Automation: a way to improve the reliability and the efficiency of cytotoxic preparation

Hôpitaux Universitaires de Genève

Pr Pascal BONNABRY
Head of pharmacy

EAHP, Hamburg
March 26, 2015

Conflict of interest

- The experimental study presented in this conference was performed on a Pharmahelp system freely loaned by Fresenius
- We received no direct financial contribution from Fresenius
- The acquisition of Pharmahelp was decided in a regular tender process
Risk

Cytotoxics = high-risk

Probability of occurrence

Complex process, based on humans

Effects or consequences
(human, economics, on the environment)

Low therapeutic margin, high impact on patients

Human reliability

« On the 6th day, God created man … »

… but God was tired, and his creation was not perfect …

In hospitals, many high-risk activities are based on human reliability, which is limited
How errors occur?

The addition of 2 errors
Commission error **AND** Control failure

- Selection error
- Calculation
- Dilution
- ... 
- Check failure
- Wrong drug / syringe swap error
- Pot-Pot Pitfall

Check Double-check...

Frequency of cytotoxic preparation errors

- Detected errors
  - Overall: 0.45 %
  - Major: 0.19 %

- High workload (>60/day) increased the risk
  (Odds-Ratio = 2)

$n=30'819$

<table>
<thead>
<tr>
<th>Error category</th>
<th>No. of error (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major errors</td>
<td></td>
</tr>
<tr>
<td>Wrong dose (confirmed or doubt?)</td>
<td>39 (27.9%)</td>
</tr>
<tr>
<td>Labelling (name, drug or dose error)</td>
<td>11 (7.9%)</td>
</tr>
<tr>
<td>Unauthorized drug</td>
<td>4 (2.9%)</td>
</tr>
<tr>
<td>Incompatible diluent</td>
<td>3 (2.1%)</td>
</tr>
<tr>
<td>Incompatible set or bag</td>
<td>2 (1.4%)</td>
</tr>
<tr>
<td><strong>Sub-total</strong></td>
<td><strong>39 (42.1%)</strong></td>
</tr>
</tbody>
</table>

| Minor errors                        |                 |
| Wrong set of infusion               |                 |
| (without incompatibility)           | 31 (22.1%)      |
| Final volume                        | 22 (13.9%)      |
| Wrong diluent (without incompatibility) | 21 (15%)      |
| Final presentation                  |                 |
| (e.g. bag instead of syringe)       | 6 (4.3%)        |
| Solvent of reconstitution           |                 |
| (without incompatibility)           | 1 (0.7%)        |
| **Sub-total**                        | **81 (57.9%)**  |
| **Overall**                          | **140 (100%)**  |

Limat S, Pharm World Sci 2001;23:102
Accuracy of cytotoxic preparation by humans

- Simulation study, worst cases
  - Data distribution of 438 preparations by 11 operators

<table>
<thead>
<tr>
<th>Accuracy</th>
<th>Deviation</th>
<th>Weakly accurate</th>
<th>Deviation</th>
<th>Inaccurate</th>
<th>Deviation</th>
<th>Error</th>
<th>Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt; 5%</td>
<td>5-10%</td>
<td>10-30%</td>
<td>&gt;30%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>58-60%</td>
<td>25-27%</td>
<td>14-17%</td>
<td>0.7%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The risk of an inaccuracy of more than 5% ranged from 13% to 88% across operators.

Carrez L, HUG, 2013
Limited performance of controls

- Detection during cytotoxic preparation process (simulation study)

Phase 1
52 %
Raising awareness

Phase 2
80 %

Demography of cancers

New cases
Deaths

Millions of persons

2008 2012 2025

WHO, 2013

Sarfati L, J Clin Pharm Ther 2015;40:55
Evolution of cytotoxic preparations

Human resources

- Facts
  - Increasing workload
  - Difficult to get more resources
  - Increased risks of
    - preparation errors
    - dissatisfaction, burn-out, …

- Need to improve the efficiency…
  - …make more with less
    (or with a constant staffing)
Summary of problems

- Cytotoxic compounding is a high risk process, with major consequences in case of errors
- Human reliability is suboptimal:
  - preparation errors are committed and
  - performance of controls is limited
- A large inter-operator variability exists, for example in preparation accuracy
- The number of preparations will continue to increase, with difficulties to adequately adapt the staffing

How to improve the safety?

- Implement strategies to
  - Increase the reliability of controls
  - Reduce the frequency of errors
How to improve the safety?

- **Reduce the frequency of errors**
  - Automation

- **Increase the reliability of controls**
  - In-process
    - Gravimetric
  - Post-process
    - Quantitative analysis

**Main objectives**
- Avoid errors (wrong drug/dose)
- Increase the accuracy
- Reduce the inter-operator variability
- Increase the efficiency, the productivity
- Improve the traceability
Avoid selection errors

- Product identification by camera and RFID

Accuracy

The filling was accurate from a volume of 3 mL for $< \pm 5\%$ limits

Mean $\pm$ CI95%, n=54/volume

Verrey AS, Carrez L, HUG, 2014
**Accuracy**

- Error to the target (based on gravimetry)

<table>
<thead>
<tr>
<th>Volume [mL]</th>
<th>≤ 3%</th>
<th>3 - 5%</th>
<th>5 - 10%</th>
<th>&gt; 10%</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>51</td>
<td>2</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>5</td>
<td>52</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>10</td>
<td>54</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>40</td>
<td>54</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>100</td>
<td>54</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Total by category
- 265
- 3
- 1
- 1

% 98.2% 1.1% 0.4% 0.4%

Non-conform preparations detected during the final gravimetric control

n=54/volume (=270)

Verrey AS, Carrez L, HUG, 2014

---

**How to improve the efficiency?**

- Increase the productivity
  - 10 bags, mean time 45 min (32 min automated)
  - From 6.5 min (3 mL) to 86.5 min (250 mL)

Pre-processing
Production
Post-processing
How to improve the efficiency?

- Implement dose-banding
  - A system whereby calculated doses of intravenous cytotoxic drugs are fitted to pre-determined dose range (« bands »)
  - The dose of each band is provided by with pre-prepared syringe or infusions containing standard dose
  - The maximum variation of the adjustment from the prescribed dose is usually 5%


How to improve the efficiency?

- Implement dose-banding
  - ex. gemcitabine (2013)

- 613 bags produced, 111 different doses

Fleury M, HUG, EAHP GPls 2015
How to improve the efficiency?

- Implement dose-banding
  ex. gemcitabine (2013)

  ![Graph showing dose-banding bands]

- 5 bands = 90% of preparations

  Fleury M, HUG, EAHP GPls 2015

---

Our cytotoxic process TODAY

Preparation with gravimetric control

- Electronic prescription
- Bedside scanning
Our cytotoxic process **TOMORROW**

- Automated preparations (2015)
- Electronic prescription + Dose-banding (2016)
- Preparation with gravimetric control
- Bedside scanning

### Implementation challenges

- The PharmaHelp system will be delivered end of March 2015
- Qualification
- Interfacing
- Operators training
- Process reengineering
- Implementation of dose-banding
- Evaluation of performance in the real life
Take home messages

- Human reliability is limited and we have to implement robust systems to avoid errors and catch them before they reach the patient.
- The demography of cancers will continue to be increasingly demanding on cytotoxic preparations.
- Automation and dose-banding can help us to improve the safety and the efficiency.
- Automation in oncology is an emerging technology, that will be routinely used in the future...

Thank you for your attention

This presentation can be downloaded
http://pharmacie.hug-ge.ch/ens/conferences.html
Pascal.Bonnabry@hcuge.ch