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CLINICAL REPORT

Altered responses to vasopressors of a patient medicated with carvedilol, pilsicainide and enalapril

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Abstract A patient scheduled for laparoscopic rectal surgery was medicated with carvedilol, an antagonist of beta 1-, beta 2- and alpha 1-adrenergic receptors, pilsicainide, a class Ic antiarrhythmic drug and enalapril, an angiotensin-converting enzyme inhibitor. Because the patient experienced attacks of atrial fibrillation with rapid ventricular response almost weekly, carvedilol and pilsicainide were continued up to the day of surgery, while enalapril was discontinued for 24 h prior to surgery. During the operation, he showed prolonged hypotension that did not respond to usual doses of vasopressors such as ephedrine, phenylephrine and dopamine but responded to higher doses of norepinephrine. Postoperatively, he was given dopamine but exhibited tachyarrhythmia until the dopamine infusion was discontinued.

Keywords Carvedilol · Enalapril · Pilsicainide · Dopamine · Perioperative administration

Introduction

Preoperative continuation of medication with alpha- and beta-adrenergic blockers has been controversial in the past, although their continuation up to the day of surgery is now almost accepted by anesthesiologists [1–3]. A patient who was given carvedilol and pilsicainide until the day of surgery, and enalapril until 24 h preoperatively, showed hypotension refractory to the usual doses of vasopressors.

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Case report

A 61-year-old man (180 cm, 78 kg) was scheduled for a laparoscopic operation for rectal cancer. He had attacks of paroxysmal atrial fibrillation (Af) and had been medicated with beta-blockers for 2 years. The medications (daily dosage) included carvedilol (20 mg), pilsicainide (150 mg), and enalapril (5 mg). Preoperative evaluations showed sinus bradycardia and normal left ventricular function with left atrial dilatation. He complained of palpitation episodes continuing for one to several hours almost weekly.

The patient had his last dose of enalapril 24 h, and of carvedilol and pilsicainide 90 min, before transfer to the operating theater. On arrival, his blood pressure (BP) was 130/85 with sinus rhythm (58/min). After placement of an epidural catheter at the L1/2 interspace, general anesthesia was induced by propofol and remifentanil, muscle relaxation being obtained using rocuronium. Left radial artery pressure was measured continuously. Anesthesia was maintained by desflurane with small doses of intravenous narcotics (fentanyl, 0.25 mg, and remifentanil, 0.2 mg), supplemented by epidural administration of morphine (3 mg followed by 0–0.14 mg/h), and local anesthetics (lidocaine 80 mg, ropivacaine 8 mg followed by ropivacaine 0–8 mg/h). The concentration of desflurane was adjusted to maintain the bispectral index values between 40 and 50. Rocuronium (160 mg) was given during the operation and sugamadex 200 mg at the end of the operation. The operation lasted 7 h and 48 min.

The first and second hypotensive episodes (66/42 and 68/44 mmHg) occurred after the induction of general anesthesia but before starting the operation, and intravenous administration of ephedrine (8 mg) restored the patient's BP only up to around 85/55 mmHg. At the start of the operation, continuous infusion of remifentanil 0.6 mg/h

was commenced, and the BP fell again. It was restored to 95/62 mmHg only at 15 min after the discontinuation of remifentanil and administrations of atropine (0.5 mg), phenylephrine (0.2 mg), and ephedrine (4 mg). Thereafter, the BP was stable for 150 min in spite of epidural administrations of local anesthetics and morphine. At this point, his systolic BP again went down to <80 mmHg, with neither an allergic reaction, nor a surgical maneuver appearing to be responsible. This hypotension did not respond to atropine (0.5 mg), phenylephrine (0.9 mg), and ephedrine (4 mg). The continuous administration of dopamine (10 μg/kg/min) restored the patient's BP only to 82/42 mmHg; the heart rate was 60–70 beats/min with sinus rhythm and his body temperature was over 35.3 °C. Blood gas analysis revealed no abnormalities including electrolyte levels. We administered norepinephrine (up to 0.3 μg/kg/min) until the end of the operation to maintain the systolic BP over 80 mmHg. The total dose of infusion was 5,550 ml, urine output 1,480 ml, and blood loss 208 ml. All fluid and intravenous drugs were given by peripheral routes.

