SURVEILLANCE OF HAZARDOUS EXPOSURES TO LIQUID DETERGENTS CAPSULES IN ITALY: A PRELIMINARY EVALUATION OF THE IMPACT OF PREVENTIVE MEASURES

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INTRODUCTION

Liquid laundry detergent capsules (LLDCs) are unit dose fabric washing products consisting of about 32-35 mL of concentrated liquid detergent wrapped in a water-soluble membrane.
INTRODUCTION

These products are intended to improve environmental sustainability of liquid laundry detergent consumption by providing the correct dosage for washing needs and reducing packaging size (A.I.S.E.),
Following their launch in the UK, Irish, and French markets in 2001, few case reports of paediatric exposures highlighted that these products have the potential to cause corrosive eye damage, pulmonary and central nervous system toxicity, serious laryngopharyngeal injuries.

These preliminary observations on LLDCs toxic effects were confirmed by analyses of large series of cases collected in the UK and USA.
INTRODUCTION

In Italy, a major company launched LLDCs (IC-LLDCs) in August 2010

Immediately after, NPCCM started to observe an unexpected increase in the number of cases presenting with signs/symptoms associated with laundry detergent exposure.
Since the observed increase was clearly related to the newly introduced product, these preliminary observations were promptly notified to the industry and the Italian Ministry of Health to underscore the need for preventive measures.
A surveillance of hazardous exposure to laundry detergents was implemented in September 2010.

In August 2011 other companies launched their products in Italy.
AIMS OF THE STUDY

To describe the main characteristics of cases of exposure to LLDCs during a five year period and to compare them with those reported for cases exposed to traditional laundry detergents (TLDs).

To provide a preliminary evaluation of the impact of the preventive measures adopted in Italy on the occurrence of cases of exposure and related poisoning.
MATERIALS AND METHODS

The study analyses a series of cases reported to the NPPCM from September 1, 2010 to December 31, 2014. Routinely collected information were used to classify exposures according to detergent formulation, company, and poisoning severity.

The main characteristics of cases exposed to different formulations were compared.

The mean daily number of cases of exposure by month and formulation, and the number of cases exposed to LLDCs/million unit sold by month and company were calculated.
MATERIALS AND METHODS

Changes in the exposure rates were estimated.

The rates of exposure to laundry detergents before and after the observed change points were compared.

The association between exposure to LLDCs and moderate/severe poisoning was estimated.
QUESTIONS

ARE THE MAIN CHARACTERISTICS OF CASES EXPOSED TO LLDCs AND TLDs DIFFERENTLY DISTRIBUTED?

Pearson’s $X^2$ test or Fisher’s exact test
COMPARISON BETWEEN CASES EXPOSED TO LLDCs (No. 1,742) AND TLDs (No. 1,287) IDENTIFIED IN ITALY. BETWEEN SEPTEMBER 2010 AND DECEMBER 2014

CASES EXPOSED TO LLDCs AND TLDs WERE DIFFERENTLY DISTRIBUTED BY:

- site of call for assistance, p<0.001

<table>
<thead>
<tr>
<th>Site</th>
<th>LLDCs (No.)</th>
<th>TLDs (No.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital</td>
<td>68% (1,186)</td>
<td>40% (512)</td>
</tr>
<tr>
<td>Private residence</td>
<td>32% (566)</td>
<td>60% (755)</td>
</tr>
</tbody>
</table>

- class of age (years), p<0.001

<table>
<thead>
<tr>
<th>Age Group</th>
<th>LLDCs (No.)</th>
<th>TLDs (No.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;5</td>
<td>89% (1,551)</td>
<td>81% (1,042)</td>
</tr>
<tr>
<td>5-9</td>
<td>8% (146)</td>
<td>4% (47)</td>
</tr>
<tr>
<td>10-19</td>
<td>0.2% (11)</td>
<td>1% (14)</td>
</tr>
<tr>
<td>20+</td>
<td>1% (30)</td>
<td>13% (168)</td>
</tr>
</tbody>
</table>
COMPARISON BETWEEN CASES EXPOSED TO LLDCs (No. 1,742) AND TLDs (No. 1,287) IDENTIFIED IN ITALY BETWEEN SEPTEMBER 2010 AND DECEMBER 2014

CASES EXPOSURE TO LLDCs AND TLDs WERE DIFFERENTLY DISTRIBUTED BY:

