"Coffee ground" vomiting with a special smell!

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Supervisor: Dr. James James Luk

Inter-hospital Geriatric Meeting
25th May, 2012
Our patient

- 95/F
- Old Age Home Resident
- Walk with frame indoor, wheelchair outdoor
- Partially dependent for her basic activities for daily living (able to self feed)
Past Medical History

- Old stroke presented with right hemiplegia more than 20 years ago with good recovery
- Hypertension
- Fracture Right Hip with surgery done in 2004
- Alzheimer's Dementia
- Chronic renal failure (baseline Cr 130mmol/L)
- FU GOPD
Drug History

- Amlodipine 10mg daily
- Aspirin 80mg daily
- Multi-vitamin 1 tab daily
History of Present Illness

- Admit to Accident and Emergency Department (A&E) for vomiting for one time in old age home
- The vomitus was brownish in color
- No diarrhoea
- Patient claimed that she only ate food from OAH
- No chest pain
- No abdominal pain
- No shortness of breath
- No cough and sputum
- No fever
- No urinary symptoms
Physical examination

- Afebrile
- BP 162/54    P 82
- SaO2 97% on RA
- Smell of medicine oil inside her mouth
- Heme stix 6.3
- Patient conscious and alert
Physical Examination

- Cardiovascular system:
  - Pulse regular
  - Heart sound normal, no murmur

- Respiratory system:
  - Respiratory rate 20/min
  - Otherwise, clear

- Abdominal system:
  - Abdomen is soft and non tender. Bowel sound normal

- Neurological system:
  - Glasgow Coma Scale (GCS) 15/15
  - Cranial nerve intact. no power/sensory loss.

- Urine:
  - clear
Investigations

- **Complete blood picture (CBP)**
  - White cell count $9.8 \times 10^9/L$
  - Hemoglobin $9.1g/dL$ (baseline $\sim 10g/dL$)
  - Platelet $216 \times 10^9/L$

- **Clotting profile**
  - Normal
Investigations

- Renal function test
  - Sodium 141mmol/L
  - Potassium 3.7mmol/L
  - Chloride 108mmol/L
  - Urea 8.1mmol/L
  - Creatinine 132mmol/L
Investigations

● **Liver function test**
  - Albumin 35g/L
  - globulin 35g/L
  - bilirubin 5 umol/L
  - Aspartate Transaminase (AST) 250U/L
  - Alanine aminotransferase (ALT) 89U/L
  - Alkaline phosphatase (ALP) 74U/L
Investigations

- Random glucose 7.0 mmol/L
- Arterial blood gas (ABG)
  - pH 7.46
  - pCO2 3.58 kPa  pO2 12.4 kPa
  - HCO3 19 mmol/L  BE -5 mmol/L

- HbsAg: negative
- ECG: Sinus rhythm. no ischemic change
Investigations
On further Questioning…

- Patient actually complained of joint pain 1 week before admission
- Family bought a bottle of 50ml topical medicine (活絡油) which contain methyl salicylate
- Found empty bottle at the old age home bedside
- ?There is some residual topical med in patient’s cup in old age home
- Patient deny ingesting the topical medication
Investigations

- **Blood for toxicology:**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Result</th>
<th>Reference Range</th>
<th>Units</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paracetamol</td>
<td>&lt;66</td>
<td>See Below</td>
<td>umol/L</td>
</tr>
<tr>
<td>Salicylate</td>
<td>3.0 H</td>
<td>1.4 - 1.8</td>
<td>mmol/L</td>
</tr>
<tr>
<td>Ethanol</td>
<td>&lt;3.0</td>
<td>Toxic &gt;33</td>
<td>mmol/L</td>
</tr>
</tbody>
</table>
Investigations

- Urine for toxicology

Date Collected: 12/12/11 14:49

Clinical Details: DO. Temperature: DegCelsius, E:/4, V:/5, M:/6, Alleged date of poisoning (dd/mm/yyyy): dd/mm/yyyy, Alleged time of poisoning (hh:mm): hh:mm

pH 6
Ketones Negative
Glucose Negative

Toxicology screening (Urine):
Salicylate & metabolite, Amlodipine.
Investigations

