

Important Findings from an In-depth Analysis of a Medication Incident

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Contributions to this column are prepared by the Institute for Safe Medication Practices Canada, a key partner in the Canadian Medication Incident Reporting and Prevention System (CMIRPS). From time to time, ISMP Canada invites others to share learning based on local initiatives.

INTRODUCTION

In May 2007, the Alberta Cancer Board released the document *Fluorouracil Incident Root Cause Analysis*¹ for shared learning. The incident under analysis involved administration of a high dose of fluorouracil (4000 mg/m²; total dose 5250 mg) over 4 h instead of the intended 4 days. The protocol also included administration of a single dose of 100 mg cisplatin. The patient, a 43-year-old woman with advanced nasopharyngeal carcinoma, died 22 days later of the sequelae of fluorouracil toxicity, cumulative with cisplatin toxicity. The Institute for Safe Medication Practices Canada (ISMP Canada) was invited to provide external expertise for the root cause analysis of this event. Providing such assistance is one of ISMP Canada's defined roles in the Canadian Medication Incident Reporting and Prevention System. The recommendations in the report¹ were directed specifically toward safer management of high-dose fluorouracil protocols and may be relevant to the management of other chemotherapy agents and other high-alert medications. One of the recommendations was to disseminate widely the findings of the root cause analysis as a way to enhance awareness of the hazards identified. This article presents selected findings and excerpts from the report that are highly relevant to pharmacists.

Root cause analysis is a structured process for a comprehensive system-based review of critical incidents to determine what happened, why it happened, and what

can be done to reduce the likelihood of recurrence.² Root cause analysis of a medication incident identifies hazards, issues, contributing factors, and underlying causes. This information is used to develop safeguards to prevent similar adverse events or to mitigate harm to patients if an incident does occur again.

IDENTIFIED CAUSES RELEVANT TO HOSPITAL PHARMACISTS

The defined event for this analysis was the death of a patient due to the sequelae of fluorouracil toxicity, cumulative with cisplatin toxicity. This event was not the result of a single "root cause". Rather, a combination of actions and conditions, each of which on its own would not have caused the event, together were causal. Three primary causal chains were identified.

Fluorouracil overdose: The patient received fluorouracil 5250 mg over 4 h rather than 4 days. Seven causal chains led to the infusion rate being entered as 28.8 mL/h instead of 1.2 mL/h: miscalculation, opportunity for false confirmation on the pharmacy label, information required to program the pump not being part of the medication administration record (MAR), failure of the double-check process, a complex workload and multitasking, lack of feedback from the pump, and limited knowledge of the hazard.

Design of the chemotherapy protocol: The amount of fluorouracil contained in the infusion bag (4 days' supply), as per the treatment protocol for nasopharyngeal

carcinoma, was sufficient to result in an overdose. Cisplatin was administered as a single dose of 100 mg, also according to the protocol. (Some protocols use cisplatin 20 mg/m² daily for 5 days instead of a single dose.³)

Inability to mitigate harm from fluorouracil and cisplatin: The absence of an antidote or defined treatment plan for fluorouracil overdose increased the likelihood that a significant overdose would cause harm. In addition, the absence of a defined treatment protocol to reverse cisplatin toxicity increased the potential for cumulative toxicity with fluorouracil.

Through a process of cause-and-effect diagramming and analysis, each of these causal chains was expanded to provide a more detailed understanding of the underlying causes of the patient's death. The following causes and contributing factors described in the report are included here because of their high relevance to pharmacists.

Information Not in Physician Order or on MAR

Critical information was not clearly "mapped" among the medication order, the MAR, the pharmacy label, and the infusion pump.

The total dose was provided in the order and transcribed onto a handwritten MAR. The medication order, however, did not include some critical information, such as the total volume and the rate to be programmed into the pump, and this information was therefore not included on the MAR. Although this information was provided on the pharmacy label, it was not displayed in an optimal way, and additional unnecessary information was provided.

Reliance on Calculation at the Bedside

Nursing staff were required to complete a complex calculation involving multiple dimensions at the bedside (specifically, dose in milligrams divided by days, divided by hours, divided by concentration) to determine the infusion rate for administration. The calculation result was compared to the information on the pharmacy label for confirmation before the calculated rate was entered into the infusion pump.

Label Format Inconsistent with Pump Programming Requirements

Pharmacists and pharmacy technicians were not familiar with the pump's functionality; furthermore, they had not been involved in evaluating the pump, and thus were unaware of the information required for programming, the terminology used, and the required sequence of information.

No Defined Process to Periodically Review Label Requirements

The information on the label was based on an interpretation of legal requirements and professional guidelines. There was no process in place to periodically review label requirements in conjunction with changes in care processes and equipment.

