An evidence based flowchart to guide the management of acute salicylate (aspirin) overdose

P I Dargan, C I Wallace, A L Jones

Objective: To develop a flowchart to be used as a tool to guide clinicians step by step through the management of salicylate poisoning.

Methods: A comprehensive literature search was carried out.

Results: The evidence base was used to develop a management flowchart that guides the clinician through the three main steps in caring for the patient with salicylate poisoning: preventing further absorption, assessing the severity of poisoning and, where appropriate, increasing elimination.

Conclusions: Salicylate poisoning can result in severe morbidity and mortality and this flowchart provides an evidence based guideline that will guide clinicians through the management of patients presenting to the emergency department with salicylate poisoning.

Although the overall mortality in salicylate poisoning is low, such figures can be very deceptive as severe poisoning may cause metabolic acidosis, convulsions, coma, hyperpyrexia, pulmonary oedema, and renal failure. Death can occur in 5% of patients who have such features of severe poisoning and is attributable to cardiac arrest or multiple complications after severe brain damage. Critically, 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. The current problem is that because salicylate poisoning is not seen so commonly, through lack of familiarity, medical and nursing staff may underestimate the severity of poisoning or fail to administer sufficiently vigorous treatments early enough to prevent morbidity and mortality (NPIS data, not shown).

Once the severity of poisoning is recognised, management is a success story for clinical toxicology as over the past 40 years techniques to reduce the absorption of salicylate and increase its elimination have been developed. This evidence based flowchart has been developed to help guide decision making in salicylate poisoning. It is a guide however, not a protocol and individual decisions will still need to be made for each patient. Further advice on the management of salicylate poisoning is also always available from a poisons centre (in the UK the single national number, 0870 600 6266, will connect you to your local poisons centre).

DISCUSSION

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

Prevention of further absorption

A study on volunteers taking 1.5 g aspirin comparing activated charcoal, emesis, and gastric lavage had several limitations; salicylate elimination was followed up for only 24 hours, the analytical method used underestimated some salicylate metabolites, and plasma salicylate concentrations were not measured. Like similar volunteer studies in other drugs it does not accurately reflect the effect of treatment regimens in poisoned patients, but none the less taken with the other evidence shown in figure 1, it provides some rationale to support the use of activated charcoal within one hour of an overdose.

Repeated doses of activated charcoal may have the added advantage of shortening the elimination half life of salicylates. This study is controversial in clinical toxicology because the charcoal administered in this study contained bicarbonate (Medicoal) but in our view its implications have been too readily dismissed. A study in adult volunteers given 1.9 g of aspirin showed that three, four hourly 50 g doses of charcoal resulted in a significant decrease in salicylate absorption when compared with one or two doses of charcoal. Aspirin forms concretions within the stomach and it may be important to recoat surfaces of such concretions with charcoal to reduce ongoing absorption. The administration of a second dose of activated charcoal is of particular value in adults who have ingested substantial quantities of an enteric coated or sustained release preparation. Gastric decontamination in salicylate poisoning remains controversial even among toxicologists. However, we would advocate that patients with salicylate poisoning are 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.

Assessing the severity of salicylate poisoning

The serum salicylate should be determined on admission provided that more than four hours have elapsed from the time of ingestion of the overdose. Measurements made before this
**PRESENTATION**

Note: Some salicylate preparations contain other agents such as opioids, paracetamol and caffeine. This flowchart deals only with the management of the salicylate component; the other agents need separate consideration.

- **Mild poisoning**
  - Adults: 300–600 mg/l
  - Children/elderly: 200–400 mg/l
  - Clinical features: Lethargy, nausea, vomiting, tinnitus, dizziness.

- **Moderate poisoning**
  - Adults: 600–800 mg/l
  - Children/elderly: 450–600 mg/l
  - Clinical features: Drowsiness, cyanosis, tinnitus, dizziness.

- **Severe poisoning**
  - Adults: > 800 mg/l
  - Children/elderly: > 700 mg/l
  - Clinical features: Respiratory suppression, metabolic acidosis, hyperpyrexia, sweating, dehydration, loss of coordination, somnolence.

**Time related factors**

- **Urine output**
  - Monitor urine output and fluid balance carefully.

- **Repeat salicylate level every 3 hours until a peak concentration is reached**
  - This can be as late as 12 hours after ingestion, particularly with enteric-coated aspirin.

**Conversion factors**

- To convert mg/l to mmol/l, multiply by 0.0072
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**Conversion factors for plasma salicylate concentration**

- Children < 7 years: 1 g/kg
- Adults: One 50 g Oral activated charcoal

**Discharge patient if severe of dose**

Adolescents with any symptoms, particularly vomiting, tinnitus, sweating.

**Severe clinical features**

- Coma, convulsions
- Acute renal failure
- Pulmonary oedema
- If these develop at any stage:
  1. Resuscitate: airway, breathing, circulation
  2. Check ABCs
  3. Discuss with local poisons unit and ITU
  4. Consider haemodialysis

**Haemodialysis**

- Give sodium bicarbonate (cautious with volume if anuric)

**NOTE:**

- 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.
- Not all of the features described need to be present for each of the classifications of mild, moderate or severe poisoning. The plasma salicylate concentration needs to be interpreted in the context of the patient’s clinical features and degree of metabolic acidosis. Clinical features are more important in grading the severity of salicylate poisoning.

**Metabolic acidosis?**

- If arterial pH < 7.3, treat with 1 ml/kg 8.4% sodium bicarbonate to increase pH to 7.4
- If arterial pH < 7.2, consider haemodialysis

**Oral activated charcoal**

- Adults: 50 g
- Children: 1 g/kg

**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

**Check blood results**

- Is this the first salicylate level?