- **route of exposure, p<0.001**

<table>
<thead>
<tr>
<th>Route of Exposure</th>
<th>LLDCs (No.)</th>
<th>TLDs (No.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single route</td>
<td>88% (1,538)</td>
<td>94% (1,203)</td>
</tr>
<tr>
<td>Multiple routes</td>
<td>12% (208)</td>
<td>6% (77)</td>
</tr>
</tbody>
</table>

- **clinical signs/symptoms, p<0.0001**

<table>
<thead>
<tr>
<th>Clinical Signs/Symptoms</th>
<th>LLDCs (No.)</th>
<th>TLDs (No.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>None/not associated</td>
<td>25% (435)</td>
<td>74% (946)</td>
</tr>
<tr>
<td>Associated (at least one)</td>
<td>75% (1,307)</td>
<td>27% (341)</td>
</tr>
</tbody>
</table>
COMPARISON BETWEEN CASES EXPOSED TO LLDCs (No. 1,742) AND TLDs (No. 1,287) IDENTIFIED IN ITALY. BETWEEN SEPTEMBER 2010 AND DECEMBER 2014.

CASES EXPOSURE TO LLDCs AND TLDs WERE DIFFERENTLY DISTRIBUTED BY:

- Severity of poisoning*, p<0.001

<table>
<thead>
<tr>
<th></th>
<th>LLDCs (%)</th>
<th>TLDs (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>None/not associated</td>
<td>25% (No. 435)</td>
<td>74% (No. 946)</td>
</tr>
<tr>
<td>Minor</td>
<td>64% (No. 1,116)</td>
<td>25% (No. 327)</td>
</tr>
<tr>
<td>Moderate</td>
<td>10% (No. 177)</td>
<td>1% (No. 13)</td>
</tr>
<tr>
<td>High</td>
<td>1% (No. 14)</td>
<td>0% (No. 1)</td>
</tr>
</tbody>
</table>

*Assessed according to the Poisoning Severity Score, Persson et al, J. Toxicol Clin Toxicol, 1998
QUESTIONS

DID THE EXPOSURE RATES CHANGE DURING THE PERIOD UNDER STUDY?

Cumulative Sum Control Chart (CUSUM) and bootstrapping techniques
CASES OF EXPOSURE TO LLDCs AND TLDs HANDLED BY THE NATIONAL POISON CONTROL CENTRE IN MILAN, ITALY, BETWEEN SEPTEMBER 2010 AND DECEMBER 2014

Average: 1.61 cases of exposure /day

Average: 0.83 cases of exposure /day

Average: 0.86 cases of exposure /day
LLDCs exposure rates based on cases handled by the National Poison Control Centre in Milan, Italy, between September 2010-December 2014.

**PRE-CHANGE POINT PERIOD**
- LLDCs marketed by one major company (IC-LLDCs)
  - Average: 2.10 cases/million units sold
- LLDCs marketed by other companies (OCs-LLDCs)
  - Average: 0.97 cases/million units sold

**POST-CHANGE POINT PERIOD**
- LLDCs marketed by one major company (IC-LLDCs)
  - Average: 0.74 cases/million units sold
- LLDCs marketed by other companies (OCs-LLDCs)
  - Average: 1.17 cases/million units sold
LLDCs EXPOSURE RATES BASED ON CASES HANDLED BY THE NATIONAL POISON CONTROL CENTRE IN MILAN, ITALY, BETWEEN SEPTEMBER 2010-DECEMBER 2014
LLDCs EXPOSURE RATES BASED ON CASES HANDLED BY THE NATIONAL POISON CONTROL CENTRE IN MILAN. DECEMBER 2010-DECEMBER 2014

Average: 0.86 cases /million units sold

Average: 1.88 cases /million units sold

Average: 0.96 cases /million units sold
QUESTIONS

IS THE DIFFERENCE BETWEEN THE MEAN NUMBER OF CASES EXPOSED TO LLDCs IN THE PRE- AND POST-CHANGE POINT PERIOD STATISTICALLY SIGNIFICANT?

