Incidence of drug related problems

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Disposition

- Drug related problems – definition and classifications
- Incidence of drug related problems
- Examples: different settings and diseases
- Consequences of drug related problems
- Example of preventable drug related admissions in diabetes
Why is this of interest?

More people die of inappropriate drug treatment than from breast cancer, AIDS and traffic accidents all together (Kohn et al. 1999)

Adverse drug reactions are the 4.-6. most frequent cause of death in USA (Lazarou et al. 1998)

Twice as much money are use to solve drug related problems and adverse drug events than on the drug themselves (Ernst & Grizzle. 2000)
Pharmaceutical care

The responsible provision of drug therapy with the purpose to achieve defined outcomes that improve patients quality of life

Hepler og Strand (1990)
PC and drug related problems

- PC focus on identification, solving and prevention of drug related problems
- *Before* the problems results in drug related morbidity and mortality

**2 main groups**
1. Problems caused by therapeutic failures
2. Problems caused by unwanted effects that creates new medical problems for the patient (negative effects)
Drug related problems

An unwanted situation experienced by the patient that is caused by or excepted to be caused by drug therapy and which causes or have the potential to cause problems for the desired outcomes of drug therapy
DRP - dimensions

**Access to treatment**
1. Untreated indication

**Effectiveness**
2. Inappropriate choice of drug
3. Sub-therapeutic dosages
4. Inappropriate use by patient

**Safety**
5. Over dosages
6. Adverse drug reactions
7. Interactions
8. Medication without indication
Documentation database in pharmacy practice

- Electronic database developed, maintained and financed by the Danish Pharmaceutical Association and Pharmakon

- The database started primo 2003. Yearly update

- 10 different themes

- Access through: www.pharmakon.dk/dokumentationsdatabasen
Incidence of drug related problems - Evidence report 7

Drug related problems
• Drug related problems in community pharmacies
• Drug related problems in nursing homes
• Drug related problems in general practice

Adverse drug events
• Drug related hospital admission
• Admissions caused by adverse drug reactions
• Drug related emergency room visits
Data sheets

- Number and category of drug related problems
- Number and category of adverse drug events
- Drugs at risk
- Risk factors (social, demographic, treatment)
- Other health related consequences
- Economic consequences
- Psychosocial consequences
Included studies in the 2006 update

59 studies are included in the report

- DK: 11 studies
- UK: 8 studies
- Europe: another 19 studies
- USA: 15 studies
- Australia: 1 study
Settings

Drug related problems
• Community pharmacy: 6 studies + 11 studies
• Nursing homes: 6 studies
• General practice: 4 studies

Adverse drug events
• Hospital: 35 studies
• Emergency room: 4 studies
Community pharmacy

**Incidence**
- Campaigns: 30-40%
- Pharmaceutical care programs: 75-100%

**Most frequent DRP**
- Inappropriate use by the patient
- Adverse drug reactions
- Lack of knowledge about disease and drug therapy
AHProject

- Data collection by students on internship in pharmacy
- Qualitative interview with patients
- 1999: Angina pectoris patients
- 2000: Diabetes patients
- 2001: Asthma patients
- Ellen Westh Sørensen and Lotte Stig Haugbølle
### AHProject results

<table>
<thead>
<tr>
<th></th>
<th>Angina pectoris</th>
<th>Diabetes</th>
<th>Asthma</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=123 (% of DRP)</td>
<td>N=176 1154 LRP</td>
<td>N=96 394 LRP</td>
</tr>
<tr>
<td>A: Inappropriate choice of drug</td>
<td>41%</td>
<td>81 (7.0%)</td>
<td>66 (16.8%)</td>
</tr>
<tr>
<td>B: Inappropriate drug use</td>
<td>9%</td>
<td>341 (29.%)</td>
<td>109 (27.7%)</td>
</tr>
<tr>
<td>C: Inappropriate dosing</td>
<td>9%</td>
<td>65 (5.6%)</td>
<td>16 (4.1%)</td>
</tr>
<tr>
<td>D: Interactions</td>
<td>-</td>
<td>94 (8.1%)</td>
<td>2 (0.5%)</td>
</tr>
<tr>
<td>E: Adverse drug reactions</td>
<td>14%</td>
<td>42 (3.6%)</td>
<td>52 (13.2%)</td>
</tr>
<tr>
<td>F: Other problems</td>
<td>27%</td>
<td>531 (46%)</td>
<td>149 (37.8%)</td>
</tr>
</tbody>
</table>
Asthma patients – based on 6 studies

