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JOURNAL OF
Surgery and Surgical Research OPEN ACCESS JOURNAL

ISSN: 2455-2968 DOI: https://dx.doi.org/10.17352/jssr

Case Report

High dose epinephrine in the management of life-threatening hypotension from post-surgical hemorrhage with an excellent outcome in a patient with Phaeochromocytoma: A case report

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Received: 10 January , 2022
Accepted: 05 February, 2022
Published: 07 February, 2022

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Keywords: High dose epinephrine; Case report; Phaeochromocytoma

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Summary

Epinephrine is widely used in the management of severe cardiovascular instability as well as in cardiac arrest. In cardiac arrest, epinephrine has a standard dose (1mg) given at fixed intervals. We present a report on the use of high dose epinephrine (35mg in 45 minutes) during the successful management of a patient with sustained profound hypotension as a result of massive hemorrhage following laparoscopic adrenalectomy.

Glossary

BMI: Body Mass Index; eGFR: Estimated Glomerular Filtration Rate; MAP: Mean Arterial Pressure; PEA: Pulseless Electrical Activity

Introduction

Epinephrine is widely used in the management of severe cardiovascular instability as well as in cardiac arrest. Although the high dose of epinephrine has been investigated in cardiac arrest, current recommendations do not favor its use [1,2]. In hypotension secondary to cardiogenic or anaphylactic shock, low-dose epinephrine is often used as an infusion to maintain organ perfusion. Sustained intraoperative hypotension is recognized to result in significant end-organ dysfunction. There is emerging evidence to support the use of pre-emptive interventions to avoid and manage protracted hypotension in patients undergoing general anesthesia. The authors present the use of high dose epinephrine in the successful management of profound and protracted hypotension secondary to massive postoperative hemorrhage following laparoscopic adrenalectomy. At six months follow up, the patient reported no cardiovascular, neurological, or renal sequelae.

The patient provided written consent for the use of de-identified data for analysis and publication in a peer-reviewed journal.

Citation: James A, Robertson G, Bhardwaj N, Lloyd D, Niraj G (2022) High dose epinephrine in the management of life-threatening hypotension from post-surgical hemorrhage with an excellent outcome in a patient with Phaeochromocytoma: A case report. J Surg Surgical Res 8(1): 001-003.
DOI: https://dx.doi.org/10.17352/2455-2968.000145

Case report

A 77-year old male patient underwent elective laparoscopic right adrenalectomy to remove a 63mm adrenal tumor causing phaeochromocytoma. Co-morbidities included ischaemic heart disease (single stent), carcinoma of the prostate (endocrine therapy), hyperlipidemia, and hypertension. Medications included ramipril, bisoprolol fumarate, atorvastatin, and aspirin. He was commenced on phenoxybenzamine pre-operatively. He was a non-smoker with a Body Mass Index (BMI) of 27 and used to walk 30 miles a week. Preoperative hemoglobin was 125g/L. Laparoscopic adrenalectomy was performed under general anesthesia with invasive blood pressure and central venous monitoring. The surgery was uneventful with minimal blood loss. The patient was transferred to a high dependency unit as a planned admission. A norepinephrine infusion was commenced in the postoperative period to maintain blood pressure.

Over the next five hours after surgery, the patient developed worsening hypotension and the norepinephrine requirement increased to 4 mg/hour. Thereafter, he developed acute severe hypotension (60/30mm Hg) and the hemoglobin level dropped to 63g/L. The patient was given an intravenous fluid bolus (2 liters of Hartman's solution). An epinephrine infusion was commenced and increased to 4mg/h to maintain the systolic blood pressure of 80mm. Following immediate surgical review, the patient was taken to the emergency operating theatre for an exploratory laparotomy.

Following urgent transfer to the operating theatre, general anesthesia was carefully induced. A laparotomy revealed a massive amount of blood in the intraabdominal cavity and four-quadrant blood clots. It took 36 minutes from the time of skin incision to identify the source of the hemorrhage. The patient received 4 liters of crystalloids, 8 units of packed cells, 3 units of fresh frozen plasma, calcium gluconate, and sodium bicarbonate. Despite fluid and electrolyte replacement, the patient's blood pressure only responded to epinephrine bolus of 1mg every 45-60 seconds on top of a background infusion of norepinephrine (4mg/h) and epinephrine (4mg/h). Despite epinephrine 1mg bolus administration every minute, the systolic blood pressure remained between 30-50mm Hg.

Twenty minutes after the skin incision, the patient suffered loss of cardiac output (pulseless electrical, PEA) activity for five minutes that required cardiac compression. The patient received an additional bolus of 5mg of epinephrine before the return of spontaneous circulation. Once the arterial bleeder was ligated, the patient's hemodynamic function gradually improved. The surgical duration was 75 minutes and the estimated blood loss was 5 liters. In total, the patient received 35mg of epinephrine.