- **Renal function test**
  - Sodium 141mmol/L
  - Potassium 3.7mmol/L
  - Chloride 108mmol/L
  - Urea 8.1mmol/L
  - Creatinine 132mmol/L

- **Arterial blood gas (ABG)**
  - pH 7.46
  - pCO2 3.58kPa   pO2 12.4kPa
  - HCO3 19mmol/L   BE -5mmol/L

- **Anion Gap = 18**
  - \([Na^+] + [K^+] - [Cl^-] - [HCO_3^-]\)
Estimation of amount of Methyl Salicylate ingested

- Estimated volume of 活絡油 in the bottle = 45ml
- The amount of the methyl salicylate in 50ml 活絡油 (stated in the bottle) = 15g

- Estimated total amount of methyl salicylate consumed = 13.5g
Progress

- Patient was given 50g activated charcoal
- Intravenous fluid with Sodium Bicarbonate given
- Aspirin was withheld

- During alkaline diuresis, urinary pH was monitored
## Progress

<table>
<thead>
<tr>
<th>Time</th>
<th>Admission</th>
<th>2hr later</th>
<th>4hr later</th>
<th>7hr later</th>
<th>12hr later</th>
<th>21hr later</th>
<th>30hr later</th>
</tr>
</thead>
<tbody>
<tr>
<td>Salicylate Level (mmol/L)</td>
<td>3</td>
<td>2.7</td>
<td>2.6</td>
<td>2</td>
<td>1.9</td>
<td>1.5</td>
<td>1</td>
</tr>
<tr>
<td>pH</td>
<td>7.46</td>
<td>7.54</td>
<td>7.54</td>
<td>7.55</td>
<td>7.56</td>
<td>7.59</td>
<td>7.56</td>
</tr>
<tr>
<td>pCO2 (kPA)</td>
<td>3.5</td>
<td>2.9</td>
<td>3.1</td>
<td>3.3</td>
<td>3.7</td>
<td>3.6</td>
<td>4.2</td>
</tr>
<tr>
<td>HCO3 (kPA)</td>
<td>18</td>
<td>18</td>
<td>20</td>
<td>21</td>
<td>24</td>
<td>25</td>
<td>28</td>
</tr>
<tr>
<td>Urinary pH</td>
<td>6</td>
<td>6</td>
<td>6.5</td>
<td>6.5</td>
<td>6.5</td>
<td>6.5</td>
<td>6.5</td>
</tr>
</tbody>
</table>
Progress

- Patient was then transferred to the geriatric unit of Grantham Hospital for monitoring
- Patient remained well and stable
- Patient did not complain of any joint pain
- HCO3 level returned to normal and Sodium bicarbonate was off
- Liver function normalized
Progress

- **Family interview:**
  - Explained to them that patient now was pain free and we could not identify the source of pain
  - Advice them not to simply buy the over-counter pain-killer or topical oil to patient
  - Also, we have educated them not to put any medicine or topical oil in patient’s drawer

- Patient was then discharged back to old age home and will be followed up by CGAT
Salicylate poisoning
Introduction

- Salicylates represent a group of compounds that are derivatives of salicylic acid in which an ester or salt is added to modify its properties in order to make the substance suitable for therapeutic use.
- The drugs we used would be metabolized to salicylate in our body.
Epidemiology of Salicylates poisoning

- In a study conducted by Prince of Wales Hospital during 1988 to 1991, aspirin and other analgesics accounted for 10 to 18% of the adult cases of self poisoning admitted to Prince of Wales Hospital.

- Topical medications containing wintergreen oil or methyl salicylate were involved in about half of the patients who were suspected to have ingested salicylates.

