Improving Ambulatory Chemotherapy Safety: Results and Impact of a Multi-disciplinary, Multi-jurisdictional Proactive Risk Study

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Incidents with IV ambulatory chemotherapy, including the death of a patient due to a fluorouracil over-infusion, have highlighted the patient safety risks associated with administering systemic therapy. This study prospectively collected risk data from both a national survey and observations during six field studies across five Canadian provinces, and analyzed them using two proactive risk management frameworks: Rasmussen’s 1997 Proactive Risk Management Framework and a Healthcare Failure Modes and Effects Analysis. The detailed understanding of the safety issues and their associated causal chains led to the implementation of safety strategies across all levels of the Canadian ambulatory chemotherapy system.

Introduction

Incidents with intravenous (IV) ambulatory chemotherapy, including the death of a patient due to a fluorouracil over-infusion in 2006, have highlighted the safety risks associated with administering systemic therapy. A root cause analysis (RCA) of the fluorouracil incident by the Institute for Safe Medication Practices (ISMP) Canada identified 16 causal factors and made several recommendations to help mitigate the root causes (Institute for Safe Medication Practices Canada, 2007). This incident and the accompanying RCA created a heightened awareness in the Canadian oncology community that additional safety hazards may exist that were not implicated in the incident, and thus were not being actively mitigated.

In response to this concern, the purpose of this study was to:
1. Identify current practices for ordering, preparing, labeling, verifying and administering ambulatory IV chemotherapy in Canada.
2. Identify potential sources of risk in a variety of ambulatory IV chemotherapy environments.
3. Recommend strategies to reduce risks.

Methods

Data Collection

Two types of data collection activities were conducted. The first was a national survey of all types of clinicians involved in caring for patients receiving ambulatory chemotherapy, and focused on the following information:
1. Ordering, preparing, labeling, verifying and administering practices and policies
2. How aware practitioners were of the fluorouracil incident and the accompanying RCA report
3. The impact of the recommendations made in the RCA on practices in Canadian outpatient oncology centers
4. Incident descriptions (regardless of whether they were reported)

Survey responses were anonymous, although respondents could choose to identify their oncology centre and were required to disclose the province they worked in.

The second data collection method was a field study at a series of six sites in five Canadian provinces (British Columbia, Alberta, Manitoba, Ontario and New Brunswick). To ensure a broad range of practices could be observed, cancer centres were selected to represent a cross-section of academic and community facilities in both urban and rural environments.

A mixed-methods approach was conducted at each study site, which consisted of semi-structured interviews and direct observations of clinicians performing all relevant tasks associated with ordering, preparing, labeling, mixing, verifying and administering IV chemotherapy. Each site study began with a semi-structured group interview of clinical administrators (e.g., nurse and pharmacy managers), clinical educators, oncologists and administrative staff. The number and type of interview participants varied across sites based on availability. Each interview lasted 2-3 hours and focused on the unit structure, the patient flow from diagnosis to treatment,
the medication preparation process, the medication administration process, infusion technologies in use, training and education, and safety and efficiency challenges. The interviews were followed by 4.5 days of direct observations of all relevant processes by two or three human factors researchers with experience in the healthcare domain.

Qualitative ethnographic data were collected in the form of photographs (see examples in Figures 1 and 2) and written notes.

Data Analysis
The data were analyzed using the following approaches:

- Information flow mapping
- Rasmussen’s 1997 Proactive Risk Management Framework
- Healthcare Failure Modes and Effects Analysis

Information Flow Mapping
To ensure that information about all the processes associated with the delivery of outpatient oncology at each center were fully and accurately captured, a flow map of how information travels through the system, structured by person-role, was created from the field notes. The map was validated by each center’s site coordinator in consultation with appropriate staff. An example of an information flow map is presented in Figure 3.

Rasmussen’s 1997 Proactive Risk Management Framework
Factors with the potential to contribute to patient harm were identified for each site, along with their complex cause-consequence relationships using structural hierarchies. This type of structural hierarchy was originally developed as a proactive risk management tool in Rasmussen’s 1997 Proactive Risk Management Framework (Rasmussen, 1997; Rasmussen & Svedung, Proactive risk management in a dynamic society, 2000) and has been successfully applied to other healthcare related risk management analyses (Vicente & Christoffersen, 2006; Cassano-Piché, Vicente, & Jamieson, 2009). Actions and decisions with the potential to contribute to patient harm at all levels of the system were mapped for each study site (see Figure 4 for an example).
Healthcare Failure Modes and Effects Analysis

The structural hierarchy highlighted potential safety issues, many of which were present at more than one field site. The issues were prioritized using a Healthcare Failure Modes and Effects Analysis (De Rosier, Stalhandske, Bagian, & Nudell, 2002). The HFMEA rating scheme for probability, detectability, and severity were adapted specifically for the ambulatory chemotherapy context (Table 1).