The patient was transferred to the intensive care unit and required mechanical ventilation for 36 hours. Inotropic support was reduced to noradrenaline infusion within 6 hours of emergency surgery. The patient's trachea was extubated on day 2 and he was discharged from the intensive care unit on day 3. The patient did not suffer any end-organ dysfunction and there was no neurological impairment. The patient was discharged from the hospital on day 6. Pre-operative serum creatinine was 96 micromol/L and the estimated Glomerular Filtration Rate (eGFR) was 70. At six months after surgery, serum creatinine was 90 micromol/L and eGFR was 70.

The patient was reviewed in the outpatient clinic at 2 months and over the telephone at 6 months. At six months follow up, the patient reported occasional forgetfulness, continued to walk between 21-25 miles a week and did not report any cardiovascular, renal, or neurological sequelae.

Discussion

Phaeochromocytoma is a rare tumor arising from the chromaffin cells of the adrenal medulla, with an annual incidence of 0.8 per 100,000 person years [3]. Prior to adrenalectomy, the patients are often commenced on phenoxybenzamine, which is a long-acting, non-selective, irreversible alpha-adrenergic blocker. Prolonged postoperative hypotension following adrenalectomy is common. It is usually the result of a combination of factors including a sudden decrease in the level of catecholamines, persistent alpha-adrenergic blockade by phenoxybenzamine, or down-regulation of adrenoceptors [4]. Clinical predictors of prolonged hypotension include tumor size > 60mm and raised urinary catecholamine levels [4]. Patients are commenced on catecholamine infusion to maintain systemic perfusion.

In this patient, in addition to the above factors, there was a catastrophic hemorrhage that resulted in sustained, profound hypotension and subsequent PEA. Profound hypotension has been defined as a systolic blood pressure less than 50mm Hg [5]. There is increasing evidence that hypotension during anesthesia is associated with a high risk of organ damage [6]. A Mean Arterial Pressure (MAP) below 40mm Hg for over five minutes increases the risk of acute kidney injury (four folds), myocardial injury (four folds), and death (two folds). A MAP of 40mm Hg is likely to be associated with a systolic arterial pressure of approximately 55mm Hg [6-9].

Despite significant intravascular fluid replacement, administration of packed red cells, calcium gluconate and sodium bicarbonate as well as infusions of norepinephrine (3.2mg/h) and epinephrine (3.2mg/h), the hypotension was refractory and severe. A systolic blood pressure of 30-50 mg Hg was possible only with 1mg bolus of epinephrine that was administered every minute for over 30 minutes. The abdominal cavity was filled with over 2.5 liters of blood and there was a significant amount of blood clots in all four quadrants of the abdomen. The systolic blood pressure was significantly low for a prolonged period.

These factors made it challenging to promptly identify the bleeding vessel.

The use of a 1mg bolus dose of epinephrine every 45-60 seconds was more instinctive than planned. As the patient's blood pressure was responding to the bolus dose, albeit temporarily, the physician continued to repeat bolus administration. In experimental cardiopulmonary resuscitation, high dose epinephrine has been shown to increase cortical cerebral blood flow as well as coronary perfusion [6,7].

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This patient had initial moderate-severe hypotension during the first five hours after the initial surgery. Thereafter, the patient experienced profound hypotension for over 60 minutes as a result of a massive intraabdominal hemorrhage. In addition, he suffered a brief period of loss of cardiac output. Despite these catastrophic events, the patient made a significant and complete cardiovascular and neurological recovery.

At six months follow up, the patient's renal function remained unchanged. The authors believe that the excellent outcome is very likely due to the high dose of epinephrine (35mg).

Large doses of epinephrine have been used and investigated for resuscitation after cardiac arrest [1]. Current recommendations do not support a high dose of epinephrine [2]. High-dose adrenaline infusion has been reported in severe hypotension as a result of disulfiram-ethanol reaction [10].

A literature search did not reveal the use of high-dose epinephrine boluses in the management of severe hypotension. The authors present the first report on the use of high-dose epinephrine in the management of profound hypotension under general anesthesia.

In this patient, the use of high-dose epinephrine may have played a role in the excellent outcome. However, there is insufficient evidence to recommend the standard use of high-dose epinephrine. Instead, the authors suggest the early use of epinephrine bolus (in aliquots of 50-100 micrograms) in severe hypovolemic shock especially in patients under general anesthesia. This practice would help in maintaining the mean arterial pressure as well as limit the severity of profound hypotension thereby improving perfusion to the vital organs [6]. There is an emerging consensus on the critical need to commence early intensive support to manage profound hypotension in patients under general anesthesia. Our recommendation is in line with the proposal by Harper et al to commence pre-emptive chest compressions [7]. High-risk patients undergoing general anesthesia may benefit from an individualized plan for instituting early interventions [6,11].

The authors present the first report where epinephrine was repeatedly administered as a 1mg bolus for a sustained period in the management of life-threatening hypotension with no cardiovascular, renal, and neurological sequelae at six-month follow-up.

Authors' contribution statement

AJ: methodology, data collection, writing a draft of the manuscript

GR: methodology, writing a draft of the manuscript

NB: methodology, writing a draft of the manuscript

DL: methodology, writing a draft of the manuscript

GN: concept, methodology, data collection, writing a draft of the manuscript, and complete responsibility of the manuscript

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DOI: https://dx.doi.org/10.17352/2455-2968.000145