Healthcare Workers and Antineoplastic Drugs: Evaluating the Risks and Identifying Determinants of Exposure

Presented by:

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October 15, 2013
Agenda

- Background
- Methods and results for each objective (x4)
- Summary
- Strengths and limitations
- Future studies
Antineoplastic drugs

- Also known as chemotherapeutic or cytoxoxic drugs
- Primarily used for the treatment of cancer
- Inherently toxic agents; however, to patients, benefits > risks
- Occupational exposure concerns initially surfaced in the 1970’s
  - Non-selective mode of action – normal cells may also be affected
Exposure limits?

- No exposure limits listed in Ontario OHS Regulation
- No ACGIH threshold limit values (TLVs®)
- No OSHA permissible exposure limits (PELs)

The ALARA Principle applies (As Low As Reasonably Achievable)
Occupational exposure to antineoplastic drugs

- Documented health effects of exposed workers:
  - Mutagenicity \((\text{damage to genetic material})\)
  - Reproductive toxicity \((\text{e.g. miscarriages})\)
  - Carcinogenicity

- Pilot study at hospital pharmacies in BC found:
  - Surface contamination on work surfaces
  - Certain personnel had dermal contamination
Gaps in literature

- Unknown dermal contact frequency
- Only select departments/job categories assessed
- Exposure underestimate
  - Number of workers at risk
  - Urinary drug contamination levels
- Determinants of contamination and/or exposure

Pursue current study building upon pilot study findings and gaps in the literature
1. Is antineoplastic drug contamination found on surfaces located throughout the hospital medication system?

2. Are healthcare workers throughout the hospital medication system occupationally exposed to antineoplastic drugs?

3. What are the factors associated with surface contamination and occupational exposure (skin and urine contamination)?
Four study objectives

6 sites in Metro Vancouver

Objective #1: Site observations

Objective #2: Surface contamination

Objectives #3 & 4: Personal measurements (skin and urine contamination)

BACKGROUND
Notes pertaining to entire study

- Ethics approval received prior to start
- Used cyclophosphamide (CP) as marker drug of exposure
- Included six facilities in GVRD – 5 acute care hospitals + 1 cancer treatment hospital
  - All drugs prepared in biological safety cabinet
  - Closed drug system transfer devices NOT employed
- Housekeepers declined to participate
- Laboratory analyses of samples using HPLC MS/MS
- Generated mathematical models to identify determinants of surface, skin and urine contamination
Objective 1

Identify

- surfaces most likely contaminated
- job categories potentially at risk of exposure
to antineoplastic drugs throughout the hospital medication system
Objective 1 – Methods

• Key informant interviews
  • Ascertain depts/job categories

• Repeated site observations
  • Establish hospital medication system
  • Identify potentially-contaminated surfaces
  • Identify job categories which may contact drugs/surfaces (directly or indirectly)

• Contact frequency graphs and tallied job categories
Surface contact frequency by stage of hospital medication system

Stage: 1. Receiving
Stage: 2. Drug Preparation
Stage: 3. Transport
Stage: 4. Drug Administration

SITE OBSERVATIONS
Objective 1 – Results

Observed job categories at risk of exposure stratified by stage of hospital medication system

<table>
<thead>
<tr>
<th>Stage</th>
<th>Job Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Delivery</td>
<td>Shipper/Receiver; Pharmacy Receiver</td>
</tr>
<tr>
<td>2. Drug Preparation</td>
<td>Pharmacy Technician; Pharmacist</td>
</tr>
<tr>
<td>3. Transport to Ward</td>
<td>Porter; Nurse; Pharmacist; Unit Clerk; Ward Aide</td>
</tr>
<tr>
<td>4. Drug Administration</td>
<td>Nurse; Volunteer; Unit Clerk; Dietician; Oncologist; Clinic Pharmacist</td>
</tr>
<tr>
<td>5. Waste Disposal</td>
<td>Nurse; Pharmacist; Pharmacy Technician; Biopacker</td>
</tr>
</tbody>
</table>

Up to 11 job categories per site at risk
Objective 2

Quantify drug contamination levels on surfaces from Objective #1 and identify determinants.

