General Anesthesia

Programming errors contribute to death from patient-controlled analgesia: case report and estimate of probability

[Des erreurs de programmation en cause dans un décès lié à l'analgésie auto-contrôlée : une étude de cas et une estimation de la probabilité]

Kim J. Vicente PhD,*†‡§¶ Karima Kada-Bekhaled MA,† Gillian Hillel BASc,†‡ Andrea Cassano,† Beverley A. Orser MD#

Purpose: To identify the factors that threaten patient safety when using patient-controlled analgesia (PCA) and to obtain an evidence-based estimate of the probability of death from user programming errors associated with PCA.

Clinical features: A 19-yr-old woman underwent Cesarean section and delivered a healthy infant. Postoperatively, morphine sulfate (2 mg bolus, lockout interval of six minutes, four-hour limit of 30 mg) was ordered, to be delivered by an Abbott Lifecare 4100 Plus II Infusion Pump. A drug cassette containing 1 mg·mL^{-1} solution of morphine was unavailable, so the nurse used a cassette that contained a more concentrated solution (5 mg·mL^{-1}). 7.5 hr after the PCA was started, the patient was pronounced dead. Blood samples were obtained and autopsy showed a toxic concentration of morphine. The available evidence is consistent with a concentration programming error where morphine 1 mg·mL^{-1} was entered instead of 5 mg·mL^{-1}. Based on a search of such incidents in the Food and Drug Administration MDR database and other sources and on a denominator of 22,000,000 provided by the device manufacturer, mortality from user programming errors with this device was estimated to be a low likelihood event (ranging from 1 in 33,000 to 1 in 338,800), but relatively numerous in absolute terms (ranging from 65–667 deaths).

Conclusion: Anesthesiologists, nurses, human factors engineers, and device manufacturers can work together to enhance the safety of PCA pumps by redesigning user interfaces, drug cassettes, and hospital operating procedures to minimize programming errors and to enhance their detection before patients are harmed.

Objectif : *Déterminer les facteurs qui mettent en danger la sécurité des patients qui utilisent l'analgésie auto-contrôlée (AAC) et obtenir une estimation de la probabilité de décès basée sur des preuves, à partir des erreurs de programmation de l'AAC.*

Éléments cliniques : *Une femme de 19 ans a donné naissance, par césarienne, à un enfant en bonne santé. Après l'opération, du sulfate de morphine (bolus de 2 mg, période réfractaire de 6 min, limite de 30 mg en 4 h), a été administré avec une pompe à perfusion Abbott Lifecare 4100 Plus II. Une cassette de médicament contenant une solution de 1 mg·mL^{-1} de morphine n'étant pas disponible, l'infirmière a utilisé une solution plus concentrée (5 mg·mL^{-1}). On a constaté le décès de la patiente 7,5 h après le début de l'AAC. Les échantillons de sang et l'autopsie ont montré une concentration toxique de morphine. La preuve présentée est compatible avec une erreur de programmation de la concentration alors que 1 mg·mL^{-1} de morphine plutôt que 5 mg·mL^{-1} était noté. Fondée sur une recherche d'incidents semblables dans la base de données MDR de la Food and Drug Administration et dans d'autres sources, et selon un ensemble de 22 000 000 de données fournies par le fabricant du dispositif, la mortalité résultant d'erreurs de programmation par l'utilisateur a été estimée comme un incident de faible occur-*

From the Department of Aeronautics and Astronautics,* Massachusetts Institute of Technology, Massachusetts, USA; the Cognitive Engineering Laboratory,† the Department of Mechanical and Industrial Engineering; the Institute of Biomaterials and Biomedical Engineering,‡ the Department of Computer Science,§ the Department of Electrical and Computer Engineering;¶ and the Departments of Anesthesia and Physiology,# Sunnybrook and Women's College Health Science Centre, University of Toronto, Toronto, Ontario, Canada.

Address correspondence to: Dr. Kim J. Vicente, Department of Mechanical & Industrial Engineering, University of Toronto, 5 King's College Road, Toronto, Ontario M5G 3G8, Canada. Phone: 416-978-7399; E-mail: vicente@mie.utoronto.ca, URL: www.mie.utoronto.ca/labs/cel/

This research was sponsored by the Jerome Clarke Hunsaker Distinguished Visiting Professorship at MIT and by a research grant from the Natural Sciences and Engineering Research Council of Canada to the first author.

