Therapeutics – common errors and pitfalls

March 14, 2008

Dr. Alexander Woywodt

Consultant Renal Physician, RPH
Errors with therapeutics can be dangerous or even fatal

• 33 year old who suffered from rheumatoid arthritis.

• GP prescribed him 10mg oral methotrexate weekly

• The GP made a prescribing error when selecting the dose frequency for the prescription from the drop down menu on the computer. She erroneously selected daily doses instead of weekly.

• The pharmacist was distracted by an enquiry from one of his colleagues about another prescription.

• Pat. not been given any patient information about the drug.

• After 5 days he began to feel ill and was admitted to hospital with methotrexate poisoning.

familiar with the drug?

should the daily option be disabled?

human error

why not?

too late
Side effects and problems with medication: Size of the problem

- May be the cause or contributing in 50% of hospital admissions
- Have been described as the fifth most common cause of death
  (Lazarou et al., JAMA 1998)
- 40% may be preventable
- Annual costs for a 700-bed teaching hospital are between $5.6 million and $2.8 million (Bates, JAMA 1997)
### Human error

#### Accident Causes by Category (percent)

<table>
<thead>
<tr>
<th>Cause</th>
<th>1950s</th>
<th>1960s</th>
<th>1970s</th>
<th>1980s</th>
<th>1990s</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pilot Error</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pilot Error (weather related)</td>
<td>6</td>
<td>12</td>
<td>9</td>
<td>11</td>
<td>11</td>
<td>10</td>
</tr>
<tr>
<td>Pilot Error (mechanical related)</td>
<td>4</td>
<td>3</td>
<td>3</td>
<td>2</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Total Pilot Error</td>
<td>37</td>
<td>39</td>
<td>30</td>
<td>34</td>
<td>34</td>
<td>35</td>
</tr>
<tr>
<td>Other Human Error</td>
<td>2</td>
<td>5</td>
<td>5</td>
<td>4</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>Weather</td>
<td>10</td>
<td>7</td>
<td>9</td>
<td>11</td>
<td>11</td>
<td>10</td>
</tr>
<tr>
<td>Mechanical Failure</td>
<td>13</td>
<td>14</td>
<td>12</td>
<td>15</td>
<td>18</td>
<td>14</td>
</tr>
<tr>
<td>Sabotage</td>
<td>3</td>
<td>3</td>
<td>7</td>
<td>10</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Other Cause</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Undetermined or missing</td>
<td>34</td>
<td>30</td>
<td>36</td>
<td>25</td>
<td>24</td>
<td>30</td>
</tr>
</tbody>
</table>
Only multiple errors are fatal: The swiss cheese model
Simple pitfalls

- Right drug
- Right patient
- Right dose

This bag contains the dose for a 500 kg man
More simple pitfalls about dosing

- Dosing usually depends on body weight, body surface area.
- Dosing regimens are based on adults with normal weight.
- Dosing regimens are based on normal liver and kidney function.
- Dosing regimens are based on a single-drug model.
**Obese patients**

- A 300 kg patient is admitted to ICU with sepsis, needs intubation, ventilation and vasopressors.
- What is the dose of Meropenem in this patient (the dose for a 75 kg man is 1g TDS iv)?

*We do not know*
Kidney disease

• A young lung transplant patient in ICU with acute renal failure and dialysis develops heparin-induced thrombocytopenia and receives lepirudin.

• Ten hours later, she bleeds to death.

• Renal patients are problematic for non-renal doctors: Many drugs need drug adjustment
  – ask for help

• Have GFR available

Be careful in these patients! (same applies to liver disease)
Interactions

- A kidney transplant patient on cyclosporin is started on 80 mg of simvastatin by her GP.
- A few days later, she is admitted with muscle pain, a CK in the millions and dies.
- Immunosuppressants
- HIV medication
- Warfarin
- Theophyllin

Be careful with these if other drugs are added/stopped.
Another pitfall: immunosuppression

- A 72 year old patient is admitted with a broken neck of femur 10 years after bilateral lung transplantation for fibrosis.
- He is given morphine for pain, develops nausea and vomiting.
- He cannot take his immunosuppression. He develops rejection, needs intubation and dies after 39 days in ICU.

Be careful with the immunosuppression – seek expert advice.
Further pitfalls: compliance

“Drugs can’t work if the patient is not taking them.”

100% Non-compliance

100% Compliance
Compliance – the rule of six

- Punctual dosing:
  - All doses taken
  - Erratic timing
  - 5-20% of doses taken, monthly
  - 5-20% omitted
  - 3-4 drug holidays per year

- Few or no doses taken:
  - Many doses missed

- Few or no doses taken:
  - Many doses missed

- Many doses missed:
  - 3-4 drug holidays per year
Compliance and escalation of treatment

• A 66 year-old man presents to a GP with BP 180/90.
• He is started on Metoprolol 100 mg. No effect. Ramipril 5mg is added, no effect.
• He is referred to a Univ. Hosp. hypertension clinic. Amlodipine is added. MR scanning of renal arteries and numerous tests all normal. BP 180/90
• He receives 5 mg of Nifedipine in clinic. BP 140/80 after one hour.

Do not escalate treatment that ends in the bin

53% of patients referred for refractory hypertension are non-compliers (Brunner et al., Hypertension 2001)
Further pitfalls

- A 66 year-old haemodialysis patient complains of poor ability to exercise at sports (gym).
- Medication: Aspirin, Calciumacetate, Atorvastatin, vitamin prescription, Ramipril and Verapamil.
- Meticulous questioning reveals: She was put on 100 mg metoprolol by a cardiologist.

Multiple prescribers are particularly dangerous
Multiple prescribers: Another example

Voltarol

Celebrex

Vioxx
Further pitfalls: Over-the-counter drugs

- A 85 year-old patient with chronic but stable kidney disease (GFR 25 ml/min) sprains her ankle.
- Her daughter buys 4 packets of ibuprofen at ALDI because it was a bargain.
- Two weeks later she presents with nausea and vomiting and needs dialysis. She dies three months later.
Further pitfalls: Herbs

Aristolochia elegans

Chelidonium majus

Aristolochia elegans
Compliance and over-prescribing

- A 87 year-old with a history of 2 myocardial infarctions is on aspirin, metoprolol and ramipril. She is now started on simvastatin. She confuses aspirin and simvastatin, stops aspirin and dies of stroke.

- Compliance decreases with number of drugs

- Non-compliance is not related to importance of drug (but size, taste, perceived importance, sympathy with doctor)

- Over-prescribing must be avoided, particularly in the elderly
Another pitfall: Over-enthusiasm

- A 67 year-old with hypertension and renal failure is started on simvastatin, ramipril and phosphate binders.

- Three days late he presents with a rash and itching.

- All three new drugs can cause allergy

Do not start more than one drug at a time if there is no need
Take-home messages

• Be aware of human error and try everything to avoid it; try to learn from near misses
• Be aware of dosing adjustments in obesity, liver and kidney disease
• Be aware of interactions, particularly in the usual suspects
• Use resources (e.g. UptoDate and clinical pharmacologist)
• Be aware of compliance as an ever-present problem
• Avoid over-prescribing
• Be careful with multiple prescribers
• Do not forget over the counter drugs and herbs
• Use medication plans