Use of Salicylates

- **Oral**
  - Acetylsalicylic acid (aspirin)
    - Analgesic, antipyretic, anti-inflammatory, platelet aggregation inhibition.
  - Bismuth subsalicylate
    - Antacid and antidiarrheal agent
  - Choline magnesium trisalicylate
    - A non-steroidal anti-inflammatory drug (NSAID) that contains a combination of choline salicylate and magnesium salicylate.
  - Salsalate
    - Non-steroidal anti-inflammatory drug (NSAID)
  - Sodium salicylate
    - Non-steroidal anti-inflammatory drug (NSAID)
Use of Salicylates

- **Dermal**
  - Methyl salicylate
  - Oil of wintergreen
    - liquid that contains 98% methyl salicylate
  - Trolamine salicylate
    - an organic compound which is the salt formed between triethanolamine and salicylic acid.
    - It is used as an ingredient in sunscreens, analgesic creams, and cosmetics.
    - The salicylic acid portion contributes to both the sun protection effect (by absorbing UVB rays) and to the analgesic effect.
Pharmacokinetics of Salicylate

- Aspirin (Acetylsalicylic acid) is readily hydrolyzed to salicylate in the gastrointestinal tract and bloodstream (aspirin’s serum half life is 15 minutes), salicylate is principally responsible for the systemic toxic effects.

- Two major metabolic pathways of salicylate are capacity-limited

- As salicylate in the body increases, the elimination will be slower and lead to accumulation

Pharmacokinetics of Salicylate

- Healthy adults begin to exhibit saturation kinetics with acute aspirin doses of 1–2 g. This dose dependent, prolonged excretion increases a person’s risk of serious toxicity.
- A small increase in dose or those with impaired renal function can cause a greatly prolonged elimination time, and a disproportionate increase in serum salicylate concentration.
- The serum half-life of salicylate is typically 2–4 hours at low doses. But can be prolonged to 15–30 hours or more following over dosage.
Salicylate poisoning

- Salicylate poisoning after ingestion
  - Oral medication (e.g. aspirin)
    - Case review found the for those of 6 years old or above, the lowest fatal case was 13g of salicylate ingestion

Salicylate poisoning

- Salicylate poisoning after ingestion
  - Topical oil (usually contain methyl salicylate)
    - Not uncommon in HK largely due to the readily availability of a wide range of topical medication used in the self-treatment of conditions such as musculoskeletal pains
    - Methyl salicylate poses the threat of severe, rapid-onset salicylate toxicity because of its liquid, concentrated form
Salicylate poisoning

- Salicylate poisoning after ingestion
  - Topical oil (usually contain methyl salicylate)
    - One teaspoon (5ml) of wintergreen oil (98% methyl salicylate) is equivalent to approximately 7000 mg of salicylate or 87.5 aspirin (80mg) tablets.
    - Ingestion of as little as 4 ml in a child and 6 ml in an adult have been fatal, although the lethal dose in adults is estimated at 30 ml.

Salicylate poisoning

- Salicylate poisoning after dermal exposure
  - Most instances of human toxicity due to methyl salicylate are a result of over-application of topical analgesics
  - These cases are difficult to characterize because the doses could not be reliably estimated.
Salicylate poisoning

- Salicylate poisoning after dermal exposure
  - A seventeen-year-old cross country athlete at Notre Dame Academy on Staten Island, died in April 2007, because of salicylate poisoning through excessive use of topical muscle-pain relief products
  - There is another case report of a 62-year-old man presented to AED for salicylate poisoning with serum salicylate concentration of 3.73 mmol/L. He had used a methyl salicylate ointment (concentration unstated) for several weeks on his thigh, twice daily

Signs and Symptoms

- **Mild toxicity**
  - nausea, vomiting, tinnitus, lethargy, dizziness, burning in the mouth

- **Moderate toxicity**
  - Trachypnea, hyperpyrexia, sweating, dehydration, loss of coordination, restlessness

- **Serious toxicity**
  - Hypotension, renal failure, cardiovascular failure, cerebral edema, hallucination, stupor, seizures, coma
Investigation

- Complete blood picture, Liver and renal function test, Clotting profile, blood glucose
- Urinary pH
- Arterial blood gas
- Blood for salicylate level
  - The sample should be taken at least 2 hours (symptomatic patients) or 4 hours (asymptomatic patients) following ingestion as it may take several hours for peak plasma concentrations to occur.
  - A repeat sample should be taken after a further 2 hours because of the possibility of continuing absorption. Measurements should be repeated until concentrations are falling.