Table 1. Healthcare Failure Modes and Effects Analysis rating scales

<table>
<thead>
<tr>
<th>Rating</th>
<th>Severity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Treatment could be less effective; unknown potential long-term harm (e.g., unnecessary exposure to chemotherapy).</td>
</tr>
<tr>
<td>2</td>
<td>Patient could be temporarily harmed (e.g., toxicity, intense side effects)</td>
</tr>
<tr>
<td>3</td>
<td>Patient could be permanently harmed</td>
</tr>
<tr>
<td>4</td>
<td>Patient could die</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Rating</th>
<th>Likelihood</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Unlikely to occur (may happen sometime in 5 to 30 years)</td>
</tr>
<tr>
<td>2</td>
<td>Possible to occur (may happen sometime in 2 to 5 years)</td>
</tr>
<tr>
<td>3</td>
<td>Probably will occur (may happen several times in 1 to 2 years)</td>
</tr>
<tr>
<td>4</td>
<td>Likely to occur immediately or within a short period (may happen several times in one year)</td>
</tr>
</tbody>
</table>

Results and Impact

The study data resulted in a detailed understanding of the potential safety issues associated with administering ambulatory IV chemotherapy. A series of initiatives to mitigate some of these issues was undertaken. This section will present the study results, the mitigating initiatives, and the impact of the mitigating initiatives.

Study Results

Survey

A total of 331 survey responses were received. The total
number of respondents by clinician type is shown in Figure 5. Respondents reported widespread use of both electronic ambulatory infusion pumps (AIPs), which are small programmable infusion devices (Figure 6) and elastomeric infusion devices, which are mechanical (i.e., non-programmable) devices that deliver a continuous infusion via a medication-filled pressurized balloon inside a closed chamber (Figure 7).

None of the AIPs in use by respondents were “smart pumps” (pumps with drug libraries and dose limits) and the professional group responsible for programming AIPs varied widely. There was also a wide variation in the reported makes and models of AIPs in use, however only one vendor’s elastomeric infusion device was in use by 96% of respondents (Baxter Corporation).

Ninety-five percent of respondents were aware of the fluorouracil incident and the ISMP Canada root cause analysis and its recommendations. Seventy-one percent of respondents indicated that one or more of the following changes was implemented at their center in response to the incident:

- Discontinued use of electronic ambulatory infusion pumps in favor of elastomeric infusion devices (reported by respondents from at least six different organizations)
- Changes to the information on IV chemotherapy bag labels
- Improved training and education on administering ambulatory IV chemotherapy
- New procedures or policies

Survey responses provided descriptions of 213 incidents that were grouped by type and organized into common types. Because survey responses were anonymous it was not possible to identify if more than one respondent reported the same incident. However, the most important information was the categorization of incidents into 16 different types, grouped into five themes. The number of each type of issue reported in each theme is shown in Table 2. Fourteen of the 16 types of issues described by survey respondents were unrelated to failure modes described in the fluorouracil root cause analysis.

<table>
<thead>
<tr>
<th>Theme 1: Wrong drug/dose/patient</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medication administered to incorrect patient</td>
<td>5</td>
</tr>
<tr>
<td>Medication ordering error</td>
<td>7</td>
</tr>
<tr>
<td>Pharmacy mixing error</td>
<td>9</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Theme 2: Medication infused too quickly or too slowly</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type</td>
</tr>
<tr>
<td>Electronic AIP programming error</td>
</tr>
<tr>
<td>Elastomeric infusion device malfunction</td>
</tr>
</tbody>
</table>
Wrong (rate) elastomeric pump filled and administered 10
Infusion pump incident - pump type not specified 10

**Theme 3: Medication not infused**

<table>
<thead>
<tr>
<th>Type</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Line kink with elastomeric pump</td>
<td>10</td>
</tr>
<tr>
<td>Electronic AIP not started</td>
<td>6</td>
</tr>
<tr>
<td>Tubing not unclamped</td>
<td>31</td>
</tr>
</tbody>
</table>

**Theme 4: Lines and leaks**

<table>
<thead>
<tr>
<th>Type</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Issue with connection/line</td>
<td>8</td>
</tr>
<tr>
<td>Leak</td>
<td>39</td>
</tr>
</tbody>
</table>

**Theme 5: Other**

<table>
<thead>
<tr>
<th>Type</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Other electronic AIP issue</td>
<td>3</td>
</tr>
<tr>
<td>Mechanical failure of electronic AIP</td>
<td>6</td>
</tr>
<tr>
<td>Patient mishap</td>
<td>14</td>
</tr>
<tr>
<td>Extravasation</td>
<td>8</td>
</tr>
</tbody>
</table>

Total 213

Field Studies

Six structural hierarchy diagrams were generated based on the field study data (one for each field site). Each element on the hierarchy (i.e., box) represents a potential contributing factor to patient harm. The cause-consequence relationship between the factors is made explicit by a line connection, resulting in chains of elements that could sequentially lead to outcomes that cause patient harm. Factors with the potential to contribute to patient harm were identified across all levels of the system for each field study.

