Intravenous Phenytoin: Rate of Administration is Critical

Phenytoin has been in use for decades, but healthcare providers should remain alert to potential risks. Analysis of an incident report received through the National System for Incident Reporting (NSIR)* suggests opportunities to enhance system safeguards with this medication when prescribed for intravenous (IV) administration. The hospital where the incident occurred wanted to share the information and learning from the analysis, to help prevent similar incidents elsewhere.

Background

In Canada, phenytoin is approved for the management of generalized tonic-clonic seizures, simple or complex partial seizures, and status epilepticus, as well as for the treatment and prevention of seizures during or following head trauma or neurosurgery.† It is available in various dosage forms for IV, oral, or enteral administration.

In the United States, the product monograph for phenytoin has a “black box” warning about cardiovascular risks associated with the rate of IV administration. The warning states that the rate of IV administration of phenytoin to adults should never exceed 50 mg/min (because of the risk of severe hypotension and cardiac arrhythmias) and recommends cardiac monitoring during and after IV administration of the drug.‡ The Canadian product monograph suggests similar infusion rates but further recommends that rates for elderly patients and those with cardiovascular disease should be significantly lower, not exceeding 25 mg/min.

Medication Incident

An elderly patient was receiving care in an intensive care unit. Phenytoin 100 mg daily by IV push was ordered for the patient.† The phenytoin was administered at a rate of 50 mg/min. During administration of phenytoin by IV push, the patient experienced an episode of ventricular standstill (i.e., had no pulse). Treatment was implemented immediately, and the patient’s heart rate and blood pressure recovered shortly thereafter.

Review of ISMP Canada Incident Database

This incident report prompted a review of the ISMP Canada medication incident database for the period November 4, 2002, to November 4, 2012, to identify any similar incidents involving IV phenytoin. A total of 93 incidents were identified, of which 9 were reported to have caused harm (but no deaths). None of the reported “no harm” events identified “rate of

* The NSIR (provided by the Canadian Institute for Health Information) is a component of the Canadian Medication Incident Reporting and Prevention System (CMIRPS) Program. More information about the NSIR is available from: http://www.cmirps-scdpim.ca/?p=12.
† Medication administration rates for IV push will vary depending on the properties of the particular medication. Guidance is typically provided in drug information resources such as IV manuals.
‡ The incident discussed here was selected for analysis by ISMP Canada on October 5, 2011. The analysis and information reported here are based on review and follow-up with the incident reporter by ISMP Canada.
administration” as the error type or mentioned the rate of administration in a description field. Of the 9 incidents reported to have caused harm, 2 appeared to be related to the rate of administration, and 1 of these was reported to have caused severe harm.

**Incident Findings**

In collaboration with the reporting facility, the following potential underlying causes of the medication incident were identified:

- The prescription for a daily maintenance dose of phenytoin specified that the drug be given IV push daily.
- Available drug information confirmed that a nurse may administer phenytoin by IV push in the critical care setting. The routine administration of other types of medications by IV push in the critical care setting reduced the likelihood that the order would be questioned.
- There was a lack of awareness about the high risk of serious consequences if phenytoin is administered to an elderly patient at a rate exceeding 25 mg/min.

In addition to these factors, it is important for practitioners to be aware of other potential factors that may contribute to such incidents:

- The rate of administration of sodium chloride 0.9% solution (which is typically administered, by infusion pump or syringe, for flushing after IV administration of a drug) may also be critical, as the flush rate will affect the overall rate of drug administration. For example, if undiluted phenytoin (100 mg in 2 mL) is administered through the injection port of the IV tubing, some of the 2 mL volume of drug may remain in the tubing. It will be the sodium chloride 0.9% solution (and the rate at which it is administered) that will determine the rate at which the medication reaches the patient.
- Distractions in the practice environment (e.g., ventilator alarms, monitor alarms, other staff) are common and can prevent the care provider from fully attending to or accurately tracking the time of administration. For example, in an analysis of delivery of high-alert medications in an observational human factors study, administration of medications by IV push had the most interruptions per task.³