- Lack of knowledge on disease and medicine: 30-70%
- Non-compliance: 25-40%
- Adverse drug events: 25-35%
- Sub-therapeutic dosages: 16-36%
- Technical problems with inhalation techniques: 20-30%
## DRP in elderly patients

<table>
<thead>
<tr>
<th></th>
<th>UK</th>
<th>AUS</th>
<th>Can.</th>
<th>UK</th>
<th>USA</th>
<th>Can.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean no DRP</td>
<td>7.8</td>
<td>2.9</td>
<td>3.9</td>
<td>5.6</td>
<td>3.4</td>
<td>8.7</td>
</tr>
<tr>
<td>Untreated indication</td>
<td>5.2%</td>
<td>16.5%</td>
<td>40%</td>
<td>20%</td>
<td>20%</td>
<td>11.2%</td>
</tr>
<tr>
<td>Inap. drug</td>
<td>11.9%</td>
<td>5.7%</td>
<td>13%</td>
<td>18%</td>
<td>11.6%</td>
<td></td>
</tr>
<tr>
<td>Sub. dosage</td>
<td>7%</td>
<td></td>
<td>6%</td>
<td>4.5%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inap. use</td>
<td>5.5%</td>
<td>32.6%</td>
<td>12%</td>
<td>11.7%</td>
<td>17%</td>
<td>4.7%</td>
</tr>
<tr>
<td>Over dosage</td>
<td>7%</td>
<td></td>
<td>4%</td>
<td>5.5%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ADR</td>
<td>24.2%</td>
<td>13.9%</td>
<td>11%</td>
<td>15.1%</td>
<td>16%</td>
<td>34.1%</td>
</tr>
<tr>
<td>Interactions</td>
<td>1.4%</td>
<td></td>
<td>3%</td>
<td>17.7%</td>
<td></td>
<td>9.2%</td>
</tr>
<tr>
<td>No indication</td>
<td>5.4%</td>
<td>7.6%</td>
<td>7%</td>
<td>8%</td>
<td>11.2%</td>
<td></td>
</tr>
<tr>
<td>Inap. dosing regimen</td>
<td>6.3%</td>
<td>14.8%</td>
<td>11.9%</td>
<td></td>
<td>8%</td>
<td></td>
</tr>
</tbody>
</table>
Improved well-being in the elderly through community pharmacy based pharmaceutical care

- Randomised, controlled trial
- 28 pharmacies
- 523 elderly >65 years, >4 prescribed drugs
- Pharmacists consultation and medication review each quarter for 1½ years

Drug related problems
Medication review (n=143)

<table>
<thead>
<tr>
<th>Problem</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Problems with ADR</td>
<td>48.3%</td>
</tr>
<tr>
<td>Problems with effects of drugs</td>
<td>35.0%</td>
</tr>
<tr>
<td>Problems with symptoms</td>
<td>30.8%</td>
</tr>
<tr>
<td>Problems with practical use</td>
<td>17.5%</td>
</tr>
<tr>
<td>Difficulties using the drugs</td>
<td>17.5%</td>
</tr>
<tr>
<td>Afraid of ADR</td>
<td>16.1%</td>
</tr>
<tr>
<td>Afraid of effect of drugs</td>
<td>9.8%</td>
</tr>
<tr>
<td>Dissatisfied with treatment</td>
<td>9.8%</td>
</tr>
<tr>
<td>Dissatisfied with effects</td>
<td>7.7%</td>
</tr>
<tr>
<td>Afraid of discontinuation</td>
<td>7.0%</td>
</tr>
<tr>
<td>Afraid to start new treatment</td>
<td>7.0%</td>
</tr>
</tbody>
</table>

**Total 518 DRP (mean = 3.6)**
## Problems with medicine use

<table>
<thead>
<tr>
<th>Issue</th>
<th>Intervention Baseline</th>
<th>Intervention 18 months</th>
<th>Control Baseline</th>
<th>Control 18 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Difficulties to swallow medicines</td>
<td>11.6%</td>
<td>8.6%</td>
<td>6.7%</td>
<td>8.7%</td>
</tr>
<tr>
<td>Difficulties to open packing</td>
<td>35.3%</td>
<td>31.0%</td>
<td>25.5%</td>
<td>26.6%</td>
</tr>
<tr>
<td>Difficulties to get medicines out of packing</td>
<td>21.8%</td>
<td>22.8%</td>
<td>11.0%</td>
<td>16.3%</td>
</tr>
<tr>
<td>Unpleasant taste</td>
<td>12.8%</td>
<td>11.4%</td>
<td>14.3%</td>
<td>12.9%</td>
</tr>
<tr>
<td>Adverse drug reactions</td>
<td>33.2%</td>
<td>19.4%</td>
<td>25.7%</td>
<td>24.8%</td>
</tr>
</tbody>
</table>
# Problems with medicine use