Accepted for publication August 20, 2002.

Revision accepted November 29, 2002.

rence (de 1 sur 33 000 à 1 sur 338 800), mais relativement important en valeur absolue (de 65 à 667 décès).

Conclusion : *Les anesthésiologistes, le personnel infirmier, les ergonomes et les fabricants d'appareils peuvent collaborer à l'amélioration de la sécurité des pompes à AAC en repensant les interfaces-utilisateurs, les cassettes de médicaments et les modes d'emploi hospitalier, ce qui peut réduire les erreurs de programmation et hâter leur détection avant que les patients en souffrent.*

PATIENT-CONTROLLED analgesia (PCA) pumps were developed to provide for the safe, self-administration of analgesics.[1] The potential benefits of PCA include improved pain management and better utilization of nursing resources. However, analgesics are consistently a leading cause of adverse drug events (ADE).[2,3] Preventable ADE are estimated to cost $2 billion annually in the U.S. alone (not including malpractice claims).[4] Reports of safety hazards and deaths associated with PCA pumps have appeared since this technology was first introduced, and now number in the dozens.[5–19] Therefore, it is important to understand the factors that threaten patient safety with the use of PCA pumps. To contribute to this goal, we report a case where a patient died as a result of a drug overdose.

This sentinel case was brought to our attention by the lay press. We made a request through the Freedom of Information Act to obtain the patient records, autopsy report, toxicology results, and interviews conducted as part of a criminal investigation. This information provides new insights into how anesthesiologists, nurses, human factors engineers, and medical device manufacturers can work together to enhance the safety of PCA pumps.

Case report

A previously healthy, 19-yr-old, 73 kg woman underwent a Cesarean section for failure to progress. Prior to surgery, an epidural catheter had been inserted for analgesia during labour. Lidocaine 2% with 1:200,000 epinephrine (total volume 29 mL) and 100 µg fentanyl were administered for surgical anesthesia. After delivering a healthy infant, the patient received an additional fentanyl 100 µg, intravenously. Two hours later, the epidural catheter was removed and the anesthesiologist ordered morphine sulfate by a PCA pump (2 mg bolus, lockout interval of six minutes, four-hour limit of 30 mg). Two different concentrations of morphine were normally available for PCA use in the hospital (1 $mg \cdot mL^{-1}$ and 5 $mg \cdot mL^{-1}$). In this case, a cassette containing 1 $mg \cdot mL^{-1}$ solution of morphine was unavailable, so the nurse obtained a cassette containing the more concentrated morphine solution (5 $mg \cdot mL^{-1}$) and inserted it into an Abbott Lifecare 4100 PCA Plus II Infusion Pump[A] (Abbott Laboratories, North Chicago, IL, USA). The patient was transferred to the ward approximately three hours after delivery. Upon arrival, a different nurse reviewed the "history setting" on the PCA pump and noted that it was programmed to deliver morphine 2 mg, with a six-minute lockout and maximum four-hour dose of 30 mg. She stated that she did not check the setting of the drug concentration on the device, did not open the pump to check the drug cassette because she did not have a key, and thus, did not read the label on the cassette nor assess the volume of drug infused.

Four hours after delivery, the patient breast-fed her infant but complained of itching. Benadryl 25 mg was administered intravenously, followed 45 min later by a second dose of benadryl 25 mg. Six hours after delivery, the patient was noted to be alert, oriented, and awake. However, later in the evening, she was found asleep and snoring loudly. A nurse noted that 20 mg of morphine had been infused. She shook the patient but was unable to arouse her. Because the nurse considered the vital signs to be normal (blood pressure 110/51 mmHg; heart rate 123 $beats \cdot min^{-1}$; respiratory rate 20$\cdot min^{-1}$), no further action was taken. Thirty minutes later, the patient had no detectable pulse or respirations. Despite resuscitation efforts, she was pronounced dead 9.5 hr after delivery.

