RESISTANT HYPOTENSION AFTER THE ADMINISTRATION OF RENIN-ANGIOTENSIN SYSTEM INHIBITORS IN THE PEROPERATIVE PERIOD: CASE REPORT

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ABSTRACT

***Objectives**: A case of severe hypotension in the perioperative period is reported, during general anesthesia, resistant to standard treatment, followed by postoperative hypotension worsening in the three days after surgery. Both conditions were related to the perioperative use of renin-angiotensin system (RAS) inhibitors.*

***Key words**: arterial hypertension, rennin-angiotensin system inhibitors, diuretics, anti-hypertension*

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Introduction

RAS inhibitors are drugs widely used as the treatment of choice for arterial hypertension and cardiac decompensation. Hence, the study of interactions between this class of drug and common anesthetics is very important. When ACE inhibitors or sartans are administered between 8 and 24 hours before general or neuraxial anesthesia, hypotension often occurs during the perioperative period. The hemodynamic effects are more serious the higher the dose of RAS inhibitors. In most cases hypotension appears within 30 minutes of anesthesia and may be resistant to standard treatment such as liquid bolus, ephedrine, or phenylephrine.

Continuing to use RAS inhibitors may be associated with profound and persistent hypotension, above all in patients undergoing cardio-pulmonary bypass surgery. This form of hypotension is similar to distributive shock and is called vasoplegic syndrome, characterized by hypotension, decrease of central venous pressure, reduction of peripheral resistance, and normal cardiac range.

Materials and methods

The male patient was 65 years old, height 175cm, weight 85kg, and was hospitalized for right renal calculi surgery. His history was positive for arterial hypotension, being treated with zofenopril 30mg/day, and the patient was negative for other cardiovascular disease. The preoperative cardiology exam revealed arterial pressure (AP) of 150/95mmHg, so hydrochlorothiazide 12.5mg/day was added to his treatment. An echocardiogram was also performed, which found left ventricular insufficiency. The E/A ratio was inverted as in diastolic decompensation with the ejection fraction apparently preserved. The patient continued the drug treatment throughout the following week and was not suspended on the day of surgery. The preoperative fast began 6 hours before the operation. Outside the operating room the AP was 160/80mmHg, and for that reason furosemide 40mg was administered. In the operating room the patient was connected to standard monitors (temperature, non-invasive AP, 5-lead ECG, end tidal CO2, pulse oximeter, precordial phonendoscope).

The anesthesia consisted of Target Controlled Infusion, with an infusion of propofol 5 γ/ml for induction, and an infusion of ramifentanil 4-5ng/ml and 3 γ/ml propofol for maintenance. Hypotension was observed 45 minutes after induction of the anesthesia, and was initially treated with ephedrine and phenylephrine. The administration of the drugs did not have any effect, so the patient was given vasopressin. First a bolus of 4U, followed by continuous infusion of 0.05 U/min until the end of the operation, which lasted 180 minutes. Pressure at the end of the surgery was 100/60mmHg (Figure 1).

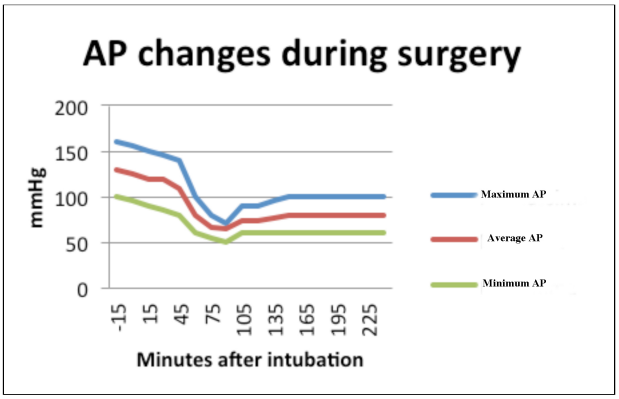

Figure 1: Arterial pressure changes during the surgical operation.

After the operation the patient was kept in the ICU for about 6 hours, and the hemodynamic values were stable during this time (AP 110/70mmHg, SO2 95%). That evening the patient was returned to his ward with continuation of ACE inhibitors and a diuretic. Over the following days the patient experienced dyspnea with pressure values lower than 110/60mmHg (Figure 2).

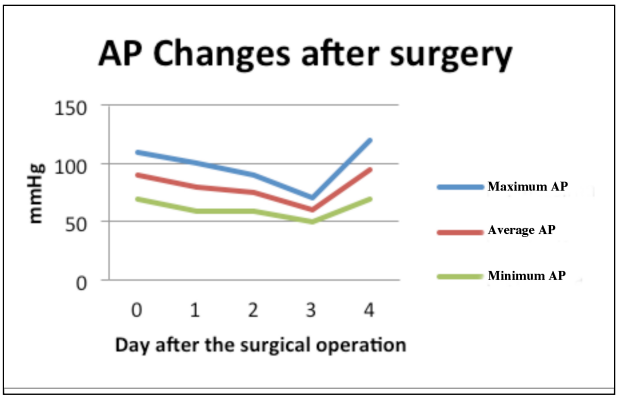

Figure 2: Arterial pressure changes after the surgical operation.

