patients on nitroprusside therapy, particularly for extended periods of time. Most importantly, therapy with nitroprusside should be as brief as possible, with oral antihypertensive agents started as soon as is practical–even shortly after the start of nitroprusside therapy.

In patients with renal insufficiency, IV fenoldopam mesylate can provide an alternative to nitroprusside, but without the threat of cyanide and thiocyanate toxicity. This drug, given at 0.03–1.6 μg/kg/min, also permits tight titration to the desired blood pressure level. Studies have been done demonstrating the safety of administration without invasive monitoring, but the clinician may choose to use invasive monitoring since fenoldopam has a similar ability to effect[8] rapid changes in blood pressure. Although much more expensive than nitroprusside, fenoldopam provides a good option in patients with renal dysfunction, or even in patients with threatened renal dysfunction, such as diabetic patients who have recently received an iodinated contrast agent. Transplant patients receiving nephrotoxic immunosuppression, such as cyclosporine or tacrolimus, may also be candidates for therapy with fenoldopam.

IV labetalol provides another effective approach in treating the patient with a hypertensive emergency. This drug is a selective α_1-adrenergic blocking agent, as well as a nonselective β-blocker.[9] Labetalol is administered to the supine patient by slow IV injection, usually of 20 mg, over 2 minutes with increasing does of 40 mg and 80 mg at 10 minute intervals until the blood pressure goal has been reached, or until a total of 300 mg of labetalol has been administered. Alternatively, a continuous IV infusion of labetalol at 2 mg/min can be started, with subsequent adjustment. As with all IV antihypertensive agents, close patient monitoring is necessary, as hypotension and heart

block can occur. As with nitroprusside, oral antihypertensive therapy with labetalol or with other agents should be started as soon as possible. While blood pressure management with IV labetalol cannot be conducted as precisely as with nitroprusside, such precision is not always necessary and may be outweighed by its several potential advantages: 1) concern and monitoring for cyanide and thiocyanate toxicity are not needed; 2) an oral form is available for easy conversion and long term use; and importantly; 3) the drug comes in a vial that can be stored at room temperature and is available for immediate administration. Unlike nitroprusside, for which administration can be delayed by the acts of finding an infusion pump, preparation and delivery of the drug from pharmacy, and placement of an arterial monitoring line, therapy with IV labetalol can be initiated immediately following the diagnosis of a hypertensive emergency.

Another antihypertensive agent that can be used during hypertensive emergencies is enalaprilat. This IV ACE inhibitor causes a rapid decrease in blood pressure and may be of particular use in patients with stroke, as it may have a beneficial effect on cerebral vascular autoregulation during hypertension.[10] IV β-blockade can be accomplished with metoprolol or esmolol and injectable hydralazine, diltiazem, and verapamil are also useful. In the very rare pheochromocytoma crisis, phentolamine is the drug of choice.

One of the most important goals in treating the patient with a hypertensive emergency is prompt institution of oral antihypertensive therapy, which should normally include a diuretic. This action will minimize the chance of IV drug related complications, minimize the need for invasive monitoring, and minimize the patient's hospital stay–particularly in the costly ICU. During this time, the patient should be educated regarding the importance of proper blood pressure control and, toward discharge, significant effort should be made to streamline the patient's antihypertensive regimen in order to enhance outpatient compliance.

HYPERTENSIVE URGENCIES

Hypertensive urgencies can usually be treated in the outpatient setting. Numerous drugs, including captopril, clonidine, labetalol, prazosin, and other agents, can be given orally and can cause reduction of blood pressure in a matter of hours. The patient should generally be seen at follow up within 24–48 hours from initiation of therapy. Subsequent treatment should be tailored to the long term treatment of the patient's hypertension, with particular attention given to the selection of an antihypertensive regimen that will be well tolerated by the patient, affordable, and effective in reaching the target goals as outlined in JNC VI.

SHORT ACTING NIFEDIPINE

The widespread practice of administering immediate release nifedipine, either orally or sublingually, during hypertensive urgencies and emergencies has resulted in numerous reports of adverse events. These are certainly related to the precipitous drop in blood pressure that this practice causes. These reports have prompted the FDA to recommend against the use of immediate acting nifedipine in the treatment of hypertensive urgencies and emergencies.[11] Unfortunately, this practice continues in many settings, as the resulting sharp drop in blood pressure accomplishes a perceived short term goal of "getting the numbers down quickly." Health care providers should discourage this use of nifedipine whenever possible as the risks far outweigh the benefit of this very temporary drop in blood pressure. If the situation is truly a hypertensive urgency or emergency, other agents, as described above, should be used.

CONCLUSION

Patients with severe hypertension need to be treated in a variety of ways depending upon their presentation. Asymptomatic patients with no evidence of ongoing target organ damage can simply be started on long term antihypertensive therapy and, if indicated, be evaluated for a secondary cause of hypertension. Patients with hypertensive emergencies require prompt therapy for their elevated blood pressure in a hospital setting. Patients with hypertensive urgencies can usually be treated as outpatients, providing rapid follow up is available. The long term goal of selecting a tolerable antihypertensive regimen for the patient's chronic use must be continuously considered and assessment of other cardiovascular risk factors, such as smoking, diabetes, and lipids, should be made at the same time as the institution of antihypertensive therapy.

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es. Finally, the Working Group will try to contribute to European nursing research by setting up an international research project in the field of cardiac nursing.

In conclusion, the Working Group on Cardiovascular Nursing is a dynamic group of nurses within the European Society of Cardiology, trying to improve the care for cardiovascular patients by facilitating international education, research, and networking. We would like to invite European and American nurses to submit abstracts for the next conference, which will be held from August 26–30, 2000, in Amsterdam, The Netherlands. For more information on the Working Group on Cardiovascular Nursing, submission of abstracts for the ESC conference in Amsterdam, or applications for Nurse Fellowship of the European Society of Cardiology, we gladly refer to the website of the ESC (http://www.escardio.org/).

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of a goal blood pressure may be the most significant move toward improving long term outcomes for the 60 million Americans who suffer hypertension. The challenge is before us.

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