Abbott Lifecare 4100 PCA Plus II Infusion Pumps have a memory feature that records 200 events. A record of the drug delivery history from the PCA pump was unavailable because the pump was not taken out of service after the ADE. During the autopsy, it was noted that the morphine cassette connected to the patient's *iv* contained 7 mL of the original 30 mL. Analysis of blood samples showed a toxic concentration of morphine (free morphine concentration 170 $ng \cdot mL^{-1}$; total morphine concentration 761 $ng \cdot mL^{-1}$). Analysis of the contents of the morphine cassette showed the morphine concentration was 3.8 $mg \cdot mL^{-1}$. The hospital had 76 Abbott Lifecare 4100 PCA Plus II Infusion Pumps, and 75 were tested for hardware and software failures (one pump could not be located). No hardware or software failures that could have caused an overmedication were detected.

A Lifecare is a registered trademark of Abbott Laboratories.

Discussion

Since 23 of the 30 mL of morphine solution had infused from the drug cassette, the patient likely received 100 mg to 115 mg of morphine over a seven-hour period. This overdose could have occurred if the PCA pump was incorrectly programmed to a morphine concentration of 1 $mg \cdot mL^{-1}$ rather than 5 $mg \cdot mL^{-1}$. This interpretation would also explain why the four-hour limit of 30 mg did not safeguard the patient, and why, about one hour before the patient was declared dead, another nurse noted that only 20 mg rather than 100 mg (i.e., 20 mL of 5 $mg \cdot mL^{-1}$) had been infused. Additional factors that may have contributed to the ADE include tampering with the PCA device, a suboptimal response by the second nurse, inadequate drug stocking procedures, and the total dose of analgesic administered at the time of surgery. However, a programming error is likely the major factor because it accounts exactly for a 5:1 ratio between the actual amount of morphine delivered and the incorrect amount displayed by the device. Notably, the nurse who programmed the PCA device had been an honour roll student, had a spotless professional record, and stated that she had programmed the PCA at least 50 times per year since 1996 without any problems. Thus, insufficient training or experience are unlikely to have been significant contributors.

To determine whether similar problems have occurred, an exhaustive search of the U.S. Food and Drug Administration (FDA) MDR database (as of July, 2000) and of the published literature was conducted for deaths attributed to user error with the Abbott Lifecare 4100 PCA system. The results are shown in Table I. All reported user error deaths with this device were explicitly attributed to programming of drug concentration. This particular type of error is extremely dangerous because entering an incorrect, lower drug concentration can cause up to four enduring problems: a) over-delivery of bolus dose by the caregiver; b) over-delivery of subsequent PCA doses; c) over-delivery of a continuous infusion dose; and d) an increase in the total amount of drug infused during a four-hour period.

Several ADE reports stated that caregivers incorrectly accepted the first concentration value presented by the device during the programming sequence. For example, in one operating configuration, the device offers an initial concentration value of 0.1 $mg \cdot mL^{-1}$. The caregiver can either accept or modify this value using the arrow controls. In at least one case, the

TABLE I Reported incidents of mortality from programming errors with the Abbott Lifecare 4100 PCA system. FDA MDR reports can be found at www.fda.gov/cdrh/mdr/

Number of deaths	*Source*	*Error type*
1	FDA MDR # 28379, report date 10/12/1995	Concentration set at 1 $mg \cdot mL^{-1}$ instead of 10 $mg \cdot mL^{-1}$
1	FDA MDR # 35355, report date 7/01/1996	Concentration set ten times lower than desired
1	FDA MDR # 2921482-1997-00058, report date 3/25/1997	Concentration set at 0.1 $mg \cdot mL^{-1}$ instead of 1 $mg \cdot mL^{-1}$
2 or 3*	ECRI (1997)[8]	Concentration set ten times lower than desired
1	ISMP (1999)[13]	Concentration (details unknown)
1	This article	Concentration set at 1 $mg \cdot mL^{-1}$ instead of 5 $mg \cdot mL^{-1}$
TOTAL	5 to 8	

* The ECRI reports are anonymous so it is not possible to determine whether there is any overlap between these two or three cases and the three cases previously reported to the Food and Drug Administration MDR database.

TABLE II Epidemiological analysis of mortality from programming errors associated with the Abbott Lifecare 4100 PCA system over a 12-yr period (1988–2000). Minimum and maximum values are based on the smallest and largest total values from Table I, respectively. Low estimates are based on a 7.7% reporting rate, and high estimates on a 1.2% reporting rate. Probability estimates were calculated using a conservative denominator of 22 million.