Assessing the Severity

- Plasma concentrations six hours after an overdose very roughly correlate with toxicity as follows:
  - Mild: 300–500 mg/l (2.16 – 3.6 mmol/L)
  - Moderate: 500–700 mg/l (3.6 – 5 mmol/L)
  - Severe: >750 mg/l (>5.4mmol/L)

- Children (< 12 y) and the elderly (> 65 y) are more susceptible to the effects of salicylate poisoning and tend to get more severe clinical effects at lower blood salicylate concentrations. So the plasma concentration for toxicity for these 2 groups would be lower than healthy adults.

Assessing the Severity

- The presence of symptoms and signs and the degree of acidosis should be considered when interpreting the plasma salicylate concentration and deciding upon management.
- The reason that the arterial pH needs to be taken into account when interpreting a plasma salicylate concentration is that in the presence of acidaemia, more salicylic acid crosses the blood brain barrier resulting in greater CNS toxicity.
- After ingestion of enteric coated tablets, plasma salicylate concentrations on admission are unreliable guides to the severity of poisoning. Salicylate levels may not peak until more than 12 hours after such an overdose.
Management

- Early diagnosis is most important. In severe salicylate poisoning, delay in diagnosis was associated with a mortality of 15% compared with a much lower rate in those patients in whom early diagnosis and initiation of treatment was made.

Management

- Salicylate poisoning include excessive topical application or ingestion of salicylate containing ointments, or agents containing methyl salicylate is dangerous.
- These agents contain liquid preparations and many of them are concentrated and lipid soluble and so there is the potential for severe, rapid onset salicylate poisoning.
- It is advise that doctors looking after a patient poisoned with one of these agents contact their local poisons centre for advice on treatment.
Management

- There is no antidote to salicylate poisoning and management is directed towards:
  - preventing further absorption
  - increasing elimination of the drug in patients with features of moderate or severe intoxication.
Management

- Prevention of further absorption
  - Patients with salicylate poisoning should be given repeat doses of activated charcoal (four hourly doses of 50 g in adults, 1 g/kg body weight in children) until the salicylate level peaks to minimise delayed absorption of salicylates.
  - The administration of repeated dose of activated charcoal is of particular value in adults who have ingested substantial quantities of an enteric coated or sustained release preparation.
Management

- Increase the elimination of salicylates
  - Alkaline diuresis
    - The elimination of salicylate may be increased by alkalinization of the urine. There is a 10-fold to 20-fold increase in renal salicylate clearance associated with an increase in urine pH from 5 to 8.
    - A urine pH of 7.5 or higher is indicated and careful monitoring of the urine pH is necessary. The pH of blood should not exceed pH 7.55 however.
Management

- Increase the elimination of salicylates
  - Alkaline diuresis
    - The most common recommendation is to continue treatment until the plasma salicylate concentration decreases to the therapeutic range.
    - Important to maintain a normal serum potassium level, as low potassium level would lead to more active potassium-Hydrogen exchange in the distal tubules, resulting in excretion of Hydrogen ion and affect the urinary alkalinization.
Management

Increase the elimination of salicylates

- Hemodialysis
  - Although haemodialysis has been used successfully for many years in the management of severe salicylate poisoning, no controlled trial comparing its efficacy with that of carefully managed alkaline diuresis has been performed.
  - Research had highlighted the importance of continuing urinary alkalinisation in patients who are undergoing haemodialysis in order to reduce plasma concentrations quickly, prevent acidaemia, and promote elimination of as much salicylate as possible via the kidneys.

Management

- Increase the elimination of salicylates
  - Hemodialysis
    - Use when:
      - Altered mental status
      - Pulmonary or cerebral edema
      - Renal insufficiency that interferes with salicylate excretion
      - Fluid overload that prevents the administration of sodium bicarbonate
      - A plasma salicylate concentration >100 mg/dL (7.2 mmol/L)
      - Clinical deterioration despite aggressive and appropriate supportive care
PRESENTATION
Note: some salicylate preparations contain other agents such as opiates, paracetamol and caffeine. This flowchart deals only with the management of the salicylate component; the other agents need separate consideration.

