Language Independent Description of Poisoning Symptoms in RAS-CHEM Using MedDRA Terminology

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Herbert Desel, Stacey Wyke, Rob Orford, Raquel Duarte-Davidson, Nicholas Edwards, Katherine Kennedy, Maeve McParland, Alison Good, Hugo Kupferschmidt, Andreas Schaper, Gabi Ochsenfahrt, Al Bronsten, Gabriella Dragelyte, Monique Mathieu-Nolf, Daniela Pelcova

Harmonisation of Description of Poisonings

- began with IPCS working group results,
- authority lists for many items needed to describe poisonings
- especially with the poisoning severity score

Introduction: A fundamental requirement for RAS-CHEM to operate successfully (in an interdisciplinary multi-language environment) is to adopt standardised terminology to describe clinical effects.

Methods: All clinical effects identified in the CEPs were compared to symptoms reported in internationally standardised terminology systems such as MedDRA, Snomed-CT, WHO-ART and poison centre specific terminology.

Results: From the 118 chemical agents included in the literature review, 1011 clinical effects were identified. These effects were described using the terminology systems under investigation.

EAPCCT Bordeaux 2010, Abstract #128:
The Evaluation of Standard Medical Terminology Systems to Describe Symptoms of Poisoning, an Output of the ASHTII Project


Bordeaux #128: The Evaluation of Standard Medical Terminology Systems to Describe Symptoms of Poisoning, an Output of the ASHTII Project

Conclusions:
- In the development of the alerting system it is intrinsically important that RAS-CHEM can capture the wide spectrum of clinical effects associated with toxic chemical exposure and poisonings.
- The use of a limited terminology system containing broad definitions of clinical effects may result in reduced sensitivity of the alert system.
- As a result an internationally standardised terminology system such as MedDRA or Snomed-CT has been recommended for inclusion in EUPC Forum and RAS-CHEM.
- The terminology system chosen for alert systems may become a basis for collation or exchange of cases from poisons centres for different purposes in the future.

Final decision

- The Medical Dictionary for Regulatory Activities (MedDRA) was chosen as the most suitable independent terminology to describe poisonings in several European languages.
- It was carefully evaluated and recommended as the most appropriate symptom description terminology to be incorporated into RAS-CHEM.

The Medical Dictionary for Regulatory Activities (MedDRA)

- ... is a hierarchic multilingual terminology system of medical symptoms
- maintained by the MedDRA Maintenance and Service Organisation (MedDRA MSSO).
- MedDRA terminology is widely used for a variety of medical purposes, especially for exchanging reports on adverse drug reactions between companies and authorities.
- The European Medicines Agency (EMA) uses MedDRA for symptom-related communication.
- The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) strongly supports MedDRA use.

Structure of MedDRA

- System Organ Class (SOC):
  - Respiratory, thoracic and mediastinal disorders
- High Level Group Term (HLGT):
  - Respiratory disorders NEC (i.e. not elsewhere classified)
  - Breathing abnormalities
- High Level Term (HLT):
  - Respiratory Depression
- Preferred Term (PT):
  - Dyspnoea
- Low Level Term (LLT):
  - Difficulty breathing

Methods

- All CEP data were combined in a single spreadsheet/database table (column titles: agent name, symptom, related organ, time course).
- All terms chosen by ASHTII to describe poisoning symptoms were corrected for spelling errors.
- Subsequently all terms were matched with MedDRA low level terms (LLT) (version 13.0) by automatic and manual procedures.
- Change requests to add missing poisoning symptoms was submitted to MedDRA MSSO.
- These changes were included in the revised version of MedDRA (version 13.1). Finally all symptoms identified in any CEP were matched to MedDRA version 13.1 terms.
- All CEP data including all MedDRA matched symptom terms were imported into a test database (DEV-EU PC Forum). Detailed evaluation was done with special attention to reporting in different languages.
Methods

➢ All CEP data were combined in a single spreadsheet / database table

Results

➢ In total 4036 symptom-by-agent relations were included in
the data analysis.
➢ After editing the symptoms list to erase double entries,
correct typo errors and minimal spelling variations 1565
different medical symptoms were listed.
➢ 1492 symptoms (95%) could be matched with MedDRA
terms either
  ➢ automatically (41%)
  ➢ semi-automatically (algorithmic match with expert checking,
e.g., „Difficulty breathing“ -> „breathing difficulties“, 22%)
  ➢ or manually (33%)
➢ 83 symptoms (5%) could not be described or identified in
MedDRA version 13.0

Results

➢ 83 symptoms that could not be described
or identified in MedDRA version 13.0 and
were submitted for addition to MedDRA
version 13.1 (‘change requests’)
➢ ... and were accepted.
➢ After acceptance, 
  ➢ all 1565 ASHT symptom terms could be
matched with
  ➢ 1139 MedDRA terms.
➢ After import into the test database, search
and reporting functions tested satisfactory.

Conclusion

➢ 1139 terms were needed to describe all symptoms
of more than 100 (mostly severe) intoxications.
➢ It was shown that MedDRA, a systematic
nomenclature developed for reporting adverse
drug effects, can be used to precisely describe
poisonings.
➢ Cooperation with MedDRA MSSO gave substantial
support for the project.
➢ The mapping of symptoms in the technical
environment of a relational database enables
multiple functions of data retrieval and reporting.

Conclusion

➢ The mapping of symptoms in the database
enables multiple functions of data retrieval
and reporting:
➢ Thus,
  ➢ the hierarchic ordering of symptoms in MedDRA
enables searching not only for
  ➢ cases with identical symptoms but also for
  ➢ those with similar symptoms.