		Estimates of true Mortality incidence		*Estimates of true Mortality probabilities*	
	Reported deaths	*Low*	*High*	*Low*	*High*
Min	5	65	417	2.95×10^{-6}	1.89×10^{-5}
Max	8	104	667	4.72×10^{-6}	3.03×10^{-5}

incorrect initial value of 0.1 $mg \cdot mL^{-1}$ was accepted rather than modified to the correct value of 1.0 $mg \cdot mL^{-1}$, causing a ten-time overdose. In the factory preset configuration, this device sequentially offers four default options for programming of the drug concentration (i.e., morphine 1 $mg \cdot mL^{-1}$, morphine 5 $mg \cdot mL^{-1}$, morphine 0.5 $mg \cdot mL^{-1}$, and meperidine 10 $mg \cdot mL^{-1}$). In several cases, the caregiver likely accepted the initial lower concentration value rather than modifying it to 10 $mg \cdot mL^{-1}$ or 5 $mg \cdot mL^{-1}$, thereby causing a ten- or five-time overdose. The commonality in these cases is important; recent laboratory research shows that redesigning the programming interface for this particular device may virtually eliminate concentration programming errors.[20]

It is well known that voluntary and mandatory reporting systems for adverse events and ADE, including the FDA MDR database, suffer from severe underreporting; epidemiological studies revealed reporting rates that ranged from a low of 1.2% to a high of 7.7%.[2,21–23] We used these extreme values to transform the minimum and maximum reported frequencies in Table I into evidence-based high and low estimates of the true incidence of patient mortality associated with programming errors with this device. The results are shown in Table II. These estimates can be transformed into probability and likelihood estimates using the total number of patients treated as a denominator; in March, 2001, the manufacturer reported: "Since Abbott's LifeCare PCA system was introduced in 1988, more than 22 million patients have used it safely".[24] These results, also shown in Table II, suggest that PCA mortality from user programming error is a low probability event, ranging from 3.03×10^{-5} to 2.95×10^{-6} (i.e., 1 in 33,000 to 1 in 338,800) for this device. Nevertheless, because PCA usage with this device is so widespread, mortality events may be relatively numerous, ranging from 65–667. Clearly, the true number of deaths is unknown, but is likely to be higher because the MDR data are from the U.S., while this device has been used in many other countries. Note also that these estimates are only for deaths attributed to user errors, and thus do not include deaths caused by other factors (e.g., inappropriate prescription, patient tampering, hardware failure, software failure). By way of comparison, the likelihood of death from general anesthesia is 1 per 200,000 to 300,000.[25] Therefore, efforts to enhance the safety of PCA pumps even further are worthwhile.

This case report suggests several recommendations. First and foremost, user interfaces for PCA pumps should be redesigned to make them easier to program based on human factors engineering techniques.[20] Second, caregivers should always report any difficulty, near miss, injury, or death associated with PCA pumps and other medical devices using Health Canada's Medical Devices Problem Report Form so that the true magnitude of the problem can be established. The required form is easy to fill out and can be found on the internet (www.hc-sc.gc.ca/hpfb/inspectorate/md_pro_rep_form_tc_e.html). Third, caregivers should check and chart the amount of solution missing from the cassette (not simply the value presented on the pump display). Fourth, labels on drug cassettes should be designed to facilitate reading the amount of infused drug at a glance. Gradations on these labels should be scaled to the concentration of the analgesic and display the mass directly, thereby removing the need for mental arithmetic (i.e., converting volume and concentration to mass). Fifth, hospitals should require an independent "double-check" by a second caregiver when the PCA pump is programmed. This safeguard is not fool-proof, but provides an added means of detecting error. Sixth, a single concentration of morphine (e.g., 1 $mg \cdot mL^{-1}$ cassettes) should be generally stocked to avoid confusion. Special precautions should be instituted when cassettes with higher concentrations are required for patients with exceptionally high analgesic requirements. Finally, when an adverse event occurs, the room and equipment should be secured and the investigation started immediately to maximize the available information and to increase the chance of learning from experience.

Anesthesiologists, nurses, human factors engineers, and device manufacturers are keenly interested in ensuring patient safety. By working together to implement these recommendations, this important goal can be advanced.

Acknowledgements

We would like to thank Jeff Cooper and the reviewers for their comments.