Gastric lavage\textsuperscript{24, 25}
- If sure of dose and time of ingestion. Ensure that the airway is protected.
- < 1 hour
- > 1 hour

When taken?

Dose taken?

< 125 mg/kg and asymptomatic\textsuperscript{24, 27}

Discharge patient if sure of dose
Advise to return if develops any symptoms, particularly vomiting, tinnitus, sweating.
- Before the patient is discharged an assessment of their mental state and risk of repeated episodes of deliberate self harm should be carried out, ideally by a psychiatrist or psychiatric liaison nurse.

≥ 125 mg/kg or unknown\textsuperscript{24, 27}

50 g Oral activated charcoal\textsuperscript{24, 28-30}
(children 1 g/kg bodyweight)
Ensure that the airway is protected.

Haemodialysis
- Give sodium bicarbonate (cautious with volume if anuric)\textsuperscript{11, 22}

Conversion factors for plasma salicylate concentration:
- to convert mmol/l to mg/l divided by 0.0072
- to convert mg/l to mmol/l multiply by 0.0072

Does the patient have any of the severe clinical features?\textsuperscript{1}
- Coma, convulsions
- Acute renal failure
- Pulmonary oedema
If these develop at any stage:
1. Resuscitate i.e. airway, breathing, circulation
2. Check ABGs
3. Discuss with local poisons unit and ITU
4. Consider haemodialysis

Rehydrate the patient and take blood for salicylate level, U&E, FBC, INR (at least 4 hours after ingestion)
ABG should be checked in symptomatic cases

Metabolic acidosis?
1. If arterial pH < 7.3, treat with 1 ml/kg 8.4% sodium bicarbonate iv to increase pH to 7.4
2. If arterial pH < 7.2, consider haemodialysis

Check blood results
Prevention of Salicylate Poisoning
Prevention

- In Hong Kong, medication oils containing methyl salicylate are widely available.
- The risk of salicylate poisoning after ingesting the medication oil is greater if:
  - the methyl salicylate concentration is higher;
  - the bottle is larger;
  - the bottle opening is bigger.
- Improvements in the packaging of these products should reduce the risk of severe salicylate poisoning after accidental or deliberate ingestion.

Reference: TYK Chan. Ingestion of medicated oils by adults: the risk of severe salicylate poisoning is related to the packaging of these products. Human & Experimental Toxicology (2002) 21, 171 ± 174
Prevention

- A retrospective study of adults performed by Prince of Wales Hospital in Hong Kong on patients ingested two different medicated oils (White Flower Oil and Red Flower Oil).

- In this study, subjects who had taken `Red Flower Oil` tended to have higher plasma salicylate levels than subjects who had taken `White Flower Oil`.
Prevention

- The possible explanations:
  - The ‘Red Flower Oil’ had a bigger bottle size and its content could be emptied much more easily.
  - There are only 1 brand of ‘White flower Oil’, but there are about 3 brands of ‘Red Flower Oil’. ‘Red Flower Oil’ usually contained a higher methyl salicylate concentration than ‘White Flower Oil’.
Red Vs White Flower Oil
## Prevention

### Table 1 Packaging of medicated oils containing methyl salicylate

<table>
<thead>
<tr>
<th></th>
<th>White Flower Oil*</th>
<th>Red Flower Oil*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>Brand 1</strong></td>
<td><strong>Brand 2</strong></td>
</tr>
<tr>
<td>Methyl salicylate (%)</td>
<td>40</td>
<td>67</td>
</tr>
<tr>
<td>Bottle size (mL)</td>
<td>2.5, 5, 10 and 20</td>
<td>60</td>
</tr>
<tr>
<td>Internal diameter of opening (mm)</td>
<td>3.04†</td>
<td>11.44</td>
</tr>
<tr>
<td>Rate of emptying of content (mL/s)‡</td>
<td>0.15†</td>
<td>2.5</td>
</tr>
</tbody>
</table>

Data based on Ref. [5]. *There is only one manufacturer for ‘White Flower Oil’. There are several manufacturers for ‘Red Flower Oil’, but only the data from 3 brands previously tested by us are shown here. †Based on the findings from one bottle size (20 mL). ‡The bottles were tilted at 30° angle from the horizontal and the time needed to empty half of the content was noted.
Prevention