The patient was then transferred to the pulmonology department where he was treated with omeprazole 40mg, zofenopril 30mg, hydrochlorothiazide 12.5mg, furosemide 25mg x 2, levofloxacin 500mg, and enoxaparin sodium 4000UI. During the next 3 days the pressure gradually decreased to 70/50mmHg and cardiac frequency of 110beats/minute on the morning of the third day after surgery. Echocardiography was performed and showed the same inversion of the E/A ratio, with 40% of the walls of the vena cava collapsed. The anti-hypertension treatment was then suspended and an infusion of colloids 500ml and crystalloids 1000ml began, which proved to be appropriate because that evening the AP returned to acceptable values (100/65Hg), and the following morning the values reached 120/70mmHg. So the anti-hypertension treated was resumed and there were no further complications.

Discussion

The anti-hypertension treatment must be considered first. We believe it was a mistake to continue treatment with zofenopril and add hydrochlorothiazide. The ACE inhibitor should have been replaced by an anti-hypertension drug with a different mechanism of action. For example, nifepidine was a valid alternative because it may be used despite surgery and also because it has a brief half-life. The second mistake was certainly the administration of furosemide in a patient who was already unstable because of the RAS inhibitor. Considering the above and the minor side-effects of the vasopressin dose used, the best treatment is prophylaxis[1]. When the correct treatment is not followed and resistant hypertension appears, the best choice is a bolus of vasopressin with continuous infusion throughout the operation. Continuous infusion of vasopressin is an excellent technique because the dose may be increased, decreased or suspended easily and quickly. It also has a brief half-life of 6 minutes[2].

In contrast, terlipressin has a much longer half-life and hence is more difficult to control. Methylene blue has not been studied sufficiently for systemic use yet, and there are more complications compared to vasopressin[3]. The third mistake occurred in the department of pulmonology, where furosemide, zofenopril and hydrochlorothiazide were administered at the same time. Even though the patient's sympathetic system was functional, it wasn't able to balance the precarious hemodynamic state and led to acute cardiac decompensation. Vasopressin wasn't administered because its vessel-

restrictive effect leads to chronic inhibition of the RAS and would have caused a glomerular blockage as well as a decrease in oxygen concentration (in a patient already dyspneic) and hence metabolic acidosis that would not be compensated by respiratory alkalosis in a patient in this respiratory condition. The nitrate could not be used also because its vasodilator effect would have worsened the hypotension.

We chose not to use dobutamine in order to avoid worse tachycardia and thereby risk decompensation. Furosemide is another bastion of cardiac decompensation treatment, which had already been administered to the patient, so we believe the association between ACE inhibitors and the two diuretics at high dosage interfered with proper hemodynamic compensation. We chose euvolemia for reintegration as recommended by the ACP[4], according to the echocardiography that confirmed the decompensation was on the right and due to hypovolemia, which provided the safety to fill the patient without danger of problems. As a consequence, our treatment consisted in increasing blood volume and suspending the ACE inhibitor, which resulted in hemodynamic stabilization of the patient. The patient was no longer in crisis even after RAS inhibitors were reintroduced.

Conclusions

This case indicates the need to suspend RAS inhibitors during the perioperative period. Although hypotension commonly appears within 30 minutes of the induction of anesthesia, in our case hypotension began much later. AP did not return to normal even after continuous infusion of vasopressin, and for a few days there was another crisis of hypotension, which ended only after the ACE inhibitors were suspended and the patient received colloid and cristalloid solutions. The postoperative hypotension occurred probably because the balance between vasopressin and NO leaned toward the latter, and despite the treatment the persistent block of the RAS prevented hemodynamic compensation. The sympathetic system functioned perfectly in the postoperative period and the simple increase in blood volume in association with elimination of the primary block of the RAS allowed the return to normal physiological pressure. Hence, in the perioperative period it is fundamental to study the patient who takes RAS inhibitors regularly. Railton et al. demonstrated that in major surgery the use of RAS inhibitors during the perioperative period increases mortality during the 30 days after surgery because it increases the rate of myocardial infarction, congestive cardiac decompensation, and acute renal insufficiency[5]. Except for patients with left ventricular dysfunction, in our opinion RAS inhibitors must always be suspended before surgery, since morbidity in average risk operations becomes the same as in major surgery. Finally, the interactions between opioid anesthetics (fentanil, ramifentanil) and RAS inhibitors must be investigated since the interaction may provoke a hypotension crisis in the perioperative and postoperative period.

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