Opportunity for False Confirmation on Pharmacy Label

The design of the pharmacy label was not in accord with the information needed by nurses to administer the medication. For example, a 24 hour infusion rate and an hourly infusion rate were both included. Human factors engineering principles such as prominence of critical information and optimal sequence of information display would have enhanced the label design.

Lack of Coordinated Team Response

There was no system in place to triage incidents for potential harm, nor was there a protocol for managing patients with an unexpected adverse medication incident. In the setting of chemotherapy overdose or infusion error, the need for immediate and short-term mitigation measures must be determined as soon as possible for best outcome.

PRIORITY RECOMMENDATIONS OF HIGH RELEVANCE TO PHARMACISTS

Of the 40 recommendations in the analysis report,¹ the following 15 require the direct involvement and commitment of pharmacists working as part of a multi-disciplinary team (e.g., the Pharmacy and Therapeutics Committee).

- Include critical information required for medication administration as part of standardized order sets in manual and electronic orders. For example, if optimal programming of an infusion pump requires data input of "total volume" and "rate of infusion", these data should be available in the medication order.
- Standardize communication of orders for infusion of medication to refer to rates as "millilitres per hour" instead of "millilitres per 24 hours".
- Standardize administration protocols for high-dose fluorouracil infusions; include this information and the critical calculations required as part of electronic order sets and/or preprinted manual orders.
- Design medication orders, MARs, and medication labels to ensure that the critical information required to program infusion pumps for administering



medications is available and provided in a logical sequence, with consistent terminology.

- Review pharmacy-generated medication labels in the context of medication administration requirements. Consider human factors design principles to improve readability (e.g., prominence of critical information, font size, contrast, white space).⁴⁵
- Develop standardized order sets for computerized prescriber order entry and pharmacy information systems that reflect the administration information needed by nurses.
- Incorporate checklists and calculations into medication order forms and MARS to embed check procedures where required.
- Enhance the institutional information system to provide a direct interface between the computerized prescriber order entry and pharmacy information systems.
- In the absence of “smart pump” technology for ambulatory infusion pumps, use pumps with safeguards such as controlled-rate delivery (e.g., elastomeric pumps or preset maximum rates for pumps with delivery in millilitres per hour, where this functionality is available).
- Develop a triage process for medication incidents to ensure timely medical review of incidents with a high potential to cause patient harm, regardless of the severity rating on the incident report.
- Create a multidisciplinary rapid response team that can be quickly convened to provide assistance in managing medication incidents with potential for serious harm.
- Develop a protocol for dealing with potentially serious medication incidents that includes the need to consider contacting the regional poison information centre.
- Participate in evaluation and usability testing of infusion pumps in current use and under consideration for purchase.
- Develop a mechanism to ensure adequate consultation with multiple front-line staff regarding medication use.
- Work with other health care leaders to improve awareness of the attributes of high-reliability organizations through ongoing education efforts and implementation of high-visibility safety-promotion activities.

IMPLEMENTATION UPDATE FROM THE ALBERTA CANCER BOARD

The Alberta Cancer Board has selected a pharmacist to lead implementation of the recommendations throughout the organization’s facilities in Alberta.

It was recognized that key organizational decisions were required with respect to the use of ambulatory continuous infusion pumps within the Alberta Cancer Board. The provincial Pharmacy and Therapeutics Committee reviewed current options available for ambulatory infusion pumps and considered the hierarchy of effectiveness of various safety strategies. A decision has been made to switch to elastomeric pumps for all fluorouracil protocols until smart pump technology for electronic ambulatory infusion pumps becomes available. Other drugs delivered by ambulatory continuous infusion will be evaluated to determine if they are compatible with elastomeric pump delivery. If continued use of electronic pumps is required, additional safety measures will be implemented. Centres within the Alberta Cancer Board will eliminate use of any pumps that require programming in millilitres per 24 hours. In addition, participation in clinical trials will be contingent on the ability to utilize the pumps that are in standard use in these centres.

Immediately after this incident occurred, pharmacy labelling procedures were changed, such that the “millilitres per 24 hours” information no longer appears. Further recommendations regarding incorporation of human factors engineering principles into the design of pharmacy labels will be reviewed over the coming months.

Work has also begun on a number of the other recommendations at the local level. In addition, a national committee has been convened to address implementation of the recommendations across the country. Further information on progress will be shared in future publications.

CONCLUSIONS

The system failures that were identified in this event analysis are known to exist in other cancer treatment centres; therefore, the same or a similar incident could happen elsewhere. In fact, ISMP Canada research has discovered 7 previous similar cases in which patients died. As well, a usability test conducted at another cancer centre with the same pump and label information resulted in programming of the same incorrect rate into the pump.

As medication and pharmaceutical care experts, pharmacists have the opportunity to provide leadership to enhance the safety of the medication-use process. Pharmacists in both clinical and administrative roles must make implementation of these recommendations a top priority to reduce the likelihood of this or a similar event anywhere in Canada.



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