Recognition of new occupational diseases by the method of pharmacovigilance

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Lessons learnt

- What is pharmacovigilance
- Causality assessment
- Relation between pharmacovigilance and new Occupation diseases
- Lessons to learn
- ADR reporting
- Final remarks
The aim is

- to assess the importance of pharmacovigilance in the occupational pathology, discovering new information about the unknown risk and identify adverse reactions and symptoms of occupational diseases.
Wouter van Doeveren presented "Remedio morbi", 8. February 1779.

Remedio morbi
Digitalis intoxication, 19 people died
The word Pharmacovigilance

- Being vigilant regarding drugs
- Started in France in the regional centres
- Internationally introduced around 1980 by prof. Rene Royer
- Definition by WHO in 2002: science and activities
Definition

Pharmacovigilance

- The science and activities relating to the detection, assessment, understanding and prevention of adverse drug effects or any other drug related problem

WHO definition

- The science and activities relating to the detection, assessment, understanding and prevention of various risk factor effects or any other environmental working place related problem
Definition

Adverse Drug Reaction (ADR)

- A response to a drug which is noxious and unintended, and which occurs at doses normally used in men for prophylaxis, diagnosis or therapy

  WHO definition

- A response to a exposure to workplace factor which is noxious and unintended, and which occurs at permissible doses in working environmental for everyday work

ADR in OH= adverse effects of work on health
Post- signals and symptoms surveillance

- Spontaneous Reporting Surveillance - RAPID ALERT SYSTEM-RAS (urgent information system)
- Active surveillance, such intensive monitoring
- Epidemiological studies
- Phase IV clinical studies
Pharmacovigilance in OH

- Application of pharmacovigilance in occupational medicine involves the collection, monitoring, assessment and evaluation of information on adverse effects of work on health.

- All functions of pharmacovigilance is compatible with the discovery of new occupational hazards and new occupational health disorders- signal detection.
Causality assessment

- Clinical information
- Metabolism: pharmacological and toxicological or pathological mechanism
- Time-course
  - period of latency: challenge and rechallenge in OH: period of exposure
- Involvement of co-factors
  - indication, risk-factors, worsening factors
Patient characteristics

- Confounding by indication
- Co-morbidity
- Individual characteristics
Quantitative approach: screening database

- Screening all associations for possible signals
- Prescription based on:
  - Number of reports
  - Labelled ADR: yes or no
  - Minimum lower level 95% CI

Complementary to case by case analyses !!!
Position of pharmacovigilance
Newfangledness': fascination for new things

- New Occupational Diseases: side effect of work
- Parallel with side effects of drugs/pharmaceutics
- All Occupational Diseases once were new
- Pharmacovigilance: example for OHS-vigilance
In defense of case reports and case series.

- “Case reports and series have a high sensitivity for detecting novelty and therefore remain one of the cornerstones of medical progress; they provide many new ideas in medicine. At the same time, good case reporting demands a clear focus to make explicit to the audience why a particular observation is important in the context of existing knowledge.”

- imaju visoku osjetljivost u otkrivanje novina,
- Jedan su od temelja medicinskog napretka;
- pružaju mnoge nove ideje u medicini
- dobar slučaj zahtijeva jasan fokus kako bi eksplicitno ponuditi javnosti zašto je određeno promatranje važno u kontekstu postojećih znanja.
Software for National Centres
Vigibase on-line

Dr
RC
NC

\( E2B \)

Search
Analysis

Vigibase
Lessons to learn

- **Case reports** are an important source of knowledge
- Exchange of information supports signal (symptom) detection
- Causality assessment is key
- The message counts, not the reporter

*OH- vigilence*
Case reports:
difficulties in completing the records

- Possible Occupational Diseases (toxic or infectious):
  - Happening in different, often unexpected workplaces; inadequate labeling
  - Medical aspects: cases are referred to local hospitals often lacking know-how of occupational medicine
  - Exposure assessment: in retrospect difficult to perform adequate measurements

OH-vigilence
Impact of (patient) report

- Awareness of a (new) signal
  patients often provide more detailed information
- Publication
- Information
- Information in organization
- ADR is reported without a medical filter
<table>
<thead>
<tr>
<th>Category</th>
<th>Examples</th>
</tr>
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<tbody>
<tr>
<td>New diseases due to changes in work / conditions</td>
<td>• Allergy to biological pesticides</td>
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<tr>
<td></td>
<td>• Neuropathy in swine slaughterhouse workers</td>
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<td></td>
<td>• Legionnaires disease</td>
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<td>• Popcorn workers lung</td>
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<td>• Povrede ponavljanih opterećenja pri radu za komjuterom (eng. Repetitive Strain Injury)</td>
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<tr>
<td></td>
<td>• Legionnaires` discharge</td>
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<tr>
<td>New risks from known forms of stress</td>
<td>• Cardiovascular diseases caused by fine dust</td>
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<td>• Breast cancer and work at night</td>
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<td>• Lung infections due to welding fumes</td>
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<td>Consequences of parents occupational exposure on off spring</td>
<td>• Congenital abnormalities</td>
</tr>
<tr>
<td></td>
<td>• Cancer in children</td>
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<td>• Delayed neuropsychological development</td>
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Spontaneous Reporting Systems

Regarding the detection of adverse drug reactions, experience learns us that Spontaneous Reporting Systems can not be replaced by any other method yet.

Geneeskde,1986

What should be reported

- Serious ADRs
- NEW ADRs
- ADRs from new drugs, .....new risks, new technology, new workplace

- What you think: it should be reported!
Goals of ADR reporting

- Signal detection: finding new signals/symptoms
- *Awareness of occupational physicians* (and pharmacists):
  - prevention of ADRS
  - recognition of ADRs
- ADR reporting is a quality indicator for pharmacotherapy
- ADR reporting in OH is a quality indicator for intervention and therapy at workplace
- Signals/ Symptoms of OD reporting is a quality indicator
ADR reporting system in OH
Method of pharmacovigilance (vigilance)

Follow 6 steps (work includes occupational health physicians)
1. registration of cases in the field of detection signals of adverse reactions;
2. registration of workers;
3. detection and screening during the implementation of preventive periodic inspections;
4. installation data in the relevant database;
5. synthesis, evaluation, selection and active medical supervision and monitoring;
6. and secondary epidemiological analysis of survey data in the population of patients- workers.
Final remarks

- Detected the first suspicious signals, signs or symptoms as adverse reactions or side effects of work are starting activities before launch epidemiological and experimental research.

- The method of pharmacovigilance is not able to demonstrate causality.

- Application of pharmacovigilance is a challenge in tracking, identifying and preventing unknown risks and illnesses at the time of continuous changes in the field of the work.
Circle of knowledge and practice

Knowledge

Practice

OH- vigilence
WHO programme for international Drug Monitoring

**TOP 10 COUNTRIES**

- USA 46%
- GBR 13%
- DEU 6%
- CAN 5%
- AUS 5%
- FRA 4%
- ESP 3%
- SWE 3%
- THA 2%
- NLD 2%
- OTHERS 11%
Reporting system ADR as symptoms and signals: tip of the iceberg

Thank you for your attention