The data elements on the hierarchy coupled with the issues identified in the survey incident data yielded 37 unique issues that were prioritized using the HFMEA scoring matrix. Eleven issues had a hazard score greater or equal to 16, and were therefore deemed “critical”. Mitigating strategies for the critical issues were investigated. The 11 critical issues were grouped into three themes:

1. Elastomeric AIPs and IV access devices
2. Orders and labels
3. Pharmacy Practices

Table 3 shows the issues grouped by theme.

Table 3. Critical issues grouped by theme

<table>
<thead>
<tr>
<th>1. Elastomeric AIPs and Access Devices</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1  Unexplained elastomeric AIP malfunctions</td>
</tr>
<tr>
<td>1.2  Elastomeric AIP selection errors</td>
</tr>
<tr>
<td>1.3  Homecare and AIPs</td>
</tr>
<tr>
<td>1.4  Access devices used with elastomeric AIPs</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>2. Orders and Labels</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.1 Change orders</td>
</tr>
<tr>
<td>2.2 Pre-printed orders: reuse of forms, handwriting, usability, flexibility</td>
</tr>
<tr>
<td>2.3 Large volume general purpose infusion pump programming errors and labeling</td>
</tr>
<tr>
<td>2.4 Free-form orders</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>3. Pharmacy Practices</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.1 Organization of materials and work</td>
</tr>
</tbody>
</table>

In addition to the 11 issues, by comparing the content of each structural hierarchy, overarching organizational structure and practice variations between field sites were identified. These stemmed from actions and decisions made primarily at the higher levels of the system (e.g., organizational, regulatory), and had the potential to impact safety, including:

- The role of the provincial cancer organization in overseeing and funding treatment protocols
- Patient scheduling model (e.g., time between clinic visits, blood work, and chemotherapy treatment for each cycle)
- Chemotherapy ordering technology (e.g., paper-based vs. electronic ordering)
- Use of electronic versus elastomeric infusion devices
- Overall complexity of work processes and degree of distribution of tasks across professionals
- Models of teamwork (e.g., how closely the various care providers work together)
- Efficiency pressure (e.g., time pressure experienced by clinicians based on the work structure)

Impact of Mitigating Initiatives

A report summarizing the study’s findings and recommendations (Health Technology Safety Research Team, Healthcare Human Factors, ISMP Canada, 2011) was widely disseminated through the Canadian Association of Provincial Cancer Agencies (CAPCA)’s website, with co-promotion through each of the provincial cancer agencies. Several initiatives targeting one or more issues in each of the three themes were also undertaken. The impact of these initiatives will be discussed.

Elastomeric AIPs and IV Access Devices

A common response by chemotherapy clinics to the fluorouracil incident was a migration away from using AIPs to exclusive use of elastomeric infusion devices. Therefore, the number of reports of unexplained elastomeric device malfunctions in the survey and field studies was concerning. In several instances the devices were noted to infuse the chemotherapy a day too quickly or slowly. Discussions with the vendor revealed that a number of factors have the potential to impact flow rate, and that, in combination, these factors can cause the flow rate to deviate by as much as 36.5%, which could explain some malfunction reports. Factors with the potential to impact elastomeric device flow rate and the maximum flow rate impact of each factor are shown in Table 4.

Table 4. Impact of deviations on elastomeric device flow rate

<table>
<thead>
<tr>
<th>Departure from Calibration Setting</th>
<th>Example</th>
<th>Rate Increase</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>Physical properties of the</td>
<td>+10%</td>
</tr>
</tbody>
</table>
It was clear that these factors and their impact were not widely understood by pharmacists, nurses, or patients – all of whom require this knowledge to ensure the best possible flow rate accuracy. To this end, a series of user-specific educational materials pictorially highlighting these factors was developed by the research team in collaboration with Baxter Canada. These have been distributed widely and demand for the materials has exceeded the previous demand by Baxter Canada customers for any related materials. A second printing was required. These materials are available for download at: (http://www.capca.ca/current-issues/patient-safety/research#download)

Orders and Labels

Chemotherapy can be ordered in several ways (e.g., handwritten on free-form prescription pads, electronically, on pre-printed orders), often within the same organization. Orders must specify several cycles’ worth of medication, patient’s physiological parameters (e.g., height, weight) that can result in standard dose adjustments by pharmacy, and must change in conjunction with a patient’s highly dynamic condition. Field study observations revealed several risks associated with the miscommunication and mistiming of communication about orders and order changes, stemming from the limitations of ordering tools.

