Fluorouracil Mistake Ends With a Fatality

Applying the Lessons Learned Can Save Lives

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PROBLEM: The following scenario describes many breakdowns that led to a fatality with the use of a commonly used chemotherapy agent.

A 43-year-old cancer patient was being treated in an ambulatory clinic with a protocol that included high-dose fluorouracil and cisplatin (Platinol AQ, Bristol-Myers Squibb). She received 5,250 mg of fluorouracil (4,000 mg/m^2) over a period of *four hours* instead of *four days*, as intended. The order for fluorouracil was written as follows:

> *5-fluorouracil 5,250 mg (at 4,000 mg/m^2) intravenous once continuous over 4 days ... Continuous infusion via ambulatory infusion pump (baseline regimen dose = 1,000 mg/m^2/day = 4,000 mg/m^2/4 days).*

After a nurse reviewed the patient's orders, laboratory results, height, and weight, a pharmacy technician prepared the two medications. A pharmacist then checked the drugs before dispensing them to the clinic.

The fluorouracil bag contained about 130 mL of solution (a final concentration of 45.57 mg of fluorouracil/mL) before priming of the intravenous (IV) administration set was performed. The nurse used a calculator to determine the infusion rate and programmed the infusion pump to deliver fluorouracil at a rate of 28.8 mL/hour. However, 28.8 mL was the total volume of solution that should have been infused in *24 hours*, not in *1 hour*. The correct hourly infusion rate was 1.2 mL.

Another nurse was asked to confirm the calculation. She could not find a calculator and thus did the math in her head and on a scrap of paper; however, she did not recognize the first nurse's miscalculation. The infusion was started, and the patient was discharged with instructions to return four days later for the pump to be disconnected. The patient also received 100 mg of IV cisplatin that day.

Four hours after the patient was discharged from the clinic, she noticed that the pump was beeping and the IV bag was empty. The patient returned to the clinic immediately, where the error was recognized. An evening nursing supervisor notified an on-call physician about the mistake; the on-call physician suggested that no treatment was needed and that the patient should call again the next morning. The error was disclosed to the patient, and she was advised to drink plenty of liquids because of the large amount of drug that had been administered.

Two days after the wrong dosage was given, the physician called to check on the patient. Arrangements were made for the patient to come in the next day for assessment, although she was still feeling well. When the patient visited the clinic the next day, she complained of nausea, vomiting, and throat discomfort. She was treated and discharged. Because no beds were available, admission to the hospital was arranged for the next day.

The following day, the patient was hospitalized. During the next few weeks, profound mucositis and pancytopenia, hemodynamic collapse, and multiorgan failure ensued. Sadly, the patient died 22 days after the error had been made.

Unfortunately, the design of the treatment protocol (four days of high-dose fluorouracil in one infusion bag, combined with a single 100-mg dose of cisplatin) increased the likelihood that a mishap would occur. The cause of death was determined to be complications from fluorouracil toxicity, compounded by cisplatin toxicity. Several contributory factors played a role in the execution of the fluorouracil error. Some examples follow.

Miscalculations. The two nurses who programmed the pump and verified the settings carried out complex calculations at the bedside to determine the infusion rate in milliliters per hour. However, both nurses omitted a step, forgetting to divide the daily dose by 24 hours. The infusion rate (in mL/hour) did appear on the label of the infusion bag but not prominently. The first nurse did not notice that the infusion would last only four hours at her calculated rate of infusion.

Design of the pharmacy label. The label was difficult to read and unnecessarily listed the mL/24-hour rate of infusion (28.8 mL/24 hour) first and then the mL/hour rate of infusion (1.2 mL/hour) in parentheses. The nurses who miscalculated the hourly rate displayed confirmation bias; they thought that their erroneous computations were correct when they saw "28.8" as the first entry for the "rate" on the label. The nurses did not realize that the pharmacy had listed the mL/24-hour rate of infusion on the label *before* the mL/hour rate of infusion.

Failure of the double-check system. The nurse who double-checked the initial infusion rate calculation was distracted and was on the way to perform another task at the time. She did not use a calculator and performed the calculation mentally on paper. The checking process was thus informal and unstructured; further, there was no requirement to perform calculations independently or to document calculations or any other aspects of a checking process.