Conclusion

➢ Further evaluation will show whether
MedDRA may be used for other tasks and
projects where information of poisoning
symptoms need to be compiled or
exchanged in a harmonized and
multilingual way, e.g.
  ➢ case documentation in poisons centres and
  ➢ case data exchange between poisons centres.
Acknowledgement

- Thanks to Eva Rump, member of the maintenance team, MedDRA MSSO
- delivered strong support
- in the symptoms matching process and
- integration of poisoning specific term into MedDRA
### Example Search by Symptom

#### Table

<table>
<thead>
<tr>
<th>Organ</th>
<th>Symptom</th>
<th>Initial Search</th>
<th>Secular Search</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immune system</td>
<td>Hypersensitivity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory</td>
<td>Wheezing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nervous system</td>
<td>Tumoral change</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
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<td></td>
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<td></td>
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<td>Nervous system</td>
<td>Incontinence</td>
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#### Diagram

- **Venn Diagram**: Three overlapping circles labeled "Search", "Vehicle", and "Location".
- **Clinical Effect**: "Wheezing effect".
- **Symptom Search Mode**: "Broader Search".

#### Text

- **Note**: 65 agents found.

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#### Text

- **Note**: 65 agents found.
Conclusion: The ASHTII project team has further developed the concept of the RAS-CHEM to provide DG SANCO with a central alerting system for chemical agents. CEPs were produced for 118 chemical agents included in RAS-CHEM to be accessed easily by both the poisons centres and public health authorities. The list included chemicals of concern in deliberate release scenarios, those posing a major threat from accidental release, and agents identified as interesting from a poisons centres perspective. The list was used as a reference point for the literature review, which resulted in the production of acute-exposure Clinical Effect Profiles (CEPs) for a representative list of chemical agents. The poisoning severity score developed by Deutsche Gesellschaft für Forensische Medizin (DGFM) in 1998 was used to grade the severity of acute poisoning, and agents were classified as single-organ, multi-organ, or whole-body effects. The CEPs were updated, peer reviewed, referenced, and easily accessible in a concise tabulated format according to body system and ordered chronologically. The poisoning severity score developed by Deutsche Gesellschaft für Forensische Medizin (DGFM) in 1998 was used to grade the severity of acute poisoning, and agents were classified as single-organ, multi-organ, or whole-body effects. The CEPs were updated, peer reviewed, referenced, and easily accessible in a concise tabulated format according to body system and ordered chronologically. The poisoning severity score developed by Deutsche Gesellschaft für Forensische Medizin (DGFM) in 1998 was used to grade the severity of acute poisoning, and agents were classified as single-organ, multi-organ, or whole-body effects. The CEPs were updated, peer reviewed, referenced, and easily accessible in a concise tabulated format according to body system and ordered chronologically. The poisoning severity score developed by Deutsche Gesellschaft für Forensische Medizin (DGFM) in 1998 was used to grade the severity of acute poisoning, and agents were classified as single-organ, multi-organ, or whole-body effects.

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Methods: Following a review of resources, the Meta-Directory ToxSeek was used as the initial starting point for all literature reviews. The literature review resulted in the production of acute-exposure Clinical Effect Profiles (CEPs) for a representative list of chemical agents. The literature review was updated, peer reviewed, referenced, and easily accessible in a concise tabulated format according to body system and ordered chronologically. The poisoning severity score developed by Deutsche Gesellschaft für Forensische Medizin (DGFM) in 1998 was used to grade the severity of acute poisoning, and agents were classified as single-organ, multi-organ, or whole-body effects.

Objective: For RAS-CHEM to operate successfully in an interdisciplinary multi-language environment, it is important to adopt an agreed standard to describe symptoms of poisoning. An agreed symptom terminology system is necessary to facilitate communication among the different stakeholders, such as medical professionals, emergency services, and public health authorities. The aim of the project was to develop a symptom terminology system that could be used by the RAS-CHEM project to describe symptoms of poisoning.

Pelclova et al.


References Pelclova et al.
Introduction: An Alerting System for Chemical Threats (ASHTII) is currently under development to improve the speed and effectiveness of detection, evaluation and public health response to accidental and deliberate chemical release. This new system, which is being developed by the European Commission’s 7th Framework Programme (FP7) Project, is intended to provide an early warning, alerting and information distribution capability to European Union (EU) members, as well as being connected to the Global Public Health Emergencies Information Network (GPHIN). A fundamental requirement for ASHTII is to adopt standardised terminology to describe clinical effects in both systems.

Methods: A literature review of symptoms associated with exposure to relevant chemicals was undertaken; this included chemicals that have a high risk of accidental or deliberate release and chemicals of interest to poisons centres. Clinical Effect Profiles (CEPs) were produced to provide concise tabulated summaries of clinical effects reported in the available literature; all clinical effects identified in the review were compared to symptoms reported in internationally standardised terminology systems such as MedDRA, SNOMED-CT, WHO-ART and poisons centre specific terminology such as NPDS and GfKT.

Results: From the 118 chemical agents included in the literature review, 1011 clinical effects were identified. 108 individual CEPs were produced; seven were grouped as ‘organophosphates’ and three as ‘cyanides’.

Conclusion: In the development of the alerting system it is intrinsically important that both the EUPC Forum and RAS-CHEM can capture the wide spectrum of clinical effects associated with toxic chemical exposure and poisonings. The use of a limited terminology system containing broad definitions of clinical effects may result in reduced sensitivity of the alert system. As a result an internationally standardised terminology system such as MedDRA or SNOMED-CT has been recommended for inclusion in EUPC Forum and RAS-CHEM. The terminology system chosen for alert systems may become a basis for collation or exchange of cases from poisons centres for different purposes in the future.