**Is the peak level > 750 mg/l?**

- Yes

- No

**Severe poisoning 2**

- Adults: 800 mg/l
- Children/elderly: > 700 mg/l
- Clinical features: Nostril irritation after rehydration, nasal stuffiness (cingulum), CNS features e.g. hallucinations, drowsiness, fits, coma

**Severe clincial features 1**

- Coma, convulsions
- Acute renal failure
- Pulmonary oedema
- If these develop at any stage:
  1. Resuscitate: airway, breathing, circulation
  2. Check ABCs
  3. Discuss with local poisons unit and ITU
  4. Consider haemodialysis

**Urinary alkalinisation**

- Give sodium bicarbonate (cautious with volume if anuric)

**Urinary alkalinisation**

- Give 1 ml of 1.26% sodium bicarbonate with 20 to 40 mmol potassium as an infusion over 3 hours
- Children: Dilute 1 ml/kg 8.4% sodium bicarbonate in 10 ml/kg sodium chloride solution and add 1 mmol/kg potassium. This should be given at a rate of 2 ml/kg/h as an iv infusion
- Check urinary pH hourly, aiming for a pH of 7.5–8.5; the rate of sodium bicarbonate administration given above will need to be increased if the urine pH remains < 7.5
- Check U&E every 3 hours, the serum potassium should be kept in the range 4.0 to 4.5

**Rehydrated with oral fluids**

- Rehydrate with oral or intravenous fluids

**Repeat salicylate level every 3 hours until a peak concentration is reached**

- This can be as late as 12 hours after ingestion, particularly with enteric-coated aspirin

**Figure 1** Flowchart for management guidance in salicylate poisoning (numbers in superscripts relate to the supporting references).
when interpreting a plasma salicylate concentration is that in the presence of acidemia, more salicylic acid crosses the blood brain barrier resulting in greater CNS toxicity.

In mild or early poisoning burning in the mouth, lethargy, nausea, vomiting, tinnitus, or dizziness can occur. In moderate poisoning all of the above plus tachypnoea, hyperpyrexia, sweating, dehydration, loss of coordination, and restlessness, can occur. In severe poisoning hallucinations, stupor, convulsions, cerebral oedema, oliguria, renal failure, cardiovascular failure, and coma may be seen together with metabolic acidosis. 2 4

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. 9 11 The use of gastroscopic and other measures to remove enteric coated tablets requires further evaluation in the future. As well as aspirin tablets, other sources of salicylate poisoning include excessive topical application or ingestion of salicylate containing ointments, keratolytic agents or agents containing methylsali-cylate (for example, oil of wintergreen). 22 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. 23 We would advise that doctors looking after a patient poisoned with one of these agents contact their local poisons centre for advice on treatment.

Methods used to increase the elimination of salicylates

The elimination of salicylate may be increased by alkalinisation of the urine (see fig 1 for details). 10 There is a 10-fold to 20-fold increase in renal salicylate clearance associated with an increase in urine pH from 5 to 8 and renal excretion of salicylate depends much more on urine pH than flow rate. 10 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. The most common recommendation is to continue treatment until the plasma salicylate concentration decreases to the therapeutic range but cessation of the patient’s symptoms are also a crucial factor in the decision to discontinue alkalinisation. Although it is prudent to administer supplemental potassium to hypokalaemic patients, it is inappropriate to delay the administration of sodium bicarbonate solution until normokalaemia is achieved. Forced diuresis alone has little effect and is potentially harmful because of the potential for pulmonary oedema, hypernatremia, and hypokalaemia. 30 However, in severe poisoning the renal elimination of salicylate may be very slow as the urine becomes acidic and there may be oliguria. 31 This is when haemodialysis needs to be considered. 31 32

Haemodialysis reduces both the mortality and morbidity of poisoning and should be considered in those with severe salicylate poisoning—that is, systemic metabolic acidosis or plasma concentrations greater than 800 mg/l in adults and 700 mg/l in children or the elderly. While the plasma salicylate concentration is undoubtedly a good guide to treatment it should not be the sole determinant of when to consider extracorporeal removal and other factors such as the presence of a severe systemic metabolic acidosis, a young patient or very old patient, CNS features (for example, drowsiness, agitation, coma or convulsions), acute renal failure or pulmonary oedema make it much more likely that haemodialysis will be needed. 31 32

A recent case has emphasised the importance of continuing urinary alkalisation in patients who are undergoing haemo-dialysis in order to reduce plasma concentrations quickly, prevent acidemia, and promote elimination of as much salicylate as possible via the kidneys. 33 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 urinary alkalinisation and diuresis has been performed. Nevertheless its use has the advantage of normalising acid base balance and electrolyte abnormalities while removing salicylate, without the thrombocytopenia that frequently accompanies charcoal haemoperfusion. 21 The role of haemofiltration remains unproven in salicylate poisoning.

CONCLUSIONS

Salicylate poisoning can result in severe morbidity and mortality. It is important that clinicians caring for patients with salicylate poisoning are able to identify patients that are severely poisoned on the basis of clinical features, metabolic acidosis and their plasma salicylate concentrations so that appropriate treatment can be started. This evidence based flowchart will guide the clinician step by step through the management of salicylate poisoning.

Contributors

Paul Dargan was responsible for the literature review and together with Craig Wallace designed the management flowchart. Alison Jones reviewed the literature review and the management flowchart. All these authors were involved in the writing of the paper and all three authors will act as guarantors.

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