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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.[1,2] The mainstay of treatment involves resuscitation, supportive care, and administration of antidotes where available.[3] Activated charcoal has been used since the 1970s[4] and is the only means of gastric decontamination that is now widely used.[5–10] 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.[4,11]

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.[12] 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.[6]

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.[6,13] However, it is ineffective for some drugs such as lithium, iron, cyanide, and strong acids or alkalis which are not adsorbed.[14]

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.[13] Some drugs, for example, digoxin, are excreted via bile into the gut[10] 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.[15] 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.[16]

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.[17] 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 χ^2-test was used to determine significance of results.

Results

Gastrointestinal adverse effects

The most common adverse effects were vomiting, diarrhoea, and constipation.[4] In volunteer studies, constipation, vomiting, abdominal fullness, nausea, diarrhoea, anal irritation, drowsiness, and light-headedness have occurred.[18] 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.*[20] reported that 239 (27%) vomited. In patients presenting within 12 h of ingestion, Cooper *et al.*[21] showed no significant difference with vomiting in 25 of 166 patients of the activated charcoal group (50 g) and 23 of 161 [relative risk (RR) 1.05, 95% confidence interval (CI) 0.63–1.77, $P = 0.84$] of the control group.

Aspiration

The cause of aspiration is multifactorial. A large contribution may be attributable to the effect of the toxin, spontaneous vomiting, or aspiration secondary to loss of protective reflexes. This is likely to be dependent on toxin load, and could explain why few cases of aspiration were picked up in mild-to-moderate overdose patients.[22]

Cases of pulmonary aspiration have been reported,[23] resulting in pneumonia, protracted respiratory insufficiency, severe bronchospasm, and need for mechanical ventilation. Activated charcoal has been administered directly into the lung by nasogastric tube[24]; late complications like recurrent pneumothoraces have also occurred.[25]

A retrospective review of 878 patients treated with MDAC, with a discharge diagnosis of 'poisoning', identified five patients with clinically significant pulmonary aspiration (of whom none suffered any long-term sequelae).[26] In the activated charcoal alone arm of two RCTs, Albertson *et al.*[27] reported no aspiration pneumonia in a group of 107 mild-to-moderate overdose patients and Merigian *et al.*[22] reported no aspiration in 194 symptomatic overdoses. In the study by Eddleston *et al.* of the 97 patients receiving MDAC and 109 SDAC patients, who subsequently died, none had significant aspiration at judicial postmortem.[28]

In an RCT, Cooper *et al.*[21] commented on aspiration, reporting it in one of 166 patients in the activated charcoal group, compared with 1 of 161 in the no activated charcoal groups (RR = 0.97, CI 0.10–9.37, $P = 0.98$). Intubation rates (after randomization), commented on in two RCTs, were cumulatively 154 of 3241 patients in the activated charcoal group vs. 79 of 1755 when no activated charcoal was administered (RR 1.03, CI 0.79–1.34, $P = 0.69$).[21,28]

Bowel obstruction (constipation, ileus)

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

Bowel obstruction was explicitly commented on in two RCTs. No patients experienced gastrointestinal obstruction in 401 hospital inpatients treated after yellow oleander poisoning (SDAC 50 g or MDAC 50 g × 12 doses).[19] In a second RCT, although 24 of 3075 patients treated with activated charcoal (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, $P = 0.36$).[28] 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.[28]

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.[31] A randomized crossover study of 19 healthy volunteers showed that the oral absorption of acetylcysteine was reduced by activated charcoal, with peak concentrations 29% lower.[32]

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.*[28] 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.[33] 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 Clinical studies of poisoned patients receiving activated charcoal

Author	Study type	Subject group	Size	Interventions compared	Primary outcome(s)	Adverse reactions
AC vs. no gastric decontamination						
Merigian *et al.*[4,22]	Open-label pseudo-randomized controlled trial (even–odd day protocol)	Self-poisoning patients Presenting to the emergency department (unspecified time) All overdoses excluding acetaminophen >140 mg/kg, lithium, monoamine oxidase inhibitors, heavy metals, formaldehyde, mushrooms, digitalis, methanol, ethylene glycol, iron, or sustained release products	451	50 g dose of oral AC ($n = 220$) vs. no AC ($n = 231$).	Clinical deterioration in 4 h after treatment Symptomatic patients requiring admission for further observation were assessed until hospital discharge Clinical deterioration was based on GCS, temperature, blood pressure, pulse, and dysrhythmias	No clinical deterioration or adverse events reported in either group
Cooper *et al.*[21]	Open-label randomized controlled trial (sealed sequentially numbered envelopes)	Self-poisoning patients Presenting within 12 h of ingestion All overdoses, but mainly pharmaceuticals	327	One 50 g dose of AC ($n = 166$) vs. no gastric decontamination ($n = 161$)	Medical length of stay of patient	There was no significant difference in adverse effects when comparing AC with no gastric decontamination Vomiting 25/166, 15% vs. 23/161, 14% in control group Aspiration 1/166, 0.6%, vs. 1/161, 0.6% in control group Intubation 8/166, 4.8% vs. 3/161, 1.8% in control group