**Recommendations**

Several facilities were contacted in follow-up to the incident described above. Some reported that they had already implemented restrictions relating to the use of IV phenytoin. With this information in mind, the following recommendations are provided:

- Avoid routine administration of an intermittent dose of phenytoin IV push. If oral or enteral therapy (preferred) is not an option, consider IV administration via an infusion pump (e.g., dilution in a minibag with administration as a secondary infusion). If applicable, ensure that smart infusion pumps include programmed limits within error-reduction software.
- If phenytoin must be given by IV push, ensure that this method of administration is restricted to patient care areas where close supervision and continuous cardiac monitoring are available.
- Review and revise facility-specific drug information (such as IV medication manuals) used to guide IV administration of phenytoin. Ensure that the information includes the following details:
  - Maximum administration rate of 25 mg/min for elderly patients or adults with a history of cardiac problems (e.g., patients at risk of arrhythmia and those with labile blood pressure or low cardiac output).¹
  - Prominent warning statement describing the cardiovascular risks if phenytoin is administered too rapidly.
  - Monitoring required (e.g., vital signs), as this is a key component of patient care that can provide an opportunity to identify unanticipated adverse effects.
  - Consider including guidance for the IV flush rate (whether manual or via infusion pump), which will affect the rate of delivery of the medication remaining in the IV tubing.
- Share this bulletin widely to raise awareness about the importance of the administration rate when giving phenytoin by the IV route.

¹ Phenytoin for IV administration should be admixed only in sodium chloride 0.9% because of incompatibility with other IV solutions. However, even when sodium chloride 0.9% is used for admixture and dilution of phenytoin, a precipitate may form. Use of an in-line filter (0.22 to 0.5 micron) is therefore recommended.¹²⁴
Phenytoin can play an important role in the control of seizures. However, to prevent an incident similar to the one described here, precautions must be taken to address the risks of severe hypotension and cardiac arrhythmias related to the rate of IV administration. It is hoped that this bulletin and the recommendations presented here will assist organizations as they endeavour to reduce such serious, yet preventable adverse events.

**Conclusion**

A physician wrote a medication order for a patient who needed analgesia for pain (Figure 1).

![Prescription for morphine received.](image)

After writing the prescription for “morphine 1 mg”, the physician changed the order by writing the number “2” over top of the “1” in the dosage. As a result, the order was misinterpreted as “morphine 8 mg”. The patient received several doses at quadruple the intended amount before the error was identified and corrected. The patient did not experience any harm, although additional monitoring was required.

Whenever information in a handwritten communication (e.g., a prescription or a transcription) must be altered, it is best to cross out the incorrect information and start over.

**Brand Name Change for Dabigatran: Pradax Is Now Pradaxa**

In 2011, ISMP Canada published a safety alert (based on voluntary reports received) to highlight the potential for confusion between the brand names Pradax (dabigatran etexilate) and Plavix (clopidogrel). As an update, the brand name for dabigatran etexilate has recently been changed from Pradax to Pradaxa. As of January 2013, the new brand name will appear on packaging and labelling; however, any products labelled “Pradax” that are still in stock may be distributed and used as directed by a physician until the expiry date stated on the package. For additional information about the name change and transition, please visit the manufacturer’s website at: [http://www.boehringer-ingelheim.ca/content/dam/internet/opu/ca_EN/documents/humanhealth/Pradaxa_name_Change_HCP_Letter.pdf](http://www.boehringer-ingelheim.ca/content/dam/internet/opu/ca_EN/documents/humanhealth/Pradaxa_name_Change_HCP_Letter.pdf)

**Reference**

Phenytoin can play an important role in the control of epilepsy, as well as for the treatment and prevention of ventricular arrhythmias related to the rate of IV administration. It is hoped that this bulletin and the recommendations presented here will assist organizations as they strive to improve medication safety in all healthcare settings. ISMP Canada’s mandate includes analyzing medication incidents, making recommendations for the prevention of harmful medication incidents, and facilitating quality improvement initiatives.

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References