Sinus node dysfunction associated with discontinuation of cilostazol in a patient taking atenolol

Editor—We wish to report a case of cardiac arrest followed by an episode of severe bradyarrhythmias associated with discontinuation of the antithrombotic agent cilostazol in a patient taking atenolol. Cilostazol is recognized to have cardiovascular effects.1

A 72-yr-old man (157.6 cm, 49.2 kg) with atherosclerotic disease in arteries of his right lower leg was scheduled to undergo femorotibial reconstruction. He had a history of hypertension and diabetes mellitus. His medication included cilostazol 100 mg daily, atenolol 25 mg daily, amlopidine 5 mg twice daily, doxazosin 1 mg twice daily, and insulin 5 units three times daily. Cilostazol was discontinued five days before the operation. The heart rate gradually decreased from 75 beats min⁻¹ to 60 beats min⁻¹ over the next 2 days. Atenolol, amlopidine, and doxazosin were continued up to the day of surgery. Insulin was stopped on the day of operation.

Before induction of general anaesthesia, the heart rate was 60 beats min⁻¹ and blood pressure was 140/62 mm Hg. General anaesthesia was induced with propofol. Tracheal intubation was facilitated by vecuronium. Anaesthesia was maintained with sevoflurane 0·6–0·8% and nitrous oxide 67% in oxygen and fentanyl.

After induction, the patient had a heart rate of 50 beats min⁻¹ and a blood pressure of 130/40 mm Hg. Approximately 2 h after induction of anaesthesia, the deep femoral artery was clamped to remove thrombus. The cross clamping time was 68 min. Before unclamping, heart rate and blood pressure were 50 beats min⁻¹ and 130/40 mm Hg. Arterial blood gas analysis revealed pH 7.41, P\textsubscript{a}CO\textsubscript{2} 40 mm Hg, and a base excess +0.7, with a serum potassium of 4.6 mmol litre⁻¹. Four minutes after unclamping, the patient had a cardiac arrest (asystole). After 4 min of closed-chest cardiac massage, and administration of atropine 1 mg and epinephrine 1 mg, cardiac rhythm was restored. Thereafter, heart rate and blood pressure were stabilized at 80 beats min⁻¹ and 130/40 mm Hg using dopamine 5 μg kg⁻¹ min⁻¹, and arterial blood gas analysis revealed a pH 7.43, P\textsubscript{a}CO\textsubscript{2} 35.6 mm Hg, P\textsubscript{a}O\textsubscript{2} 373 mm Hg, and a base excess +0.4, with a serum potassium of 4.9 mmol litre⁻¹. Electrocardiogram showed no ST segment elevation before or after the event. The patient was transferred to the intensive care unit on dopamine and a propofol infusion. Approximately 30 min later, severe bradyarrhythmia (26 beats min⁻¹) was noted. Epinephrine 1 mg was administered and the heart rate returned to 60 beats min⁻¹.

Coronary angiography, echocardiogram, and 24 h Holter monitoring revealed no abnormalities. The patient was discharged from hospital on the 17th day after surgery without further sequelae.

Cilostazol increases heart rate, whereas atenolol decreases it. In this patient, cilostazol was stopped 5 days before surgery and atenolol was continued up to the day of operation. The heart rate gradually decreased after stopping the cilostazol. It may be that discontinuation of cilostazol combined with continuation of a β-blocking agent impaired the balance between the tachycardiac effect of cilostazol and the bradycardic action of atenolol, leading to perioperative sinus node dysfunction.

As the base excess and serum potassium did not change after unclamping of the deep femoral artery, which was performed 4 min before the cardiac arrest, metabolic factors would have only had a minor influence on the cardiac arrest. In addition, the likelihood of myocardial infarction, coronary spasm, or sick sinus syndrome, occurring during general anaesthesia in this patient should be small.

As cilostazol has antiplatelet properties, it is commonly stopped before surgery. In contrast, β-blocking drugs should be continued perioperatively. However, discontinuation of cilostazol in a patient taking β-blocking drugs may result in sinus dysfunction. Adjustment of the dose of a β-blocker should be considered when cilostazol is discontinued preoperatively.

Control of the phaeochromocytoma patient revisited

Editor—We read with interest the article by Tauzin-Fin and colleagues.1 The authors report on 18 patients, over a period of 6·5 yr, being operated upon for removal of a phaeochromocytoma using the laparoscopic surgical technique. This technique is growing in popularity both in Europe and the USA. The authors point out that insufflation of carbon dioxide into the peritoneal cavity can cause a hypertensive episode because of the pressure increase within the cavity. This increase in pressure can cause an efflux of catecholamines from the tumour at any time during the procedure. Once the pressure is maintained at 15 cm H\textsubscript{2}O, the intra-abdominal pressure should stabilize. Intraoperative insufflation of carbon dioxide can also lead to release of vasopressin, with an increase in systemic vascular resistance and gradual decrease in cardiac output.2 Carbon dioxide pneumoperitonium can produce significant hypercapnia and respiratory acidosis.3 These complications are rarely a problem in younger patients, but older patients with pre-existing pulmonary disease and those with increased respiratory dead space may have difficulty eliminating the carbon dioxide burden despite mechanically increased minute ventilation.4 Helium has been investigated as an alternative insufflating gas in a porcine model.5 Further investigation on the use of helium for pneumoperitonium is warranted. We believe that it may be an excellent alternative to carbon dioxide, especially in those patients with pre-existing cardiopulmonary disease or with decreased respiratory reserve.

