Adverse effects of activated charcoal used for the treatment of poisoning

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Summary
The incidence of adverse effects of activated charcoal in poisoned patients is unclear. We performed a search of PubMed, EMBASE, and Ovid to identify large cohorts, and both randomized and pseudorandomized controlled trials, finding nine articles. The most commonly described adverse events were vomiting, aspiration, and intubation. Other adverse events such as bowel obstruction, corneal abrasions, electrolyte disturbances, and seizures were rarely reported in the trials. Activated charcoal was associated with few clinically significant adverse events in the treatment of poisoned patients.

Introduction
Acute self-poisoning is a major clinical problem worldwide. The mainstay of treatment involves resuscitation, supportive care, and administration of antidotes where available. Activated charcoal has been used since the 1970s and is the only means of gastric decontamination that is now widely used. It is a colourless, insoluble, black powder. 'Activation' involves treatment with steam and strong acids, creating a network of pores through the charcoal, thereby increasing the surface area available for the adsorption of poisons.

Current UK guidelines recommend a single dose of activated charcoal (SDAC) in the treatment of overdose, preferably within 1 h of ingestion, for drugs that have been shown to adsorb to it. Ambulance and emergency department staff likely to encounter such patients are recommended to have activated charcoal available at all times. However, the American Academy of Clinical Toxicology (AACT) and the European Association of Poisons Centres and Clinical Toxicologists (EAPCCT) statements on SDAC concluded that there is no evidence that activated charcoal administration improves clinical outcome and that activated charcoal should only be considered in patients with a protected airway after a life-threatening overdose.

Mechanism of action
Soon after ingestion, SDAC reduces absorption of a wide range of drugs by adsorbing the poison in the stomach and small bowel. However, it is ineffective for some drugs such as lithium, iron, cyanide, and strong acids or alkalis which are not adsorbed.

Activated charcoal may still have an effect after the drug has been absorbed from the gastrointestinal tract. Multiple doses of activated charcoal (MDAC) interrupt enterohepatic and enterovascular cycling of poison. Some drugs, for example, digoxin, are excreted via bile into the gut before being reabsorbed in the terminal ileum (the enterohepatic circulation). Other drugs, such as theophylline, diffuse back and forth between the plasma and the gut lumen. In these situations, activated charcoal in the small bowel can sequester the poisons, before reabsorption, so they are excreted via faeces. Late activated charcoal confers pharmacokinetic benefit, but perhaps no clinical benefit, after overdose with drugs such as digoxin and phenobarbital.

Benefit from administration of SDAC or MDAC is unclear. Here we consider the safety of activated charcoal.

Methods
We systematically searched Ovid, EMBASE, and PubMed from January 1960 to August 2010 to identify articles reporting clinical trials or case series of poisoned patients receiving activated charcoal, using key words ‘activated charcoal’, ‘adverse effect’, ‘side effect’, ‘toxicity’, ‘complications’, and ‘anaphylaxis’.

We found 349 articles; review of the abstracts revealed that 60 were possibly relevant. Review of these articles, as well as textbooks and the bibliographies of articles identified by the search, revealed a total of 10 large (over 100 patients) studies relevant to the question (Table 1). Five reported randomized controlled trials (RCTs), four were pseudo-RCTs (pRCTs, alternate day allocation rather than random allocation), and one was a retrospective cohort. One pRCT was excluded because of methodological concerns.

No study had ‘adverse events’ or ‘complication rate’ as a sole primary outcome. Two RCTs and 2 pRCTs compared activated charcoal with no activated charcoal. We collected data from these trials. A χ²-test was used to determine significance of results.
Results

Gastrointestinal adverse effects

The most common adverse effects were vomiting, diarrhoea, and constipation. In volunteer studies, constipation, vomiting, abdominal fullness, nausea, diarrhoea, and irritation, drowsiness, and light-headedness have occurred. Although relatively minor, these effects may influence patient compliance with treatment.

de Silva et al. showed that of 201 patients poisoned with yellow oleander, who were treated with MDAC (50 g × 12 doses), three developed diarrhoea and 13 developed abdominal discomfort. These effects were transient and resolved without any specific treatment. No comparison was made with the SDAC group.19