<table>
<thead>
<tr>
<th></th>
<th>Intervention Baseline</th>
<th>Intervention 12 months</th>
<th>Control Baseline</th>
<th>Control 12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Difficulties to read label</td>
<td>15.0%</td>
<td>13.1%</td>
<td>25.7%</td>
<td>24.8%</td>
</tr>
<tr>
<td>Difficulties to read insert</td>
<td>10.4%</td>
<td>11.9%</td>
<td>10.5%</td>
<td>13.8%</td>
</tr>
<tr>
<td>Confusion on when to take medicine</td>
<td>3.9%</td>
<td>2.5%</td>
<td>2.1%</td>
<td>3.5%</td>
</tr>
<tr>
<td>Mean number of problems</td>
<td>1.36</td>
<td>1.18</td>
<td>1.04</td>
<td>1.16</td>
</tr>
</tbody>
</table>
Nursing homes - Results

Nursing home residents experiences many DRP

- Most frequent problems
  - Inappropriate choice of drugs
  - Over dosages
  - Interactions
  - Risk of adverse drug reaction

- **Drugs at risk**
  - Anti-depressant
  - Sedatives/hypnotics
  - Antibiotics

- **Risk factors**
  - Risk of DRP increase with increased number of drugs
Aim: To evaluate if the use of benzodiazepines and cyclopyrrolones are used in accordance to guideline for rational drug use

- Medication review
- Residents using benzodiazepines and/or cyclopyrrolones
- > 3 prescribed drugs
Results

- 163 residents in the nursing home
- 25% of the residents use benzodiazepines and/or cyclopyrrolones and were poly-pharmacy patients (37 residents)
- 117 potential DRP were identified (3.2 DRP/residents)
- Adverse drug events could not be judged
• Lengths of therapy too long: 28 (17%) and 54% of patients
• Over dosages: 24 (20.5%)
• Interactions: 23 (19.7%)
• Inappropriate time of administration: 20 (17.1%)
• Sub-therapeutic dosages: 9 (7.7%)
• Inappropriate choice of drug: 4 (3.4%)
General practice - Results

- Lack of evidence

- Medication review (3 studies)
  - 43-44% of patients experienced DRP
  - 56% of the drugs resulted in DRP

- Prescription service
  - 24.5% of the patients experienced adverse drug events
Clinical pharmacy in general practice

- Medication review of poly-pharmacy patients
- Review of medical record for patients in the consultation
- Implementation of treatment guidelines

Christine Dinsen, Bente Kirkeby, Peter Stæhr, Birthe Søndergaard
Medication review – Results
N=40 (Mean 2.6 DRP)

Access to treatment
  1. Untreated indication 6 (5.6%)

Effectiveness
  2. Inappropriate choice of drug 19 (18.4%)
  3. Sub-therapeutic dosages 8 (7.7%)
  4. Inappropriate use by patient 22 (21.4%)

Safety
  5. Over dosages 18 (17.5%)
  6. Adverse drug reactions 16 (15.5%)
  7. Interactions 2 (1.9%)
  8. Medication without indication 12 (11.7%)
Medication review and local guidelines

- 7 pharmacies and 19 general practices (10 intervention and 9 control)
- 82 patients >4 prescribed drugs
- Local guidelines
  - Hypertension
  - Pain
  - Ulcers
- 6 months follow-up on PEM
- Bente Kirkeby, Birthe Søndergaard m.fl.
DRP - Results

Access to treatment
1. Untreated indication 21 (18%)

Effectiveness
2. Inappropriate choice of drug 10 (8%)
3. Sub-therapeutic dosages 11 (9%)
4. Inappropriate use by patient 41 (35%)

Safety
5. Over dosages 6 (5%)
6. Problems caused by GS 6 (5%)
7. Adverse drug reactions 12 (10%)
9. Interactions 9 (8%)
10. Medication without indication 2 (2%)
Drug related admissions

Meta-analyses: 6-14%
Individual studies: 4 – 10%

ADR: Meta-analyses: 3-5%
ADR: Individual studies : 2.5-12%

3% of drug related admissions are fatal
80% of drug related admissions are ‘serious’
60% of the admissions were preventable
35% of the ADR admissions were preventable
Drug related admissions

