Clinical Reports

An anaesthetic drug error: minimizing the risk

Beverley A. Orser MD FRCPC,
Donald C. Oxorn MD CM FRCPC

A medication error caused a near fatal cardiac arrest in a previously healthy patient undergoing elective surgery. Inadvertent epinephrine injection induced ventricular dysrhythmias, hypertension, hypotension and pulmonary oedema. The case was investigated using critical-incident technique and was reviewed by the Risk Management Team of the Department of Anaesthesia. The purpose of this report is to present the recommendations resulting from the investigation. These include: improved resident training in intravenous drug management, the use of anaesthetic drug ampoules with distinct labels, and the development of a standardized colour code system for labels on anaesthetic drug ampoules. Furthermore, it is recommended that all anaesthetic drug errors be reported to the Canadian agencies responsible for drug packaging in order to identify patterns in anaesthetic drug errors, and to facilitate the implementation of effective drug identification systems.

Pendant une opération non urgente, une erreur de médicament provoque un arrêt cardiaque chez un patient non taré. De l'épinéphrine injectée par mégarde provoque des dysrythmies ventriculaires, de l'hypertension, de l'hypotension, et de l'oedème pulmonaire. Cet accident fait l'objet d'une investigation par la technique de l'incident critique et est révisé par l'équipe de gestion du risque de département d'anesthésie. Ce rapport expose les recommandations qui découlent de cette investigation. Ils comprennent l'amélioration de la formation des résidents au regard de la manipulation des préparations intraveineuses, l'utilisation d'ampoules étiquetées distinctivement et l'élaboration d'un code de couleur standard pour les étiquettes de préparation anesthésiques. On recommande aussi que toutes les erreurs de drogues anesthésiques soient rapportée aux organismes canadiens responsables de l'emballage des drogues de façon à identifier la tendance des erreurs médicamenteuses en anesthésie et faciliter l'implantation de systèmes d'identification réellement efficaces.

Key words
COMPLICATIONS: arrhythmia, misidentification;
EDUCATION: quality assurance;
MEASUREMENT TECHNIQUES: chromatography;
SYMPATHETIC NERVOUS SYSTEM: pharmacology, epinephrine.

From the Department of Anaesthesia, Sunnybrook Health Science Centre and the University of Toronto, Toronto, Ontario, Canada.

Address correspondence to: Dr. Beverley Orser, Department of Anaesthesia, Sunnybrook Health Science Centre, 2075 Bayview Ave., Toronto, Ontario M4N 3M5.

Accepted for publication 24th August, 1993.

Anaesthetic drug errors occur with alarming frequency, and the reported incidence likely underestimates the true number of events. An analysis of "critical incidents" during anaesthesia indicated misidentification of syringes and drug ampoules as the most common cause of preventable mishaps.[1] Another retrospective analysis of anaesthetic accidents or near accidents reported that the injection of the wrong drug or dose was responsible for 9.4% of mishaps.[2] Thirty per cent of anaesthetists in one survey admitted to having administered the wrong drug at least once in their careers.[3] This report describes yet another medication error due to misidentification of a drug ampoule. The case was reviewed by the Risk Management Committee of the Department of Anaesthesia and recommendations aimed at preventing similar occurrences are presented.

Case report

A 43-yr-old, 44 kg woman was scheduled for total abdominal hysterectomy for uterine fibroids. The patient had no concurrent medical problems and had never received a general anaesthetic. Her haemoglobin concentration was 110 $g \cdot L^{-1}$ and the rest of the laboratory tests were normal.

Standard anaesthetic monitors were applied, and general anaesthesia was induced with fentanyl, d-tubocurarine, propofol and succinylcholine. Following tracheal intubation, anaesthesia was maintained with nitrous oxide, isoflurane, and intermittent doses of vecuronium. The surgery was uneventful, and the patient re-