Complex workload. The work processes on the unit required multitasking, and the various tasks that needed to be accomplished were not in sequence in a stepwise fashion. Assignments included checking laboratory results, weighing the patient; assessing the patient's condition; reviewing the order, label, and calculations; programming the pump; and educating the patient. In this instance, the nurses performed many high-risk tasks—including attending to the infusion pump—simultaneously with other tasks.

Pump design. Flaws in the pump's

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design increased the cognitive burden associated with programming the pump. For example, programming choices were listed as mg/mL, µ/mL (for clarity, this should be written as mcg/mL), and mL (i.e., mL/hour). The prompt for container size actually required that the staff member enter the volume to be infused, and the review screen did not indicate the duration of the infusion that had been programmed. In addition, the pump was not a "smart" pump; it lacked dosage error-reduction software that could have detected excessive doses or programming errors.

Lack of familiarity with protocols. The nurse who programmed the pump had a low index of suspicion regarding the high infusion rate. She was new to the unit and had never administered a four-day fluorouracil infusion. The calculated rate of 28.8 mL/hour was not unusual, compared with other infusions delivered in the clinic.

Lack of preparation for managing overdoses. Staff members were uncertain how to best treat and support the patient after the overdose was detected. Depending on the degree of toxicity that occurs with chemotherapy, patients who are treated promptly for overdoses or serious adverse effects from prescribed doses of chemotherapy may be less likely to experience irreversible harm.

SAFE PRACTICE RECOMMENDATIONS. To prevent errors with programming of IV pumps and chemotherapy, staff members should follow several steps, as outlined next:

Standardizing key information on pharmacy labels. The information needed to program an infusion pump (e.g., total volume, concentration, hourly rate of infusion) should be displayed prominently in a standard, consistent fashion on pharmacy labels. Extraneous information, such as mL/24 hours, should be eliminated, and infusion rates should be communicated as an hourly rate. The pharmacy staff should be familiar with the pumps in use and with the programming processes.

Reviewing certification processes for chemotherapy. The organization should review the procedures by which certification is granted to nurses who administer chemotherapy. Supervisors should make any changes necessary to ensure that staff members demonstrate and maintain an appropriate level of skills, knowledge, and abilities before working independently.

Using pumps with safeguards. The use of smart pumps should be encouraged to maximize safety features such as dose alerts, limits for dosing and flow rates, and operator feedback to allow detection of pump-programming errors.

Enhancing independent double-checks. A structured process for conducting and documenting independent double-checks should be developed. Instructions related to this process should be incorporated into staff orientations and annual competency evaluations. Critical thinking should be emphasized during the preparation and checking of all chemotherapy agents. The need for calculations should be minimized as much as possible.

Reviewing the pump screens with patients. When teaching patients about their therapy, staff members should include a review of pump data-input screens. This step can provide a last chance for nurses or other health care professionals to review data input and detect any incorrect programming.

Defining treatment protocols for accidental overdoses. A treatment protocol for a fluorouracil overdose should be specified, and a description of aggressive supportive care in the immediate treatment plans should be provided in case an overdose occurs. Examples of topics to be covered include hospitalization, IV hydration and forced diuresis, timely administration of hematopoietic growth factors, and prophylactic antibiotics. All staff members who prescribe, dispense, and administer chemotherapy should be required to demonstrate proficiency in identifying and managing chemotherapy-induced toxicities.

REFERENCES

1. Institute for Safe Medication Practices Canada. Fluorouracil incident root cause analysis. Final draft, April 5, 2007; final report, April 30, 2007; online May 22, 2007. Available at: www.ismp-canada.org/download/reports/FluorouracilIncidentMay2007.pdf. Accessed May 5, 2011.
2. Institute for Safe Medication Practices Canada. Fluorouracil incident root cause analysis: Follow-up. August 20, 2007. *ISMP Canada Safety Bulletin* 2007;7(4):1–4. Available at: www.ismp-canada.org/download/safetyBulletins/ISMPCSB2007-04Fluorouracil.pdf. Accessed May 5, 2011.

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