In 1103 patients administered SDAC (50 g), Mohamed et al. reported that 23 of 161 patients with a discharge diagnosis of chest pain (control) admitted to hospital (RR 1.34, 95% confidence interval (CI) 1.05–1.71). Of these, 17 were subsequently admitted to intensive care with respiratory failure. None of the patients readmitted developed pulmonary aspiration (of which none suffered any long-term sequelae).20

In 221 symptomatic patients treated after yellow oleander poisoning (SDAC 50 g or MDAC 50 g × 12 doses) had absent bowel sounds, only two required surgical review, and there was no statistically significant difference compared with the control group (absent bowel sounds 17 of 1554, P = 0.36).21 In two other RCTs, although not explicitly mentioned, obstruction was not reported as an adverse event.21,22

Although bowel obstruction is theoretically more likely with drugs that impair gut motility, in one RCT over 2000 patients received atropine and activated charcoal without significant problems.23

Drug interactions

One potential problem with the use of charcoal is unwanted adsorption and elimination of routine medications. The bioavailability of any drug that is adsorbed by activated charcoal will be reduced, potentially resulting in subtherapeutic concentrations. This has been noted in a case report for warfarin. A randomized crossover study of 19 healthy volunteers showed that the oral absorption of acetylcysteine was reduced by activated charcoal.28

None of the RCTs assessed drug interactions. It seems sensible to delay administration of regular medication until some time after activated charcoal is given, but the interval to wait is unclear.

Miscellaneous adverse effects

Eddleston et al.25 reported a nonsignificant difference in seizures frequency (27 of 3075 patients, 0.9% in the activated charcoal group vs. 7 of 1554, 0.5% in the control group) (RR 1.95, 95% CI 0.85–4.47, P = 0.15). A retrospective review of 878 patients treated with MDAC revealed 53 with serum sodium more than 155 mmol/L and 27 with serum magnesium more than 1 mmol/L. One patient had a corneal abrasion. No other complications were identified. The electrolyte disturbances, which were generally asymptomatic, are difficult to attribute directly to activated charcoal.26 None of the above was monitored in the RCTs listed in this review.

Table 1

| Study type | Study group | Self-poisoning patients receiving activated charcoal | Self-poisoning patients receiving no gastric decontamination | Adverse event | Adverse event | Primary endpoint | Cochrane review of AC vs. no gastric decontamination (n = 161) | P value |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | |
| All overdoses, but mainly pharmaceuticals | | | | Acute deterioration | Acute deterioration | No | 0.36 | 0.36 | 0.36 |

Table 1 Clinical studies of poisoned patients receiving activated charcoal

Adverse effects of activated charcoal

Activated charcoal lodging in the bowel lumen can cause bowel obstruction, for which some patients have required emergency surgery.29,30

Bowel obstruction or ileus

Cases of pulmonary aspiration have been reported, resulting in pneumonia, protracted deterioration in clinical condition, and even death. Aspiration pneumonia in a group of 107 asymptomatic, mildly-to-moderate overdose patients and those with peak acetylcysteine concentrations 29% lower.30

Activated charcoal was reduced by activated charcoal, with peak concentrations 29% lower.30