ceived one unit of autologous blood. Following closure of the abdominal fascia, the choice of drugs available to reverse neuromuscular blockade was discussed with the anaesthesia resident who was asked to prepare a syringe containing neostigmine 2.5 mg (5 ml of a 0.05% solution, prostigmine, ICN Canada) and glycopyrrolate 0.6 mg (3 ml of a 0.2 mg · ml^{-1} solution, Robinul, A.H. Robins). During skin closure, isoflurane was discontinued, and a syringe containing 8 ml of solution and labeled "glycopyrrolate 0.6 mg, prostigmine 2.5 mg" was handed to the staff anaesthetist. Half the reversal mixture was administered intravenously. Within one minute, multifocal ventricular premature beats were noted on the ECG tracing. Nitrous oxide was discontinued. The patient's blood pressure was 130/70 mmHg, pulse oximetry indicated a haemoglobin saturation of 99%, and her $P_{ET}CO_2$ was 32 mmHg. The cardiac rhythm rapidly deteriorated into pulseless ventricular tachycardia, and cardiopulmonary resuscitation was initiated. The cardiac rhythm spontaneously converted to ventricular bigeminy during external cardiac massage and the blood pressure increased to 210/130 mmHg. Lidocaine 50 mg was administered, and a sinus rhythm of 65 beats · min^{-1} was established. The blood pressure decreased to a systolic pressure of 50 mmHg and the patient remained hypotensive despite an infusion of 1500 ml of Ringer's lactate and phenylephrine 100 μg · min^{-1}. The patient developed bradycardia which was treated with atropine 1.2 mg. Over 15-min, her blood pressure increased to 90/50 mmHg and copious pink, frothy fluid began to bubble up the endotracheal tube. The patient was transferred to the Intensive Care Unit for further management and investigation. Before leaving the operating room, the anaesthetist instructed the operating room staff to seal the room, and to leave all equipment and drugs untouched. Subsequent cases were postponed until the preliminary investigation was completed.

Abnormal laboratory results in the Intensive Care Unit were: Haemoglobin 98 g · L^{-1}, WBC 14.3 × 10^9 · L^{-1}, arterial blood gases (F_IO_2 = 1.0) pH 7.39, PaO_2 91 mmHg, $PaCO_2$ 32 mmHg, serum electrolytes (mmol · L^{-1}) potassium 2.5, phosphate 0.7 (normal 0.8–1.5), magnesium 0.5 (normal 0.7–1.1), and calcium 1.68 (normal 2.2–2.6), and albumin 24 g · L^{-1}. Chest *x*-ray showed severe pulmonary oedema, and transoesophageal echocardiography revealed a mild septal hypokinesis, normal right ventricular function, and no valvular abnormalities. The ECG showed non-specific repolarization changes in leads V_1 through V_3.

The pulmonary oedema resolved after furosemide 40 mg, and the trachea was extubated the following day. Subsequent ECG's were normal, and there was no enzymatic evidence of myocardial infarction. The patient had no recall of the event, and had no detectable neurological deficit.

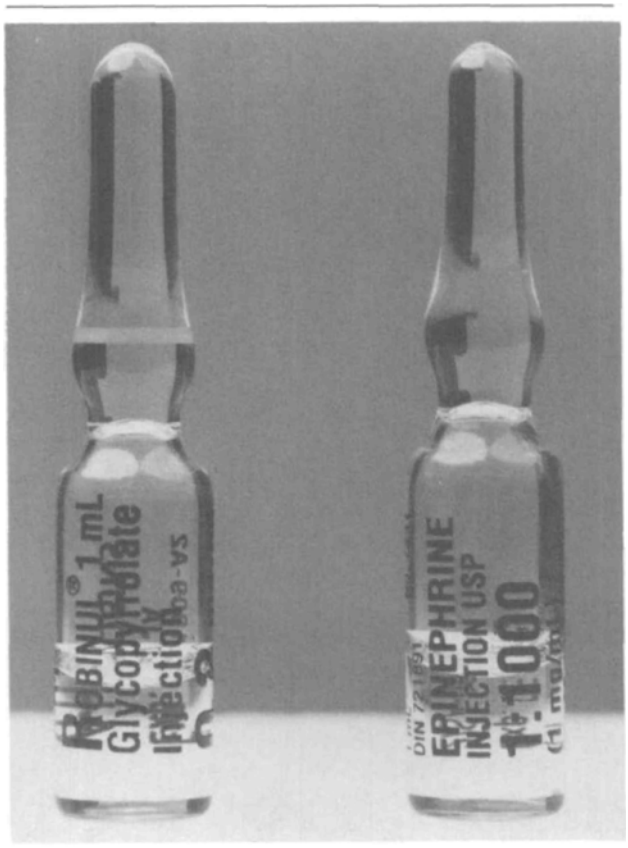

FIGURE 1 One ml ampoules of glycopyrrolate (Robinul, A.H. Robins) and epinephrine (USP-Abbott). The ampoules have the same size and shape, and the labels are printed with similar letter size, style and colour. Not evident in this illustration is the thin yellow band around the glycopyrrolate ampoule.

