Phenylephrine toxicity

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EDITOR:

Phenylephrine is an α-1 agonist used primarily in the perioperative period and in the ICU. It is also found in proprietary nasal decongestants. Its vasoconstricting properties are utilized for preparation of the surgical field to control haemorrhage in procedures involving the ear, nose and throat (ENT) or for pupillary dilatation. Given intravenously (i.v.) as an infusion or in small incremental boluses, its α-1-mediated vasoconstriction can be used to increase systemic vascular resistance to maintain blood pressure (BP). The use of small i.v. boluses is a common technique to overcome vasodilatation and hypotension caused by anaesthetic agents or regional techniques such as spinal or epidural anaesthesia. Similarly, it can be used as an infusion to counteract vasodilatation caused by sepsis, anaphylaxis or spinal shock. It may be necessary to change previously common practice when drugs are removed after loss of patent [1]. With the loss of certain other α-1 agonists and replacement in many centres with phenylephrine for i.v. injection in highly concentrated form, the potential for inadvertent overdose is increased. We describe a case of phenylephrine toxicity caused by systemic absorption after topical overdose and the incorrect use of a β-2 antagonist as part of a therapeutic response to subsequent hypertensive crisis.

A 30-yr-old male was admitted for day case surgery to stent a tear duct.

He was fit and well, not on any medications and had never had an anaesthetic before. Induction of anaesthesia was smooth and his vital signs remained initially unremarkable with a pulse of 90 bpm and BP of 135/78. The patient's nose was prepared for surgery with injection of 2 mL of lidocaine 1% + epinephrine 1 in 80 000 to the skin, followed by a nasal pack which was soaked in 2 mL of 5% cocaine (total dose 100 mg) and, erroneously, ten 0.5 mL vials of 10% phenylephrine (total dose 500 mg). It was estimated that only two-thirds of this pack was actually inserted into the nose.

The patient's BP began to rise quickly reaching 210/146 with a corresponding decrease in heart rate to 45 bpm. The initial management was to give glycopyrrolate 300 μg and fentanyl 50 μg and to deepen the anaesthetic by increasing the isoflurane concentration. The nasal pack was removed and labetalol was given in increments to a total of 15 mg. Significant ST depression was noted on the electrocardiogram (ECG) monitor, but despite the BP returning to normal levels with the above management, the ischaemic changes and occasional ventricular ectopics continued. A 12-lead ECG was performed which showed ST depression across the lateral leads in keeping with the pattern of strain caused by the sudden increase in BP, and a decision was made to abandon surgery. Anaesthesia was maintained for 25 min with a now-stable pulse and BP. The patient was extubated under deep anaesthesia avoiding the risk of a further hypertensive response.

The patient was admitted to the coronary care unit for further investigation and monitoring, where he recovered uneventfully apart from a headache that resolved later that day. Repeat ECG showed resolution of all the changes and a myocardial infarction screen was negative. An echocardiogram was completely normal and he was discharged the following day. Prior to subsequent readmission to perform the surgery urine collections for vanilmandelic acid were obtained to exclude an underlying phaechromocytoma, which were normal.

The patient was readmitted 3 weeks later for the operation, with a modified vasoconstrictive regimen, which was completed uneventfully.

Though other diagnoses such as phaeochromocytoma were considered, the nasal pack was implicated as a cause of these events both by the onset of symptoms after its insertion and the improvement seen after its removal. In addition, it became apparent later that the ophthalmologist had erroneously used ten 0.5 mL vials of phenylephrine 10% (total dose 500 mg) instead of the usual dose of two vials (total dose 100 mg).

Topical vasoconstrictor doses exceed those given i.v. for hypotension because of the belief that little is absorbed. Although commonly used, there is no consensus on which vasoconstrictor or what concentration to use [2]. After topical phenylephrine caused the death of a 4-yr-old child in New York, an advisory committee circulated guidelines to the New York hospitals with seven key recommendations [3].

Correspondence to: Michael Macmillan, Department of Anaesthetics, Royal Alexandra Hospital, Paisley, Glasgow, UK. E-mail: mhmacmillan@aol.com; Tel: +141 887 9111; Fax: +141 314 7127

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The first four recommendations suggest an initial dose of 0.5 mg applied as four drops of a 0.25% solution for ENT procedures. This dose is the product literature i.v. dose for hypotension and assumes 100% absorption. In children the recommended dose was 20 $\mu g\,kg^{-1}$. In clinical practice, only the minimal amount required for preparation of the surgical field should be given, vital signs monitored and the anaesthetist informed [3].

Although phenylephrine is predominantly a selective agonist, at very high doses β activation does occur. Our patient demonstrated a marked bradycardia in response to hypertension suggesting he had mainly an α-1-mediated vasoconstriction and a baroreceptor-mediated bradycardia without evidence of β activation. It is common practice to deepen anaesthesia in response to hypertension, which will reduce peripheral vascular resistance but may also impair cardiac performance that may already be compromised by a high afterload. There is insufficient evidence to either recommend or discourage this management [3].

The use of glycopyrrolate did appear to prevent further bradycardia and may also have prevented further complications of using labetalol in subsequent management. Labetalol is a mixed α and β antagonist although the β effects are about seven times stronger than the α effects. It is readily available and is a drug most anaesthetists have experience using. Although used in the successful management of other cases of phenylephrine toxicity [4], the Phenylephrine Advisory Committee highlighted a pattern of management in cases who were pre-treated with anticholinergics and did not demonstrate a bradycardic response to phenylephrine toxicity. The subsequent use of β antagonists may result in an inability to compensate for the increased afterload and they are thus associated with pulmonary oedema. Labetalol was used in all three cases that resulted in cardiac arrest [3]. The report went on to recommend that severe hypertension or associated complications (pulmonary oedema or ECG changes) should be treated with direct vasodilators or α antagonists such as phentolamine.

The patient in our case made an uncomplicated recovery, however the case highlights the need for good communication between surgeon and anaesthetist, and the responsibilities of phenylephrine use and dosage. With drug companies ceasing production of drugs such as methoxamine, the use of alternative α agonists such as phenylephrine has increased. The highly concentrated presentation of phenylephrine means that errors made in preparation of i.v. doses may have significant consequences in terms of toxicity, in addition to its topical use as in this case. It is therefore important to be aware of dilution protocols and the correct management of overdose.

M. Macmillan
Department of Anaesthetics
Royal Alexandra Hospital
Paisley, Glasgow, UK

K. Barker
Department of Anaesthetics
Raigmore Hospital
Inverness, UK

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Anaesthesia for Worster-Drought syndrome

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EDITOR:
A 29-yr-old, 100 kg female (body mass index 38) presented for day case bilateral hip injection of steroids. At a preoperative assessment clinic, she had been noted to have moderate learning difficulties (IQ 65), eat a special thickened diet due to 'swallowing problems' and have Worster-Drought syndrome (WDS) but the anaesthetic implications of her syndrome had not been appreciated. She had received general anaesthesia as an 11-yr-old, for surgical correction of bilateral slipped femoral

Correspondence to: Stuart M. White, Department of Anaesthesia, Royal Sussex County Hospital, Brighton, East Sussex BN2 5BE, UK. E-mail: igasbest@hotmail.com; Tel: +44 1273 566295; Fax: +44 1273 609060

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