References

1 *Ferrante FM, Ostheimer GW, Covino BG.* Patient-Controlled Analgesia. Boston: Blackwell Scientific; 1990.

2 *Classen DC, Pesotnik SL, Evans RS, Burke JP.* Computerized surveillance of adverse drug events in hospital patients. JAMA 1991; 266: 2847–51.

3 *Bates DW, Cullen DJ, Laird N, et al.* Incidence of adverse drug events and potential adverse drug events. Implication for prevention. JAMA 1995: 274: 29–34.

4 *Bates DW, Spell N, Cullen DJ, et al.* The costs of adverse drug events in hospitalized patients. JAMA

1997; 277: 307–11.
5 *Baxter AD.* Respiratory depression with patient-controlled analgesia (Editorial). Can J Anaesth 1994; 41: 87–90.
6 *Doyle DJ, Vicente KJ.* Patient-controlled analgesia (Letter). CMAJ 2001; 164: 620.
7 *Doyle DJ, Vicente KJ.* Electrical short circuit as a possible cause of death in patients on PCA machines: report on an opiate overdose and a possible preventive remedy (Letter). Anesthesiology 2001; 94: 940.
8 *Emergency Care Research Institute.* Abbott PCA Plus II patient-controlled analgesic pumps prone to misprogramming resulting in narcotic overinfusions. Health Devices 1997; 26: 389–91.
9 *Etches RC.* Respiratory depression associated patient-controlled analgesia: a review of eight cases. Can J Anaesth 1994; 41: 125–32.
10 *Geller RJ.* Meperidine in patient-controlled analgesia: a near-fatal mishap. Anesth Analg 1993; 76: 655–7.
11 *Grey TC, Sweeney ES.* Patient-controlled analgesia (Letter). JAMA 1988; 259: 2240.
12 *Grover ER, Heath ML.* Patient-controlled analgesia. A serious incident. Anaesthesia 1992; 47: 402–4.
13 *Institute for Safe Medication Practices.* Evidence builds: lack of focus on human factors allows error-prone devices. ISMP Medication Safety Alert 1999; 4: 1–2.
14 *Kwan A.* Overdose of morphine during PCA (Letter). Anaesthesia 1995; 50: 919.
15 *Looi-Lyons LC, Ching FF, Chan VW, McQuestion M.* Respiratory depression: an adverse outcome during patient controlled analgesia therapy. J Clin Anaesth 1996; 8: 151–6.
16 *Notcutt WG, Knowles P, Kaldas R.* Overdose of opioid from patient-controlled analgesia pumps. Br J Anaesth 1992; 69: 95–7.
17 *Simes D, Power L, Priestley G.* Respiratory arrest with patient-controlled analgesia (Letter). Anaesth Intensive Care 1995; 23: 119–20.
18 *Weinger MB, Pantiskas C, Wiklund ME, Carstensen P.* Incorporating human factors into the design of medical devices (Letter). JAMA 1998; 280: 1484.
19 *White PF.* Mishaps with patient-controlled analgesia. Anesthesiology 1987; 66: 81–3.
20 *Lin L, Vicente KJ, Doyle DJ.* Patient safety, potential adverse drug events, and medical device design: a human factors engineering approach. J Biomed Inform 2001; 34: 274–84. (www.idealibrary.com/links/doi/10.1006/jbin.2001.1028/pdf, February 19, 2003).
21 *Cullen DJ, Bates DW, Small SD, Cooper JB, Nemeskal AR, Leape LL.* The incident reporting system does not detect adverse drug events: a problem for quality improvement. Jt Comm J Qual Improv 1995; 21: 541–8.
22 *Gardner S, Flack M.* Designing a medical device surveillance network. FDA report to Congress. 1999. (www.fda.gov/cdrh/postsurv/medsun.html, February 19, 2002).
23 *Jha AK, Kuperman GJ, Teich JM, et al.* Identifying adverse drug events: development of a computer-based monitor and comparison with chart review and stimulated voluntary report. J Am Med Inform Assoc 1998; 5: 305–14.
24 *McLeskey CH.* Patient-controlled analgesia (Letter). CMAJ 2001; 164: 620–1.
25 *Joint Commission on Accreditation of Healthcare Organizations.* Sentinel events: approaches to error reduction and prevention. Jt Comm J Qual Improv 1998; 24: 175–86.