Immediately after transferring the patient to the Intensive Care Unit, the anaesthetist and resident returned to the operating room to investigate the incident. The container used for discarded glass and needles was emptied and the contents reviewed. A 1 ml ampoule of epinephrine 1:1000 (Abbott USP) was found (Figure 1). Chromatographic analysis of the remaining 4 ml of reversal solution revealed neostigmine 0.303 mg · ml^{-1}, glycopyrrolate 0.069 mg · ml^{-1}, and epinephrine 0.188 mg · ml^{-1}, indicating that one ampoule of glycopyrrolate was exchanged with one ampoule of epinephrine (Figure 2). The patient was informed of the drug error, and assured that subsequent anaesthetics would likely be uneventful.

Discussion

The patient described manifested signs typical of epinephrine overdose; sudden unexplained hypertension and tachyarrhythmias followed by hypotension, pulmonary oe-

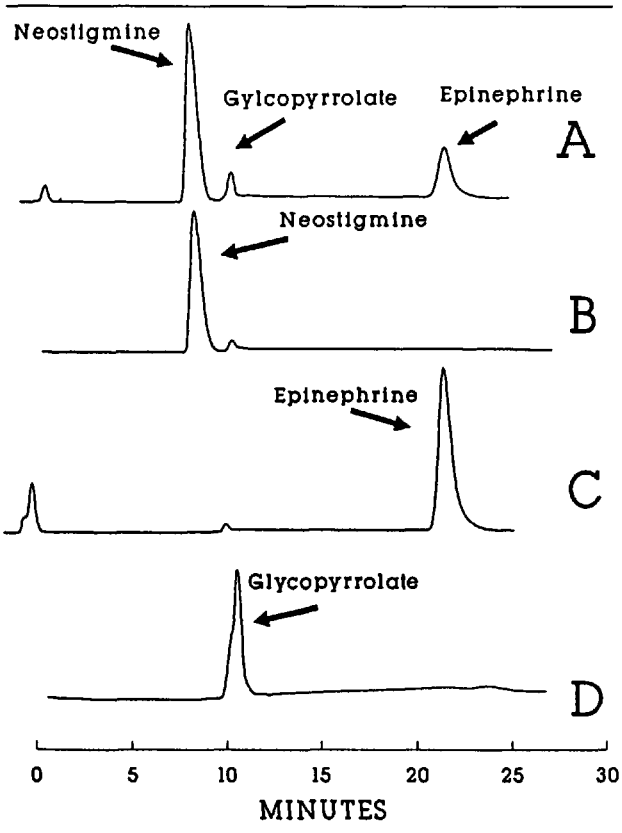

FIGURE 2 High performance liquid chromatography (HPLC) used for solution analysis. Panel A illustrates a typical chromatogram of the solution contained in the syringe. Panels B, C, D show retention times of control solutions used to measure the concentration of drug present. Ultra-violet (UV) photo-diode-array detection was then used to compare the UV spectrum of known concentration standards with the species present in the syringe. Based on identical retention times and less than a 5% difference in the UV spectra, there is no doubt that epinephrine was present in the syringe.

dema, hypokalaemia, hypomagnesaemia, hyperglycaemia and leucocytosis.[4-8] Inotrope overdose syndromes are not uncommon and their pharmacology and management have been reviewed previously.[9-14]

The need for systematic analysis of anaesthetic-related mishaps has been the subject of numerous articles in the recent literature.[15-17] The goal of risk management assessment is to identify the human errors and organizational factors that contributed to an anaesthetic mishap in order to prevent their recurrence. Guidelines to facilitate the collection and analysis of information concerning critical events have been provided.[18,19]

This case illustrates three important features of data collection. First, the investigation should begin as soon as possible. Second, the operating room should be closed and equipment left untouched until the investigation begins. Third, further cases should be postponed or transferred to another operating room until a preliminary study of the event is completed. This ensures that subsequent patients are not exposed to potential risks and that the collection of information is not hampered by the immediate need to use the operating room. When a drug error is suspected, syringes should be saved for analysis.

In addition to obvious human error, there were deficiencies in the health care "system" that also contributed to the mishap. First, the wrong drug was added to the glycopyrrolate section of the anaesthetic drug cart. In the operating rooms of our institution, epinephrine is normally stocked on the emergency resuscitation cart rather than on the anaesthetic drug cart. It was later learned that, on the day prior to the mishap, one epinephrine ampoule had been salvaged from a regional anaesthetic kit and left on top of the anaesthetic drug cart. It is likely that the same epinephrine ampoule was placed in the glycopyrrolate section of the drug drawer when the cart was cleaned. The second "systemic" deficiency was the use of similar packaging for two different drugs.