**Causes**
ADR: 23-52%
Non-compliance: 2-11%
Therapy failure: 2.5-4.5%

**Risk drugs**
Drugs for hearth diseases (diuretics)
Antibiotics
Pain revisers
CNS-working drugs
Drug related admissions

Risk factors
• Increased risk with increased number of drugs and age
• Correlation with gender is uncertain

Other consequences
• Increased lengths of stay
• Increased costs
Preventable DRA in patients with diabetes type 2
Linda Aagaard Thomsen, Birthe Søndergaard m.fl

- Indicators for preventable drug related admission (pDRA)

- Indicator: links the process and outcome
  - ADE: Hospital admission because of hyperglycaemia
  - Pattern of care: The patient is prescribed an oral hypoglycaemic agent and HbA1c was not monitored at least every 6 months
Preventable DRA

- 22 different indicators
- Register-based analysis
  - 10% random sample of the Danish population
  - All patients having oral hypoglycaemic drugs in 2001-2003 were identified
- Registers
  - Danish Medication Register
  - Population Register
  - Danish Patient Register
  - Health Insurance Register
Preventable DRA - Results

- 9,791 diabetes type-2 patients were included
- 15,645 patient year of treatment

- 12,281 preventable drug related admissions were identified
- Most events were related to
  - Kidney problems or hyperglycaemia after inappropriate HbA1c monitoring
  - Elevated serum Creatinin or kidney problems after lack of ACE-I treatment or inappropriate monitoring of
<table>
<thead>
<tr>
<th>ARE</th>
<th>Process of care</th>
<th>Number of pDRA</th>
<th>Number of patients</th>
<th>pDRA/1000 person-year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypergly.</td>
<td>Oral antidiab. and HbAc1 &lt; 6 months</td>
<td>4,447</td>
<td>842</td>
<td>284 (276-292)</td>
</tr>
<tr>
<td>Hypergly.</td>
<td>Sulfonylurea or thiazid and HbAc1 &lt; 6 months</td>
<td>81</td>
<td>13</td>
<td>5.18 (4-6.3)</td>
</tr>
<tr>
<td>Hypogly.</td>
<td>Antidiab + beta-blocker and HbAc1 &lt; 6 months</td>
<td>43</td>
<td>27</td>
<td>2.75 (1.9-3.6)</td>
</tr>
<tr>
<td>Hypogly.</td>
<td>Long acting sulfonylurea and HbAc1 &lt; 6 months</td>
<td>95</td>
<td>65</td>
<td>6.1 (4.9-7.3)</td>
</tr>
<tr>
<td>Hypogly.</td>
<td>Insulin and HbAc1 &lt; 6 months</td>
<td>62</td>
<td>35</td>
<td>3.9 (2.9-4.9)</td>
</tr>
<tr>
<td>Hypogly.</td>
<td>Sulfonylurea and NSAID/ASA and HbAc1 &lt; 6 months</td>
<td>60</td>
<td>38</td>
<td>3.8 (2.9-4.8)</td>
</tr>
<tr>
<td>ARE</td>
<td>Process of care</td>
<td>Number of pDRA</td>
<td>Number of patients</td>
<td>pDRA/1000 person-year</td>
</tr>
<tr>
<td>-------------------</td>
<td>---------------------------------------------------------------------------------</td>
<td>-----------------</td>
<td>--------------------</td>
<td>-----------------------</td>
</tr>
<tr>
<td>Secondary AMI</td>
<td>Diagnosis AMI and no 75-150 mg ASA</td>
<td>77</td>
<td>45</td>
<td>4.9 (3.8-6.0)</td>
</tr>
<tr>
<td>Secondary AMI</td>
<td>Diagnosis AMI and no beta-blocker 2 years after first AMI</td>
<td>149</td>
<td>68</td>
<td>9.5 (7.9-11.0)</td>
</tr>
<tr>
<td>Secondary AMI</td>
<td>Diagnosis AMI and no anti-hyperlipid.</td>
<td>198</td>
<td>74</td>
<td>12.7 (10.9-14.4)</td>
</tr>
</tbody>
</table>
Estimates for Denmark

- **Drug related admissions:** 68.000 – 158.000
- **ADR admissions:** 34.000 – 56.000
- **Drug related deaths:** 1.400 – 3.200
- **Serious ADE:** 54.000 – 126.000
- **Preventable ADE:** 39.000 – 120.000
- **Emergency room visits:** 30.000 – 50.000
- **Related admissions:** 4.500 – 12.500