

POSTOPERATIVE HYPOTENSION ASSOCIATED WITH AMLODIPINE

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Abstract

Continuation of anti-hypertensive drugs peri-operatively and their influence on intra-operative hemodynamic is a major concern among anesthesiologists. Amlodipine is often favored clinically over other calcium channel blockers for its vascular selectivity and relative lack of negative inotropy, once daily dosing and prolonged duration of effect. A post renal transplant patient who was on amlodipine for control of blood pressure was scheduled for laparoscopic cholecystectomy under general anesthesia. He developed severe post-operative hypotension which required intensive monitoring and vasopressor support.

Introduction

The causes of post-operative hypotension are multi-factorial, including hypovolemia, anesthetic overdose, anaphylaxis, pre-operative anti-hypertensive use, sepsis and myocardial depression. We report a case in which a patient presented with severe hypotension in the post-operative period which persisted for many hours and did not respond to vasopressors.

Case report

A 58 year old post renal transplant patient with gall bladder calculi was scheduled for laparoscopic cholecystectomy. Post transplantation he had a creatinine of 1.5 mg/dl and a good urine output. He was on Amlodipine 5 mg once daily for control of blood pressure. All investigations including CBC, RBS, creatinine, electrolytes, electrocardiogram, echocardiography, chest x-ray and liver function tests were normal.

He had taken his usual dose of Amlodipine in the morning four hours before the surgery. In the operation theatre his pulse was 76/min and blood pressure was 120/80 mm Hg. After applying all the monitors he was pre-medicated with glycopyrrolate 0.2 mg, ranitidine 50 mg, ondansetron 4 mg and fentanyl 3 µg/kg intravenously and was induced with thiopentone sodium 7 mg/kg and succinylcholine 2 mg/kg. Trachea was intubated with 8.5 mm portex cuffed endotracheal tube and anesthesia was maintained with O₂ + air + Isoflurane + atracurium. Monitoring included ECG, NIBP, SpO₂, EtCO₂ and peripheral nerve stimulator.

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About an hour after induction, towards the end of the surgery at the time of extubation the blood pressure decreased from 120/80 mm Hg to 90/60 mm Hg. The patient was extubated. Post-operatively the blood pressure further fell to 86/60 mm Hg. One litre of normal saline was infused rapidly followed by incremental doses of ephedrine and 500 ml of Gelofusin, without much improvement in blood pressure. Dopamine infusion was started and gradually increased to 20 µg/kg/min. Later on, nor-adrenaline and vasopressin infusions as high as 0.4 µg/kg/min and 6units/hr were added sequentially which did not produce any significant benefit. A central line for CVP monitoring and arterial line for invasive blood pressure monitoring were inserted. The CVP was 8 mm of Hg. With all the three vasopressors his blood pressure was still 70/40 mm Hg.

He was shifted to ICU where a sonography of the abdomen was done to rule out hemorrhage. An arterial blood gas (ABG) sample showed mild metabolic acidosis with normal electrolytes (pH 7.2, PCO_2 32, BE -12). Simultaneously a complete blood count was done which revealed total and differential WBC counts to be within normal limits. A bedside ECG, echocardiography and cardiac enzymes assay did not reveal any abnormality. He was on high dose inotropic support with normal CVP (10 mm Hg) and a blood pressure of 80/50 mm Hg. There was a drop in his hourly urine output because of compromised renal perfusion pressure.

About eight hours after the initial episode of hypotension, the patient started improving hemodynamically. ABG at this time showed improvement in acidosis with normal electrolytes levels (pH 7.32, PCO_2 31, BE-8). Over the next 5-6 hours the inotropic support was tapered gradually and then stopped altogether. Thereafter he was stable hemodynamically with a pulse of 88/min and a blood pressure of 130/80 mm Hg. On the next day he had a slightly elevated creatinine of 2.6 mg/dl but the hourly urine output was improved. His CBC, Chest x-ray, ECG, ABG and electrolytes were normal. He was shifted from the ICU on third day with stable hemodynamics, creatinine of 1.5 mg/dl and a good urine output.

Discussion

The reasons for severe post-operative hypotension can be myocardial infarction, septicemia, anaphylaxis or anaphylactoid reaction to drugs used, hypovolemia, valvular heart disease and hyper-responsiveness to pre-operative anti hypertensives.

In our patient, the cardiac enzymes and echocardiography in the immediate post-operative period were normal which ruled a cardiac cause of hypotension. Post-operatively, an ultrasound of the abdomen was done and hemorrhage as a cause of hypovolemia was ruled out. Septicemia can also be one of the causative factors for hypotension especially in immunocompromised patients, however the patient's total and differential WBC counts before and after the surgery were within normal limits. His body temperature was normal. Anaphylactic reactions during anesthesia can also cause severe refractory hypotension, but that seemed unlikely in our case because the patient did not give any history of allergic reaction and neither were signs of anaphylactic reaction like skin redness, wheezing, hives, swelling of face and eyes or angiodema noted intra-operatively. The next probable cause of hypotension was considered to be the exaggerated response of antihypertensive medication. Pre-operatively he had taken the usual dose of amlodipine on the morning of the surgery.

Amlodipine, a dihydropyridine calcium channel blocker inhibits transmembrane influx of calcium ions into vascular smooth muscles and cardiac muscles by binding to voltage gated calcium channels causing decreased cardiac output and vasodilatation of blood vessels, thus decreasing blood pressure¹. Unlike diltiazem or nifedipine, amlodipine can also induce nitric oxide dependent vasodilatation in coronary and peripheral arteries and may inhibit the angiotensin converting enzyme itself². Peak plasma concentrations occur 6-8 hours after dosing and return to baseline at 24-72 hours. While there is no clear consensus on whether the drug needs to be withheld on the day of surgery, it is generally believed that most of the calcium channels blockers (CCB) can be continued in the peri-operative period³. There are innumerable case reports citing severe hypotension after CCB overdose^{4,5}, but the same with therapeutic dosage is scarcely reported⁶.

Though the time of peak plasma concentration of Amlodipine occurred intra-operatively, the blood pressure did not fall drastically during surgery. It may have been maintained by increased endogenous catecholamine concentration due to sympathetic stimulation during laparoscopy⁷. At the completion of surgery, catecholamine concentration may have decreased to a level at which hypotension resulted. Hypotension did not respond to any of the vasopressors. The blood pressure slowly started increasing 8 hours after the initial fall, which co-incides with the terminal elimination half-life of Amlodipine. Omitting the morning dose of amlodipine could have avoided or

at least decreased the severity of hypotension in this patient.

Conclusion

We conclude that careful titration of anti-hypertensive treatment in the peri-operative period is necessary till definite guidelines on peri-operative anti-hypertensive therapy are drawn. Blood pressure should be monitored carefully intra-operatively and it should be continued in the post-operative period as well when the stimulation of surgery has ceased.

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