The case was reviewed by the Risk Management Team of the Department of Anaesthesia comprised of an Intensivist, the Quality Assurance Committee for the Department of Anaesthesia, the anaesthetists involved in the case, and the hospital pharmacist. Recommendations resulting from the analysis of the case are presented below:

1 *Proper identification of drug ampoules*
Above all, the best way to reduce the frequency of errors in medication administration is to read carefully the name, concentration, and expiry data on each drug ampoule before it is administered.

2 *Anaesthesia resident education*
Many residents, new to the operating room, are not experienced with the administration of injectable medications. During their initial anaesthesia orientation, they should be reminded of the meticulous attention required when handling intravenous drugs. They should be instructed to read the name, concentration and expiry date on the label before and after drawing a drug into a syringe. When the contents of multiple ampoules are mixed in a syringe, the number of ampoules should be recounted after the medication is prepared.

Residents and staff should also be encouraged to develop strict routines when labeling and organizing syringes on top of the anaesthetic cart. The carts should be cleared of unnecessary ampoules before the beginning of each case. All anaesthetic personnel should use extreme caution when administering medications which they did not prepare themselves.

3 *Drug packaging*

Whenever possible, each drug available on the anaesthetic cart should have distinct and unique markings. Packaging features such as ampoule shape, size, and material (plastic versus glass), label and cap colours should be considered.

In Canada, the guidelines for packaging and identification of medications are set by the Canadian Society of Hospital Pharmacists (CSHP). The Pharmaceutical Manufacturers Association (PMA) uses these guidelines to develop product packaging. Designs are then submitted for approval to the Bureau of Pharmaceutical Surveillance, Drugs Directorate, Health Protection Branch of the Ministry of Health and Welfare Canada.

Currently, there are no requirements for unique labels on any medications. Indeed, some pharmacists and clinicians feel that all markings should be identical to necessitate the careful reading of the labels. It is difficult to believe, however, that similar markings would reduce the number of drug errors. Anaesthetists would like to believe that they would never be too distracted or fatigued to misread an ampoule label, but the incidence of drug errors suggests otherwise. Careful reading of the drug labels is mandatory, but secondary cues such as label colour may prevent a "misread" from becoming an anaesthetic catastrophe.

Despite the lack of guidelines, most drugs required on the anaesthetic cart can be selected which have distinct markings. In our institution, if similar labeling of anaesthetic drug ampoules is likely to lead to confusion, the pharmacy purchasing agent is informed and an alternative pharmaceutical supplier is sought. On the rare occasion when an alternative supplier cannot be found, the manufacturers, anaesthesia staff and residents are cautioned regarding the potential for drug error. When a drug ampoule with markings similar to one routinely stocked on the anaesthetic cart is brought into the operating room, a fluorescent adhesive label is placed over the cap to warn of its contents.

A standard colour code system should be developed for anaesthetic drug ampoules. Colour codes have already been applied to volatile anaesthetic containers, gas cylinders, and adhesive syringe labels in an effort to reduce the likelihood of a drug error.[20,21] The concept of standard colour codes for injectable anaesthetic drug ampoules is not new.[21] As the number of different drugs in the anaesthetic cart increases, so does the need for an effective identification system.

4 *Reporting of drug errors*

Currently in Canada, there is no federal programme for reporting drug packaging problems. Unlike the American Food and Drug Administration (FDA) which considers adverse events, as well as problems associated with drug packaging, the provincial Canadian Adverse Drug Reaction Programmes are only interested in adverse drug reactions. Concerns regarding packaging and all reports of drug errors associated with drug labeling should be forwarded to the Canadian Society of Hospital Pharmacists (CSHP). As well, the Pharmaceutical Manufacturers Association (PMA) and the Canadian Drug Manufacturers Association (CDMA) should also be notified. The addresses for these agencies are listed below. We strongly encourage reporting by anaesthetists as this information can be used to encourage drug companies to adopt more effective labeling systems.

5 *Drug location*

Each drug stocked on the anaesthetic cart should have a specific, labeled location. Drugs that are not normally stocked on the anaesthetic cart (e.g., antibiotic solutions, KCl solution) should not be left to collect in the corners of the drawers or on top of the cart.

6 *Drug cart check list*

The anaesthetic equipment check list should include a section for documenting errors in the stocking of the anaesthetic drug cart. This would allow recurrent errors to be identified and corrected.

As the tasks of anaesthetists become increasingly complex, systems must be adopted that reduce the potential for human error. Although anaesthetists have led the medical community in the development of risk management techniques, research into the prevention of anaesthetic accidents remains in its infancy. Studies which identify medication errors and techniques for their prevention should be encouraged and facilitated. In the interim, anaesthetists should inform the CSHP, PMA and the CDMA of drug errors associated with similar drug packaging and make their concerns known.