- In this study, patients tended to ingest a greater amount of `Red Flower Oil’ than `White Flower Oil’
- Secondly, patients who had taken `Red Flower Oil’ tended to have higher plasma salicylate levels than subjects who had taken `White Flower Oil’
- Thirdly, patients who had taken `Red Flower Oil’ were far more likely to be symptomatic or have moderate to severe symptoms
- As a result, patients who had ingested `Red Flower Oil’ were more likely to require urine alkalinization
# Prevention

## Table 2
Clinical details of 24 subjects who had ingested medicated oils containing methyl salicylate

<table>
<thead>
<tr>
<th></th>
<th>White Flower Oil</th>
<th>Red Flower Oil</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men:women ratio</td>
<td>4:14</td>
<td>0:6</td>
</tr>
<tr>
<td>Age (years)</td>
<td>21 (15–74)</td>
<td>40 (26–86)</td>
</tr>
<tr>
<td>Ingestion–admission intervals (hours)</td>
<td>3.5 (1–9) *</td>
<td>3.3 (0.5–9.5) †</td>
</tr>
<tr>
<td>Amount ingested (mL)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not known</td>
<td>11 (61%)</td>
<td>2 (33%)</td>
</tr>
<tr>
<td>≤10</td>
<td>5 (28%)</td>
<td>1 (17%)</td>
</tr>
<tr>
<td>10–20</td>
<td>2 (11%)</td>
<td>1 (17%)</td>
</tr>
<tr>
<td>30–100</td>
<td>0</td>
<td>2 (33%)</td>
</tr>
<tr>
<td>Gastric lavage/activated charcoal</td>
<td>15 (83%)</td>
<td>4 (67%)</td>
</tr>
<tr>
<td>Plasma salicylate levels (mmol/L)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.1–1.0</td>
<td>12 (67%)</td>
<td>2 (33%)</td>
</tr>
<tr>
<td>1.1–2.1</td>
<td>5 (28%)</td>
<td>0</td>
</tr>
<tr>
<td>≥2.2</td>
<td>1 (5%)</td>
<td>4 (67%) ‡</td>
</tr>
<tr>
<td>Severity of salicylate poisoning§</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No symptoms</td>
<td>7 (39%)</td>
<td>0</td>
</tr>
<tr>
<td>Mild symptoms</td>
<td>11 (61%)</td>
<td>3 (50%)</td>
</tr>
<tr>
<td>Moderate–severe symptoms</td>
<td>0 (0%)</td>
<td>3 (50%) #</td>
</tr>
<tr>
<td>Duration of stay (days)</td>
<td>2 (1–4)</td>
<td>4 (2–15)</td>
</tr>
<tr>
<td>Outcome</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Home</td>
<td>17 (94%)</td>
<td>4 (67%)</td>
</tr>
<tr>
<td>Transfer to other units</td>
<td>1 (5%)</td>
<td>1 (17%)</td>
</tr>
<tr>
<td>Unrelated death</td>
<td>0</td>
<td>1 (17%)</td>
</tr>
</tbody>
</table>
Prevention

- To reduce the amount of methyl salicylate that can be readily swallowed during accidental or deliberate ingestion of medicated oils, improvements are needed in the existing packaging of these products.
- It is unnecessary for medicated oils to have a large opening of the containers they are placed in since they are intended for topical application only.
- Therefore, changing the package of the medication oil to a smaller opening may reduce the risk of severe salicylate poisoning after ingesting it.
Prevention

- Educate family and old age home staff that Analgesic balm or medication oil can be dangerous if using inappropriately.
- Risk would even be greater for those patients who is having underlying dementia.
- We may check the surrounding of the patient’s bed when going to CGAT to look for potentially dangerous drug or health care products.
Take home message

- Pay attention to your patient’s smell!
- High index of suspicion for salicylate poisoning. Signs and symptoms of salicylate poisoning may be non specific.
- Dangerous household products should be removed from close contact with demented patient
Thank you!