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<table>
<thead>
<tr>
<th>Study Authors</th>
<th>Study Type</th>
<th>Study Design</th>
<th>Self-poisoning Patients</th>
<th>AC Regime</th>
<th>Comparison</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eddeston et al.</td>
<td>Open-label randomized controlled trial</td>
<td>Stratified block randomization by computer software</td>
<td>Presenting within 72h of ingestion</td>
<td>All overdoses, but most ingested yellow oleander seeds or pesticides</td>
<td>50g of AC vs. no gastric decontamination</td>
<td>No significant difference in adverse effects when comparing AC (both groups) with no gastric decontamination. Intubation 146/3075, 4.7% vs. 76/1554, 4.9% in control group. Seizures 27/3075, 0.9% vs. 7/1554, 0.5% in control group. Absent bowel sounds: 24/3075, 0.7% vs. 17/1554, 1.1% in control group. Two patients treated with AC were referred for surgical review for acute abdomen. None of the patients who died in the study had substantial quantities of charcoal in their lungs at judicial postmortem examination. Other adverse effects were not commented on.</td>
</tr>
<tr>
<td>Albertson et al.</td>
<td>Open-label randomized controlled trial</td>
<td>Stratified block randomization by computer software</td>
<td>Presenting to the emergency department</td>
<td>All overdoses except strong acids or bases, camphor, volatile petroleum, iron, lithium, strychnine, and substances known to be a relative contraindication to treatment with syrup of ipecac</td>
<td>1533</td>
<td>No significant difference in adverse effects when comparing AC (both groups) with no gastric decontamination. Intubation 52/163 (31.9%) vs. AC alone (41/107, 38.0%) and AC plus ipecac (7/193, 3.6%). No other significant differences in clinical deterioration, length of hospital stay, complications.</td>
</tr>
<tr>
<td>Merigian et al.</td>
<td>Open-label pseudo-randomized controlled trial</td>
<td>Even–odd day protocol</td>
<td>Presenting to the emergency department</td>
<td>All overdoses excluding acamptomycin &gt;140mg/kg, lithium, monoamine oxidase inhibitors, heavy metals, formaldehyde, mushrooms, digitalis, methanol, ethylene glycol, iron, or sustained release products</td>
<td>163 vs. AC alone (154)</td>
<td>No significant difference in clinical deterioration, length of hospital stay, complications.</td>
</tr>
<tr>
<td>Pond et al.</td>
<td>Open-label pseudo-randomized controlled trial</td>
<td>Even–odd day protocol</td>
<td>Presenting to the emergency department</td>
<td>Clinical deterioration based on Glasgow Coma Score, temperature, blood pressure, pulse, and dysrhythmias</td>
<td>Clinical course during the first 6h after treatment began, length of hospital stay, complications.</td>
<td></td>
</tr>
<tr>
<td>de Silva et al.</td>
<td>Single-blind randomized controlled trial</td>
<td>Computer-generated random allocation table</td>
<td>Presenting to the emergency department</td>
<td>Intubation 52/163 (31.9%) vs. AC alone (41/107, 38.0%) and AC plus ipecac (7/193, 3.6%). No other significant differences in clinical deterioration, length of hospital stay, complications.</td>
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<tr>
<td>Mohamed et al.</td>
<td>Randomized controlled trial</td>
<td>Stratified random sample</td>
<td>Presenting with recent (unspecified time) ingested</td>
<td>Drug overdose, (excluding crack cocaine, mushrooms, volatile, caustic agents, heavy metals, lithium, iron preparations, or more than 140 mg/kg acamptomycin)</td>
<td>50g of AC every 6h for 3 days</td>
<td>Death</td>
</tr>
<tr>
<td>Excluded study (due to methodological concerns)</td>
<td>Merigian et al.</td>
<td>Open-label pseudo-randomized controlled trial</td>
<td>Presenting within 72h of ingestion</td>
<td>All patients with a history of self-poisoning</td>
<td>559 patients received one dose of 55g AC, 544 received six doses of 50g AC</td>
<td>Patient compliance with treatment.</td>
</tr>
</tbody>
</table>

**AC** Activated Charcoal

*Both were part of the same study protocol.*

*Subgroup of Eddeston et al.*

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*Subgroup of Eddeston et al.*
Adverse effects of activated charcoal

We were unable to find any cases of activated charcoal-induced anaphalaxis.

Limitations

We excluded one pRCT because of methodological concerns. Methods were incompletely described, and there was no explanation as to why three times as many patients ended up in one arm of the study as the other. Similar, although perhaps less severe, concerns exist for the three other pRCTs. In addition, not all RCTs looked at complication rates as an outcome which limited the amount of data available.

Conclusion

This review indicates that activated charcoal can be given safely to the majority of poisoned patients. There was no significant increase in the risk of vomiting, aspiration, or intubation. A little-studied but important effect of activated charcoal is reduced absorption of therapeutics.

Acknowledgements

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References

1 Meredith TJ. Epidemiology of poisoning. Pharmacology and Therapeutics 1993;59:251–256.