Canadian Society of Hospital Pharmacists
Suite 350, 1145 Hunt Club Road,
Ottawa, Ontario K1V 0Y3
Phone: (613) 736–9733
Fax: (613) 736–5660

Pharmaceutical Manufacturers' Association
302 – 11 Prince of Wales Drive,
Ottawa, Ontario K2C 3T2
Phone: (613) 727–1380
Fax: (613) 727–1407

Canadian Drug Manufacturers' Association
Suite 606, 4120 Yonge St.,
North York, Ontario M2P 2B8
Phone: (416) 223-2333
Fax: (416) 223-2425.

Acknowledgements

The authors would like to thank Mr. S. Walker and Drs. N. Shear and S. Yamashita for their assistance with chromatographic analysis, Dr. J. Iazzetta for his suggestions, and Dr. Graeme Rocker for reviewing the manuscript.

References

1 *Cooper JB, Newbower RS, Kitz RJ.* An analysis of major errors and equipment failures in anesthesia management: considerations for prevention and detection. Anesthesiology 1984; 60: 34–42.

2 *Chopra V, Bovill JG, Spierdijk J.* Accidents, near accidents and complications during anaesthesia: a retrospective analysis of a 10-year period in a teaching hospital. Anaesthesia 1990; 45: 3–6.

3 *Smellie GD, Lees NW, Smith EM.* Drug recognition by nurses and anaesthetists. Anaesthesia 1982; 37: 206–8.

4 *Carter BT, Westfall VK, Heironimus TW, Atuk NO.* Severe reaction to accidental subcutaneous administration of large doses of epinephrine. Anesth Analg 1971; 50: 175–8.

5 *Karch SB.* Coronary artery spasm induced by intravenous epinephrine overdosage. Am J Emerg Med 1989; 7: 485–8.

6 *Fyfe AI, Daly PA, Dorian P, Tough J.* Reversible "cardiomyopathy" after accidental adrenaline overdose. Am J Cardiol 1990; 67: 318–9.

7 *Novey HS, Meleyco LN.* Alarming reaction after intravenous administration of 30 ml of epinephrine. JAMA 1969; 207: 2435–6.

8 *Rosa RM, Silva P, Young JB, et al.* Adrenergic modulation of extrarenal potassium disposal. N Engl J Med 1980; 302: 431–4.

9 *Wood M.* Drugs and the sympathetic nervous system. *In*: Wood M, Wood AJJ (Eds.).: Drugs and Anaesthesia, Baltimore: Williams & Wilkins, 1990: 375–405.

10 *Levine RD, Orkin LR.* Epinephrine overdose: a continuing problem. N Y State J Med 1981: 1669–70.

11 *Reich DL, Bucek JL, Wolf NM, Klumpe DB, Cullen DJ.* General anesthesia complicated by unexpected hypertension and tachycardia. J Cardiothorac Vasc Anesth 1992; 6: 360–5.

12 *Ryzen E, Servis KL, Rude RK.* Effect of intravenous epinephrine on serum magnesium and free intracellular red blood cell magnesium concentrations measured by nuclear magnetic resonance. J Am Coll Nutr 1990; 9: 114–9.

13 *Freedman BJ.* Accidental adrenaline overdosage and its treatment with piperoxan. Lancet 1955; 2: 575–6.

14 *Larsen LS.* Labetalol in the treatment of epinephrine overdose. Ann Emerg Med 1990; 19: 680–2.

15 *Rendell-Baker L.* Standards for anesthetic and ventilatory equipment. Int Anesthesiol Clin 1982; 20: 171–90.

16 *Eagle CJ, Davies JM, Reason J.* Accident analysis of large-scale technological disasters applied to an anaesthetic complication. Can J Anaesth 1992; 39: 118–2.

17 *Gaba DM, Maxwell M, DeAnda A.* Anaesthetic mishaps: breaking the chain of accident evolution. Anesthesiology 1987; 66: 670–6.

18 *Caplan RA.* In-depth analysis of anesthetic mishaps: tools and techniques. Int Anesthesiol Clin 1989; 27: 153–160.

19 *Cohen JA.* Quality assurance and risk management. *In*: Gravenstein N (Ed.). Manual of Complications During Anaesthesia, New York: Lippincott, 1991: 1–44.

20 *Rendell-Baker L.* Reducing syringe swap errors (Letter). Anesthesiology 1993; 78: 623.

21 *Rendell-Baker L.* Standards for anaesthesia: the issues. Contemporary Anaesthesia Practice 1984; 8: 59–88.