Antihypertensive Bridge Therapy by Continuous Drug Infusion With an Elastomeric Pump in Device-Resistant Hypertension

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To the Editor:

Over recent years, invasive hypertension treatments have led to a new clinical condition, called device-resistant hypertension (DRH). DRH is defined as blood pressure (BP) >140/90 mm Hg, with at least 3 antihypertensives at maximal doses, including a diuretic, without BP decrease after the invasive treatments. These patients are not infrequent and are obliged to visit several hypertension units for managing their BP. We have observed a significant BP decrease only by using intravenous drugs recommended for emergencies. Thus, we refined a protocol to perform a chronic intravenous antihypertensive infusion in patients with DRH via an elastomeric pump and a peripherally inserted central catheter (PICC).

After exclusion of several intravenous drugs for contraindications, urapidil was selected as the drug of choice. Here, we present the case of the first treated patient with DRH.

The Case

The patient is a 45-year-old male. He was hypertensive and undergoing treatment since 2009. He was overweight (body mass index, 29.6), a smoker and dyslipidaemic. In 2012, he underwent percutaneous transluminal coronary angioplasty plus stenting for unstable angina and a formerly inserted central catheter (PICC).

Among other available intravenous hypertensive drugs, nitroglycerin is available as a 50 mg/10 mL solution for intravenous use. In our experience, it generally acts at a dose of 8 mg/h at a concentration of >300 mL, and it is compatible with high concentrations in solution. Urapidil has several of these characteristics. It has complex pharmacodynamics: α1-blocker and weak β1-blocker, it interacts with the serotonin receptor and, it is a central depressor of sympathetic tone. Urapidil shows few contraindications and can be stored at doses sufficient for at least 5 days in an elastomeric pump, that generally cannot exceed a volume of >300 mL, and it is compatible with high concentrations in solution.

It is available as a 50 mg/10 mL solution for intravenous use. In our experience, it generally acts at a dose of 8 mg/h at a concentration of 4 mg/mL without interfering with other oral antihypertensives. Among other available intravenous hypertensive drugs, nitroglycerin...
and sodium nitroprusside are not recommended because of serious side effects: risk of thiocyanate intoxication for nitroprusside; headache, methemoglobinemia for nitroglycerin, that is also characterized by fast tachyphylaxis.3

Esmolol is a short-acting β1-blocker, available as 100 mg/10 mL, with an acceptable chemical stability of 7 days in solution. Its dosing is body weight dependent, thus a 576 mL of solution/day is required to obtain a concentration of at least 50 μg/kg per hour, that makes it unsuitable for elastomeric pumps.3 Labetalol, a combined α1- and unselective β-blocker used in hypertensive emergencies, is available as 100 mg in 20 mL vials. The maximal drug concentration in solution is 1 mg/mL and an efficacious effect can be obtained at doses of >50 mg/h, unsuitable for elastomeric pumps. The angiotensin-converting enzyme inhibitor, enalaprilat, has no indications for continuous infusion. Fenoldopam mesylate is a selective agonist of dopaminergic D1 receptors, located mainly in the renal and in the splanchnic arteries, it has been successfully used in elastomeric pumps at the doses of 0.1 μg/kg per minute in patients undergoing nephron sparing surgery.5 Fenoldopam has a good tolerability, it can generally be combined with several oral antihypertensive drugs, but there are no pharmacological studies that demonstrate its stability for >72 hours. Furthermore, it is an expensive drug. Nicardipine, is chemically stable in solution for 7 days,10 is supplied in 25 mg/25 mL vials and each vial should be diluted in 240 mL of sodium chloride (0.9%) or dextrose 5% to avoid risks of venous thrombosis and phlebitis. The requirement for its high dilution does not allow an infusion of >0.2 mg/h (2 mL/h) in elastomeric pumps.3 Clevidipine butyrate is an ultra short-acting, third-generation calcium channel blocker.11 It is insoluble in water and, thus, formulated as a 20% phospholipid emulsion.

An elastomeric infusion pump with a regulation system is recommended, it allows the preparation of a standard drug solution with the possibility of modifying the infusion speed at each follow-up. PICC in peripheral vein is the most tolerable option for the patient, who hopes to live a normal life. Our patient underwent this therapy for 6 months with a good improvement in quality of life, even if he needs periodical medications and drug renewal.

In conclusion, this approach may represent a bridge therapy for the temporary reduction of BP in patients with symptomatic and severe DRH who are awaiting an alternative therapeutic solution. In the meantime, urapidil elastomeric pump infusion allows an acceptable quality of life outside the hospital.

Disclosures

None.

References

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