SURFACE CONTAMINATION
Objective 2 – Methods

• Used a pre-moistened Kimwipe
• 100 cm$^2$ template used where possible
• For other surfaces, area most likely contacted was sampled
  • Dimensions taken and surface area calculated
• LOD 0.356 ng/wipe
Objective 2 – Methods

Independent Variables:
• CP handled prior?
• Spill or leak of CP prior?
• Surface cleaned prior?
• Hospital characteristics
  • E.g. # job categories responsible for drug transport
• Attributes of the wipe sample
  • E.g. stage of hospital medication system
Histogram of surface contamination levels

N = 438; 64% < LOD

AM = 0.201 ng/cm²

Max = 26.1 ng/cm²
SURFACE CONTAMINATION
Objective 2 – Results

Factors associated with increased surface contamination:

1. Stage of hospital medication system
   - Drug preparation
   - Drug administration

2. Having more job categories responsible for drug transport (positive association)
Personal samples

Objective #3: Assess contamination levels on hands of at-risk job categories and identify determinants

Objective #4: Determine urinary drug contamination levels in at-risk job categories and identify determinants
Objectives 3&4 – Methods

Recruitment:

• Job categories identified in Objective #1 invited to participate
  • 3 representatives/job category/site

• Based on convenience sampling
  • i.e. not worst-case
Dermal samples - Methods

- Similar to surface wipe sampling
  - Front and back of both workers’ hands were wiped
- LOD of 0.356 ng/wipe
Urine samples – Methods

• 24-hr urine samples collected
• CP and 3 stable urinary metabolites analyzed
• Tallied; results reported in nmol/L
Objective 3&4 – Methods

Independent Variables:

1) *On-site survey*
   - CP contact methods
   - Hand washing practices
   - Glove use prior to sample collection

2) *Self-administered questionnaire*
   - Demographic data
   - Duty to handle antineoplastic drugs
   - Education/training
   - Usual personal protective equipment practices
Histogram of dermal contamination levels

N=225; 80% < LOD

AM = 0.360 ng/wipe

Max = 22.8 ng/wipe
### Objective 3 - Dermal results

<table>
<thead>
<tr>
<th>Job Title</th>
<th>N</th>
<th>% &gt; LOD</th>
<th>AM (ng/wipe)</th>
<th>SD (ng/wipe)</th>
<th>GM (ng/wipe)</th>
<th>GSD</th>
<th>Max</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pharmacist</td>
<td>40</td>
<td>10.0</td>
<td>&lt; LOD</td>
<td>1.08</td>
<td>&lt; LOD</td>
<td>4.15</td>
<td>1.49</td>
</tr>
<tr>
<td>Pharmacy Receiver</td>
<td>12</td>
<td>25.0</td>
<td>&lt; LOD</td>
<td>0.39</td>
<td>&lt; LOD</td>
<td>1.09</td>
<td>1.27</td>
</tr>
<tr>
<td>Pharmacy Technician</td>
<td>45</td>
<td>17.8</td>
<td>&lt; LOD</td>
<td>1.63</td>
<td>&lt; LOD</td>
<td>1.42</td>
<td>9.29</td>
</tr>
<tr>
<td>Porter</td>
<td>11</td>
<td>9.1</td>
<td>0.404</td>
<td>1.37</td>
<td>&lt; LOD</td>
<td>1.25</td>
<td>4.55</td>
</tr>
<tr>
<td>RN (includes LPN)</td>
<td>64</td>
<td>26.6</td>
<td>0.767</td>
<td>3.11</td>
<td>0.363</td>
<td>1.46</td>
<td>22.8</td>
</tr>
<tr>
<td>Transport (includes biopacker, transporter, and shipper/receiver)</td>
<td>8</td>
<td>12.5</td>
<td>&lt; LOD</td>
<td>0.21</td>
<td>&lt; LOD</td>
<td>1.05</td>
<td>0.56</td>
</tr>
<tr>
<td>Unit clerk</td>
<td>24</td>
<td>16.7</td>
<td>&lt; LOD</td>
<td>0.98</td>
<td>&lt; LOD</td>
<td>1.31</td>
<td>2.03</td>
</tr>
<tr>
<td>Others in drug admin unit (volunteer, oncologist, dietitian, ward aide)</td>
<td>21</td>
<td>28.6</td>
<td>1.321</td>
<td>4.93</td>
<td>0.504</td>
<td>1.64</td>
<td>22.4</td>
</tr>
</tbody>
</table>
Objective 3 – Dermal results

Factors associated with increased dermal contamination:

1. Working in acute care hospital
2. Employed as porter, nurse, transport staff or in the drug administration unit
3. Female
4. Having a duty to handle antineoplastic drugs
Histogram of urinary drug contamination levels