In response to these risks, a guideline for developing ambulatory chemotherapy preprinted orders (Healthcare Human Factors, Health Technology Safety Research Team, Canadian Association of Provincial Cancer Agencies, 2011) was developed by an interdisciplinary team consisting of the human factors researchers who participated in the field studies, graphic designers from the Ontario College of Art and Design University, and oncology clinicians. The guideline specifies both content and format considerations and provides graphical examples and templates for easier adoption by oncology centers. The process of developing the guideline is described in Jeon, White, Hunt, Cassano-Piché, & Easty, 2012.

The guidelines have been widely circulated to cancer care providers by CAPCA and individual provincial cancer agencies. One year after disseminating the guidelines, CAPCA’s Systemic Therapy Safety Committee solicited feedback about their use and reported the following:

- two provincial cancer agencies had implemented the guidelines to improve their existing provincial preprinted orders,
- several individual cancer centres had applied or were planning to apply the guidelines to the development of electronic order communication tools,
- one provincial cancer agency planned to use the guideline to develop its provincial electronic order forms
- one cancer centre implemented the guideline to develop electronic order forms.

Pharmacy Practices

During the field studies, a wide range of chemotherapy mixing practices was observed with respect to workspace organization, mixing processes, and double-checks in the biological safety cabinets (BSCs). Some practices were inherently more error-prone, which is concerning since mixing errors are difficult to detect in the pharmacy and are completely undetectable once an IV chemotherapy bag leaves the pharmacy. Many concerning practices, such as separation of bags from associated labels were not in violation of Canadian or international policies or standards (American Society for Hospital Pharmacy, 2006; Chemotherapy Admixture Service, 2008; Carrington, et al., 2010).

One of the most concerning practices was the presence of multiple chemotherapy agents for multiple patients in the BSC at any given time (Figure 8). A risk with this approach is that the wrong drug vial could be selected and injected into the diluent bag, and if the correct vial is then shown to the pharmacist during the double-check, the error would go undetected. The study report recommended that only a single chemotherapy preparation should enter the BSC at a time (Figure 9). This would require changes to several upstream processes related to pre-mixing materials gathering. Some pharmacists and pharmacy technicians were concerned that these changes would increase the total time and pharmacy resources required for admixing chemotherapy.
Figure 8. Field study photograph of multiple chemotherapy agents in the biological safety cabinet.

In response to this concern, two studies have been conducted evaluating a process for migrating from many chemotherapy agents in the BSC to one chemotherapy preparation in the BSC at a time.

**Broader Impact**

In addition to the theme-specific initiatives, the study’s recommendations have informed the revision of the Ambulatory Systemic Cancer Therapy Services standards used to support Accreditation Canada in accrediting all Canadian chemotherapy centers.

Figure 9. Photograph of a single chemotherapy preparation in the biological safety cabinet

**Discussion**

The human factors proactive risk assessment conducted to identify risks in Canadian ambulatory chemotherapy centers revealed that risks were present at every level of the system, regardless of the size, location, or provincial jurisdiction of the centre. Risks at higher levels of the system not traditionally associated with a human factors analysis were made apparent by mapping the causal relationships between contributing factors on the structural hierarchy, a tool that specifically suggests the presence of these factors by providing levels to capture these details as outlined by the proactive risk framework (Rasmussen, 2007).

This study represents an example of how applied human factors research can have direct impact on patient safety in ways that are generalizable across healthcare centers providing similar types of treatment.

There are several key factors that enabled both the opportunities for impact and the success of the initiatives that followed from the research. The first is the engagement of a multidisciplinary committee of key stakeholders (i.e., CAPCA’s Systemic Therapy Safety Committee) from the earliest stages of grant writing onwards. The second is that the Systemic Therapy Safety Committee fulfilled the role of a steering committee for the research project to ensure the scope and methods would allow the findings to be both representative and generalizable. Members of the steering committee were senior administrators from across the Canadian oncology system and were able to provide access to facilities and information that allowed for a detailed analysis of the system including higher-level system factors. The third key factor, and probably the most important factor contributing to the success of this project, is that it emerged from a highly publicized incident in a relatively small clinical community, where the senior management of the organization where the incident occurred exhibited a strong safety culture. The response of senior management to the incident represented a true systems approach by admitting to the patient’s family and the center’s staff that the system had failed, not the individual nurses involved, and that leadership was committed to improving the system so that subsequent errors would not occur. This expression of intent was directly followed by actions across the organization and the country, including the submission of the grant proposal that funded this research. The safety leadership of this organization paired with the tone of the root cause analysis that followed, primed Canadian oncology clinicians to participate openly in this research and support the identification of as many risks as possible.

**References**


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