After the emergence, his systolic BP was restored to over 100 mmHg, and the administration of norepinephrine was discontinued. After extubation, he was transferred to our intensive care unit (ICU) and given a dopamine infusion (1.9 μg/kg/min). Echocardiography at this point showed results similar to preoperative data. However, as the patient's hypotension continued, the dopamine infusion rate was increased gradually to 4.3 μg/kg/min 12 h postoperatively. The urinary output was over 200 ml/h. One hour later (13 h postoperatively), he developed Af with a rapid ventricular response (130–160/min). Verapamil (2.5 mg) was given intravenously to decrease the heart rate to 100–110/min. Oral administrations of verapamil (120 mg/day) and pilsicainide (100 mg/day) were started. Twenty-four hours postoperatively, a norepinephrine infusion was restarted at 0.05–0.08 μg/kg/min and the infusion of dopamine was discontinued. Then his heartbeat returned to a sinus rhythm (100–110 beats/min). His BP and heart rates were stable even after discontinuation of the norepinephrine infusion (29 h postoperatively.) He was discharged from the ICU to a general ward on the second day (40 h postoperatively) with stable cardiovascular conditions.

Discussion

Carvedilol is an antagonist of beta 1- and beta 2-adrenergic receptors with alpha 1 blocking action [4]. It not only decreases the sensitivity to internal and external catecholamines, but also blunts the release of noradrenaline by blocking presynaptic beta 2-adrenergic receptors [5]. Thus, it may exaggerate the hypotensive effects of general or epidural anesthesia and of drugs given concomitantly, and it attenuates the effects of vasopressors.

This drug is metabolized in the liver, the plasma half-life being 7–10 h [6]. The manufacturing company (Daiichi Sankyo Co., Tokyo, Japan) recommends discontinuation of this drug 48 h preoperatively. However, it is a general recommendation to continue the administration of beta-blockers until the day of surgery [1, 3] except when an excessive effect of the drug is suspected or when its use is not indicated. Our patient had sinus bradycardia preoperatively, suggesting overactivity of the drug, but still he complained of occasional attacks of palpitations. The use of such beta-blockers is given a class I recommendation in the case of patients showing arrhythmia with symptoms [3]. Thus, the decision to continue the administration preoperatively may be justified.

Enalapril is an angiotensin-converting enzyme inhibitor (ACEI) known to facilitate hypotension following induction of general anesthesia and is recommended to be discontinued preoperatively [7]. In addition, beta-blockers reduce the renin level, and their concomitant use with an ACEI may induce profound hypotension [8]. Although in our case enalapril was discontinued for longer than 24 h prior to surgery, we cannot exclude the possible participation of this drug, or of pilsicainide [9], in the hypotension of this patient.

Usually, epinephrine [10] and norepinephrine, in high doses, can overcome the action of adrenergic blockers safely. Thus, the dosage of catecholamine administration should be increased as necessary. However, if drugs with multiple actions are used, we should pay attention to other pharmacological actions [11], as well as their side effects. Dopamine has blocking actions on alpha-, beta-, and dopaminergic receptors. In our case, dopamine functioned mainly as a dopaminergic agonist and its diuretic actions seem to have contributed to the patient's hypovolemia and induction of tachyarrhythmia.

We conclude that in a patient taking adrenergic blockers such as carvedilol, the use of norepinephrine or epinephrine at high doses can be effective, and the surgical team should be aware of the potential for adverse consequences when using drugs with multiple actions.

Conflict of interest None.

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