Tauzin-Fin and colleagues1 used urapidil, an α\textsubscript{1} adrenergic blocker, intermittently, to control the intraoperative surges in blood pressure attributable to either tumour manipulation or the pneumoperitonium. In the USA, urapidil is an investigational drug and can not be used in clinical practice.

The authors’ paper reminds us of the one we had published in the British Journal of Anaesthesia in 1994.6 This paper recommends the use of metyrosine, an agent that reduces biosynthesis of catecholamines (often to normal levels) and also phenoxybenzamine, a non-competitive long-acting mixed α-antagonist. Both are continued to the morning of surgery. In the Lippmann paper,7 desflurane was used, then a new inhalational agent released by the Federal

References

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Although slower in onset, isoflurane or sevoflurane, which also have a vasodilating effect, is a selective short-acting \( \alpha \)-blocker that, given orally, improves the management of phaeochromocytoma only in the preoperative phase.11 All these drugs may exert delayed effects that can be controlled with \( \beta \)-blockers.13 Prazosin is a selective, competitive \( \alpha \)-adrenoceptor blocker that, given orally, improves the management of phaeochromocytoma only in the preoperative phase.11 All these drugs may exert delayed effects that can increase the incidence of severe hypotension after tumour removal. An alternative treatment is urapidil, a competitive and selective short-acting \( \alpha \) blocker, administered by continuous i.v. infusion preoperatively and throughout anaesthesia, to block \( \alpha \) adrenergic receptors before any acute catecholamine release during surgery.1 Its pharmacological profile renders it effective in this situation. If severe rises in blood pressure occur, nicardipine at low doses is an effective adjuvant treatment, whose action is potentiated by sevoflurane.12 13 Desflurane should be avoided as it is associated with catecholamine release if given rapidly in high concentrations.14

We totally share Dr Lippmann’s conclusions that the unprepared patient is most at risk, and we believe that the use of urapidil represents a modern, pathophysiological approach to the perioperative management of phaeochromocytoma.

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Editor—We appreciate the interest of Drs Lippmann and Kakazu in our study.1 Indeed, laparoscopic surgery for phaeochromocytoma is now widely considered to be the gold standard, and the anaesthetist should be aware of the pathophysiological repercussions from both the phaeochromocytoma and pneumoperitoneum. In an animal study, vasopressin release has been shown to be involved in haemodynamic instability.2 This situation has not been reported in humans undergoing normovolaemic anaesthesia with adequate monitoring of the depth of anaesthesia.3 Hypercapnia in relation to the carbon dioxide pneumoperitoneum induces small changes in plasma catecholamine levels.4 Hypercapnia can be of importance in patients with pre-existent cardiorespiratory disease. Close monitoring of \( \text{E}_2 \text{CO}_2 \) and more precisely of \( \text{P}_2 \text{CO}_2 \) avoids the consequences of hypercapnia in such patients. Helium can be used as an insufflating gas in laparoscopic surgery for phaeochromocytoma.5 However, because of its low water solubility, helium is more prone to induce gas embolism than carbon dioxide.9 10 Creation of the pneumoperitoneum is the main triggering factor for catecholamine release, even when close monitoring of intra-abdominal pressure during insufflation is performed.

We agree with Dr Lippmann’s view that the key to success is pre- and intra-operative \( \alpha \)-blockade, probably using short-acting agents. Unfortunately, the ideal short-acting \( \alpha \) blocker has not yet been determined. Metyrosine reduces the biosynthesis of catecholamines without establishing haemodynamic stability, thereby causing possible cardiovascular collapse after tumour gland removal.11 Phenoxbenzamine, a non-selective \( \alpha \)-adrenoceptor antagonist, has a long duration of action and a pharmacological half-life of about 24 h. Its chronotropic and inotropic effects can be controlled with \( \beta \)-blockers.13 Prazosin is a selective, competitive \( \alpha \)-adrenoceptor blocker that, given orally, improves the management of phaeochromocytoma only in the preoperative phase.11 All these drugs may exert delayed effects that can increase the incidence of severe hypotension after tumour removal. An alternative treatment is urapidil, a competitive and selective short-acting \( \alpha \) blocker, administered by continuous i.v. infusion preoperatively and throughout anaesthesia, to block \( \alpha \) adrenergic receptors before any acute catecholamine release during surgery.1 Its pharmacological profile renders it effective in this situation. If severe rises in blood pressure occur, nicardipine at low doses is an effective adjuvant treatment, whose action is potentiated by sevoflurane.12 13 Desflurane should be avoided as it is associated with catecholamine release if given rapidly in high concentrations.14

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Successful use of remifentanil for major head and neck surgery in a heart–lung transplant recipient

Editor—We would like to describe the successful use of remifentanil in a patient undergoing major head and neck surgery, who had previously received a heart–lung transplant. Remifentanil’s unique pharmacokinetic profile may be advantageous in head and neck procedures.1 Intense intraoperative analgesia can be required for prolonged periods, but postoperative pain may not be severe, and prompt recovery is normally desired. In addition, remifentanil can help to ensure immobility in the absence of neuromuscular