# The adverse effects of inadvertent intraoperative intravenous phenylephrine administration: a case report

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## Abstract

Inadvertent intravenous injection of 1% phenylephrine (10 mg) induced severe hypertension and tachycardia in a previously healthy female patient undergoing elective gynaecological surgery. This medical error was investigated using the critical-incident technique that is available in our department. This case report highlights the cardiovascular sequelae of phenylephrine overdose and the human factor that is associated with a medication error. We discuss these two factors, as well as the organisational factors that contributed to this medical error, in order to prevent its recurrence.

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## Case report

We present the case of a 24-year-old woman who was scheduled for an elective diagnostic laparoscopy for chronic pelvic pain. At the preoperative anaesthetic assessment, she was categorised as American Society of Anesthesiologists physical status I. She had no known drug allergy. The anaesthetic plan was to give her a standard intravenous anaesthetic induction and endotracheal intubation while maintaining anaesthesia with an oxygen-air mixture with sevoflurane.

Prior to induction of anaesthesia, midazolam 2 mg and fentanyl 100 µg were given intravenously. The anaesthetist trainee inadvertently administered 1% phenylephrine (10 mg) to the patient, instead of dexamethasone 8 mg. Shortly afterwards, the patient developed tachycardia with a heart rate up to 160 beats per minute (bpm) and severe hypertension with an unrecordable systolic blood pressure (SBP) and diastolic blood pressure (DBP) of 120-130 mmHg on the noninvasive blood pressure (BP) monitor. The drug error was realised immediately, assistance requested. Two consultant anaesthetists were at hand to help immediately.

Anaesthesia was immediately induced with propofol 200 mg, and endotracheal intubation secured after administering a standard dose of atracurium. The decision was taken to proceed with the planned surgery, as the patient was haemodynamically stable after induction of anaesthesia.

## Clinical course and follow-up

Immediate and appropriate emergency care was given to the patient after securing a patent airway and ensuring adequate ventilation.

An arterial line was inserted to facilitate monitoring of the BP and for serial gas sampling. A right internal jugular vein was cannulated for vasoactive drug infusion and for central venous pressure monitoring.

The patient remained tachycardiac with a heart rate of 120-130 bpm and hypotension during the surgery. At this stage, a bolus of colloid (gelofusine) was given to maintain the SBP > 100 mmHg. She became normotensive after a few minutes, but remained tachycardiac (100-110 bpm), without any other arrhythmias.

Laparoscopy was negative and uneventful. At the end of surgery, she was extubated without complications and transferred to the recovery room for close monitoring. She was oriented with appropriate cognition and informed of the drug error that had occurred in theatre. She was updated on her clinical situation.

A 12-lead electrocardiogram (ECG) showed ST depression on all leads, and troponin levels of 0.68 µg/l (0-0.1 µg/l). The cardiologist was consulted and a transthoracic echocardiogram (TTE) was performed, which demonstrated normal valves, good left ventricular function, no abnormal wall motion, no pericardial collection, and no evidence of myocardial infarction. The cardiologist recommended observation of the patient and repeated troponin levels.

The patient spent five hours in our recovery room. Her BP was maintained at 90-110/40-50 mmHg, and heart rate was 80-90 bpm. The second troponin level had decreased to 0.36µg/l (0-0.1 µg/l), while the ST depression on the ECG improved. The results of the blood gases were essentially within normal limits. She was discharged to the ward after uneventful recovery room monitoring. In the ward the patient remained haemodynamically stable, and was discharged two days later.

Four weeks after discharge from the hospital, repeat TTE studies were normal. An exercise stress test demonstrated a normal haemodynamic response with no significant ST changes, while a Holter study was normal. The cardiologist planned to follow her up in another three months' time. The patient made a complete recovery. She planned to participate in a winter marathon race.

## Critical incident investigation

This drug error was investigated using the critical-incident technique that is available in our department. The General Medical Council study (GMC)[1] on human error used the James Reason's system[2] to classify human error. Unintentional acts, such as "slips" which are a skill-based error, are due to attention failures resulting from a busy workload, multi-tasking, fatigue and lack of concentration.[1,2] Lack of concentration may occur because of distractions in the anaesthetic room. This may have contributed to the error in this case. The environmental factors that may have also contributed to this drug error include the storage of anaesthethic drugs. The dexamethasone and phenylephrine ampoules, though not similar (Figure 1), are kept in the same drawer, and both drugs have similar cap seals, and are of a similar size and shape.