Analysis of variance (ANOVA)
COMPARISON BETWEEN THE MEAN NUMBER OF CASES EXPOSED TO IC-LLDCs IN THE PRE- AND POST-CHANGE PERIOD

Cases aged <5 years

In the post-change point period the mean number of cases of exposure was reduced by 19.6 exposures/month (95% CI: -23.2; -16.1), p<0.0001 (adjusted by quantity sold)

Cases aged ≥5 years

In the post-change point period the mean number of cases of exposure was reduced by 2.1 exposures/month (95% CI: -3.1; -1.1), p<0.0001 (adjusted by quantity sold)
COMPARISON BETWEEN THE MEAN NUMBER OF CASES EXPOSED TO OCs-LLDCs IN THE PRE- AND POST-CHANGE PERIOD

Cases aged <5 years

in the post-change point period the mean number of cases of exposure was reduced by 2.2 units/month (95% CI: -5.0; 0.6), NS (adjusted by quantity sold)

Cases aged ≥5 years

in the post-change point period the mean number of cases of exposure was reduced by 0.2 units/month (95% CI: -2.6; 3.0), NS (adjusted by quantity sold)
IS THE ASSOCIATION BETWEEN EXPOSURE TO LLDCs AND MODERATE/SEVERE POISONING STATISTICALLY SIGNIFICANT?

Logistic regression models, odds ratio (OR) maximum likelihood estimate
## Model A: including cases <5 years old (No. 1,385)

<table>
<thead>
<tr>
<th>Type of product</th>
<th>No.</th>
<th>moderate/high severity (%)</th>
<th>Crude OR</th>
<th>Adjusted OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>TLDs</td>
<td>223</td>
<td>0.9</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>IC-LLDCs</td>
<td>839</td>
<td>15.3</td>
<td>19.9</td>
<td>22.5</td>
<td>5.5 - 91.9</td>
</tr>
<tr>
<td>OCs-LLDCs</td>
<td>323</td>
<td>10.2</td>
<td>12.6</td>
<td>12.4</td>
<td>2.9 - 52.1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Period</th>
<th>No.</th>
<th>moderate/high severity (%)</th>
<th>Crude OR</th>
<th>Adjusted OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-change point (Sept 2010-Nov 2012)</td>
<td>888</td>
<td>10.8</td>
<td>1</td>
<td>1</td>
<td>--</td>
</tr>
<tr>
<td>Post-change point (Dec 2012-Dec 2014)</td>
<td>497</td>
<td>13.5</td>
<td>1.3</td>
<td>1.6</td>
<td>1.2 - 2.3</td>
</tr>
</tbody>
</table>
### Model B: including cases ≥5 years old (No. 255)

<table>
<thead>
<tr>
<th>Class of age (years)</th>
<th>No.</th>
<th>moderate/high severity (%)</th>
<th>Crude OR</th>
<th>Adjusted OR</th>
<th>Adjusted OR 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-19</td>
<td>134</td>
<td>11.9</td>
<td>1</td>
<td>1</td>
<td>--</td>
</tr>
<tr>
<td>20+</td>
<td>121</td>
<td>21.5</td>
<td>2.0</td>
<td>7.3</td>
<td>3.0-17.8</td>
</tr>
</tbody>
</table>

**Type of product**

<table>
<thead>
<tr>
<th>Type of product</th>
<th>No.</th>
<th>moderate/high severity (%)</th>
<th>Crude OR</th>
<th>Adjusted OR</th>
<th>Adjusted OR 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>TLDs</td>
<td>113</td>
<td>10.6</td>
<td>1</td>
<td>1</td>
<td>--</td>
</tr>
<tr>
<td>IC-LLDCs</td>
<td>94</td>
<td>20.2</td>
<td>2.1</td>
<td><strong>7.9</strong></td>
<td>2.9-21.7</td>
</tr>
<tr>
<td>OCs-LLDCs</td>
<td>48</td>
<td>22.9</td>
<td>2.5</td>
<td><strong>8.5</strong></td>
<td>2.8-25.5</td>
</tr>
</tbody>
</table>

**Period**

<table>
<thead>
<tr>
<th>Period</th>
<th>No.</th>
<th>moderate/high severity (%)</th>
<th>Crude OR</th>
<th>Adjusted OR</th>
<th>Adjusted OR 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-change point (Sept 2010-Nov 2012)</td>
<td>147</td>
<td>16.3</td>
<td>1</td>
<td>1</td>
<td>--</td>
</tr>
<tr>
<td>Post-change point (Dec 2012-Dec 2014)</td>
<td>108</td>
<td>16.7</td>
<td>1.0</td>
<td><strong>1.2</strong></td>
<td>0.6-1.4</td>
</tr>
</tbody>
</table>
CONCLUSIONS

The occurrence of exposures to LLDCs has been halved; this may be because of using obscure/opaque or partially covered outer packaging.

The strength of the association between exposures to LLDCs and moderate/severe poisoning is not lowered by obscuring the outer packaging of these products.

Further efforts should be devoted to prevent hazardous exposure to LLDCs and reduce their intrinsic toxicity.
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