Suggests that participants have opportunities for higher exposure
Objective 4 – Urine results

Factors associated with increased urinary contamination:

1. Employed as pharmacy receiver, pharmacy technician, porter, nurse, or unit clerk

2. Having more job categories responsible for drug transport (positive association)
Summary of results

- No dermal sample exceeded DOEL of 3360 ng/wipe (Bos et al., 1998)
- However, limit is based on daily exposure

- 10 (4.5%) urine samples > NSRL of 1000 ng of CP/day (Cal EPA)
- Based on mean CP levels, lifetime cancer risk of 1.89 per million (Sargent et al., 2002)
- 8 (2%) surface samples > threshold level of 1 ng/cm² (USP Chapter 797)
- Unclear if cumulative exposure will exceed this limit

SUMMARY
“Take home” messages

- Surface contamination found throughout the hospital medication system
- Occupational exposure potential
  - More job categories than previously believed are at risk of exposure
- Overall, contamination and occupational exposure levels are low
  - Controls working; unable to eliminate contamination/exposure
- Adds to the list of occupational hazards in hospital settings
Policy implications

• Indicate potential exposure risk throughout the hospital medication system
• All job categories at-risk should be trained
• Implement control measures at every stage of the hospital medication system
  • Examples:
    a) Reduce number of transport job categories
    b) Clean surfaces including vials
    c) Use closed system drug transfer devices
Study strengths

• Looked at entire hospital medication system
• Sampled surfaces where contact is known to occur
• Large sample size
• Sensitive analytical method
• Looked at CP and metabolites in urine samples
• Duplicate samples collected
Study limitations

• Cross-sectional design
• Only examined one analyte
• Unequal representation of job categories and one cohort not included
• Two sites did not have random selection of potential subjects
• Unknown wipe recovery from surfaces/hands
• Unable to accurately assess amount of CP handled
• Most independent variables collected via self-report
Future studies

- Surface cleaning
- Evaluate health risks
- Determine mechanism of spread
- Identify determinants for each stage/job category separately


# Associated conference presentations

<table>
<thead>
<tr>
<th>Date</th>
<th>Conference</th>
<th>Presentations</th>
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<tbody>
<tr>
<td>May 2013</td>
<td>American Industrial Hygiene Conference and Exposition (Montreal, QC)</td>
<td>• Urinary Contamination of Healthcare Workers to Antineoplastic Drugs Throughout the Entire Hospital Medication Circuit</td>
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</table>
| May 2012 | CARWH-RRSSTQ 2012 Conference (Vancouver, BC)                                 | • Urinary Contamination Levels of Healthcare Workers Exposed to Antineoplastic Drugs at British Columbian Hospital Pharmacies  
  • Nurses’ exposures to antineoplastic drugs in Canada and risk assessment of lifetime cancer incidence |
| Mar 2012 | 30th Congress of the International Commission on Occupational Health (Cancun, Mexico) | • Occupational dermal exposure to antineoplastic drugs throughout the hospital medication system at Canadian hospital                          |
| Sep 2011 | Association of Occupational Health Professionals in Healthcare 2011 AGM (Minneapolis, MN) | • Antineoplastic Drugs in Hospitals – Toxicology, Exposure Potential and Recommendations for Reducing Exposure                                |
| May 2011 | American Industrial Hygiene Conference and Exposition (Portland, OR)        | • Antineoplastic drug contamination levels throughout the medication circuit in British Columbian hospitals                                      |
| Sep 2010 | International Occupational Hygiene Association 8th International Scientific Conference (Rome, Italy) | • Identifying healthcare workers at risk of exposure to antineoplastic drugs: More than just pharmacists and nurses |
Acknowledgements

• All participating sites and subjects
• PhD Committee members: Kay Teschke, Scott Venners and Paul Demers
• OEH laboratory at UBC
• Research assistants
• Study supporters: BCNU, HSA, HEU, HEABC and OHSAH
• Funding provided by WorkSafeBC Research Secretariat
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- More details: antineoexposure.spph.ubc.ca
- Website: www.ryerson.ca/sophe
Questions
Laboratory analyses

- Analyzed for cyclophosphamide (CP) (surface and dermal) and its metabolites (urine)
- HPLC MS/MS
  - Very sensitive – detection limit (LOD) in nanogram (ng) range
- QC: field, travel, and lab blanks
- QA: freeze-thaw experiments; storage stability testing