**Figure 1**: The ampoules of phenylephrine and dexamethasone

The other element to this case is the "second victim" concept, as elucidated by Wu.[3] Consideration should also be given to the physician who is responsible for the drug error. Counselling should be offered. The anaesthetic trainee was given a day off, and was followed-up by the consultant anaesthetist and supported by colleagues in the department.

## Discussion

Drug errors in anaesthesia are increasingly being recognised as an important cause of medical errors and a contributor to morbidity and mortality with significant healthcare costs.[1,4,5] However, more recent large prospective studies of drug errors in anaesthesia indicate that although drug administration errors are common, they infrequently cause major morbidity or mortality.[6,7] This case report underlines the reality of the complex nature of modern day anaesthetic practice.

Topical phenylephrine toxicity during ophthalmological surgery, that leads to a hypertensive crisis without cardiac failure, has been reported.[8] Groudine et al reported nine case records of topical phenylephrine toxicity during ear, nose and throat procedures. All nine patients developed severe hypertensive crisis, eight had symptoms of pulmonary oedema, and three of the patients had cardiac arrest that led to death.[9] Recently, Dubost et al[10] reported the first case of intravenous phenylephrine overdose in a previously healthy 29-year-old male scheduled for an ambulatory coelioscopic cholecystectomy. Their patient presented with a hypertensive crisis similar to that of our patient. However, in addition, their patient developed cardiac failure and unexpected bilateral pulmonary embolism, which ours did not. Their patient experienced a full recovery, with no cardiovascular impairment, as did our patient. These cases highlight the cardiovascular sequelae of inadvertent phenylephrine overdose and patient safety issues.

Severe hypertension, pulmonary oedema, tachycardia, cardiac arrest and death have been reported following phenylephrine toxicity.[8-10]

Phenylephrine causes vasoconstriction by stimulating the post-synaptic alpha receptors, resulting in increased systemic vascular resistance, decreased cardiac output, increased stroke volume and bradycardia.[9]

The fact that phenylephrine can cause tachycardia with marked hypertension in large doses is not well known. Usually, following phenylephrine administration, the "pure" $\alpha$ effect predominates with a reflex bradycardia. However, in large doses, a $\beta_1$ effect can occur, which explains the tachycardia.

The onset of the effect of intravenous phenylephrine is immediate, with the peak effect achieved after approximately 2-5 minutes. The effect has a short duration of 15-20 minutes.

Hypertension may resolve spontaneously before treatment is started. However, severe hypertension needs immediate treatment. The treatment recommendation for hypertension includes the use of antihypertensives with direct vasodilator activities or alpha-receptor antagonists.

The use of beta blockers and calcium-channel blockers are not recommended treatment choices for phenylephrine-induced hypertension, as they may increase the risk of mortality.[9]

## Recommendations

As illustrated in this case report and in similar case reports,[8,10] the risk of drug error and the attendant harm of these potent vasoactive drugs is great. The National Patient Safety Agency[11] and the General Medical Council[1] have published guidance on mechanisms to reduce drug administration errors. A decision was made to remove the phenylephrine box from the same drawer as other anaesthetic drugs in the anaesthetic rooms and the emergency carts, and to store them in a separate cupboard. An information leaflet has been posted on the drug cupboard re-emphasising the need for double control checking, where practicable. An ongoing critical incident anaesthesia trainee education programme, with an emphasis on meticulous attention when handling intravenous drugs, has been effected. A system is being encouraged that promotes reporting of medical errors. Without knowledge of the error, nothing can be altered.

It is believed that the above safeguards and the recommendations below will help to minimise phenylephrine toxicity and drug administration errors.

- Phenylephrine should be available in a safer, lower dosage, and a more diluted formulation, in addition to the standard formulation.
- The higher-dosage (more concentrated) phenylephrine should be marketed with a label that states that the drug should be diluted before use.
- The use of bar-coded drug readers, as a potential method of decreasing drug administration errors, should be considered.
- There is a need for improved ampoule labelling.

## Conflict of interest

There was no conflict of interest.

## Conclusion

The tasks of anaesthetists have become increasingly more complex. This case report highlights the risks of human error in medical practice, especially in anaesthesia. Systems that will help to reduce the potential for human error should be promoted and employed. The development of a safety culture and a robust error-reporting system should be encouraged and facilitated.

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