Eddleston *et al.*[28]	Open-label randomized controlled trial (stratified block randomization by computer software)	Self-poisoning patients Presenting within 72 h of ingestion All overdoses, but most ingested yellow oleander seeds or pesticides	4632	Six 50 g doses of AC ($n=1533$) vs. one 50 g dose of AC ($n=1545$) vs. no gastric decontamination ($n=1554$)	All-cause mortality during hospital admission	Other adverse effects were not commented on There was 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
Comparisons of different AC regimes						
Albertson *et al.*[27]	Open-label randomized controlled trial (randomized by hospital unit numbers)	Self-poisoning patients Presenting to emergency department (unspecified time) 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	200	Syrup of ipecac (30 ml orally repeated in 30 min if no response) plus 1 g/kg of AC (in AC–water–sorbitol mix) ($n=93$) vs. AC alone ($n=107$)	Time in emergency department, days of intensive care treatment, days hospitalized, percentage hospitalized/ admitted to intensive treatment unit, complication rates	AC plus ipecac: 5/193, 2.6%: four cases of aspiration, one threatened abortion (possibly related to ipecac) AC alone: 1/107 0.9% complication rate Persistent occult blood-positive stool (in an aspirin overdose) 0/107 aspiration/pneumonitis in AC-alone group
Merigian *et al.*[a,22]	Open-label pseudo-randomized controlled trial (even–odd day protocol)	Self-poisoning patients Presenting to the emergency department (unspecified time) All overdoses excluding acetaminophen >140 mg/kg, lithium, monoamine oxidase inhibitors, heavy metals, formaldehyde, mushrooms, digitalis, methanol, ethylene glycol, iron, or sustained release products	357	Ipecac-induced emesis (gastric lavage if obtunded) and AC ($n=163$) vs. AC alone ($n=194$)	Clinical deterioration in 4 h after treatment Symptomatic patients requiring admission for further observation were assessed until hospital discharge Clinical deterioration was based on Glasgow Coma Score, temperature, blood pressure, pulse, and dysrhythmias	Intubation 52/163 (31.9%) with gastric emptying and AC, compared with 16/194 (8.2%) treated with AC alone Aspiration pneumonia 8/163 (4.9%) with gastric emptying and AC, compared with 0/194 (0%) treated with AC alone No other significant differences in complications (hypotension, dysrhythmias, pulmonary oedema, seizures)
Pond *et al.*[34]	Open-label pseudo-randomized controlled trial (even–odd day protocol)	Self-poisoning patients Presenting to emergency department within 12 h Overdose of substances known to be adsorbed by charcoal	876	AC ($n=417$) vs. AC plus gastric emptying by ipecac-induced emesis or gastric lavage ($n=459$)	Clinical course during the first 6 h after treatment began, length of hospital stay, complications	No significant differences between the groups The first AC dose was vomited in 55% of the ipecac-induced emesis patients, 13% of the gastric lavage group, 23% of the oral AC-only group, and 17% of nasogastric charcoal group No other complications were reported in the AC-alone group
de Silva *et al.*[19]	Single blind randomized controlled study (computer-generated random allocation table)	Self-poisoning patients Presenting to the emergency department within 24 h Yellow oleander ingestion only	401	50 g AC every 6 h for 3 days ($n=201$) vs. one single dose ($n=200$)	Death	Multiple-dose AC: diarrhoea 3/201 (1.5%) abdominal discomfort 13/201 (6.5%). These side-effects were transient and resolved without any specific treatment. Comparative data not reported for single-dose group Aspiration 0/401 (all patients) Intestinal obstruction 0/401 (all patients)
Mohamed *et al.*[b,20]	Randomized controlled trial (stratified random sample)	All patients with a history of self-poisoning (unspecified time)	1103	559 patients received one dose of 50 g AC, 544 received six doses of 50 g AC	Patient compliance with treatment	Overall 239 (21.7%) of patients vomited after AC administration Of 98 patients receiving AC via NG tube, 15 vomited after administration
Excluded study (due to methodological concerns)						
Merigian *et al.*[33]	Open-label pseudo-randomized controlled trial (even–odd day protocol)	Self-poisoning patients Presenting with recent (unspecified time) ingestion Drug overdose, (excluding crack cocaine, mushrooms, volatiles, caustic agents, heavy metals, lithium, iron preparations, or more than 140 mg/kg acetaminophen)	1525	One 50 g dose of oral AC ($n=455$) vs. no gastric decontamination ($n=1075$) Discrepancy in group sizes with no explanation given	Clinical deterioration, length of stay in emergency department, complication rate	Significantly greater vomiting in AC group, but no other significant differences Vomiting 105/455, 23% AC vs. 73/1075 6.7% in control group Aspiration pneumonia 2/455, (0.4%) vs. 2/1075 (0.2%) in control group Intubation 2/455, (0.4%) vs. 2/1075 (0.2%) in control group No other significant differences in adverse reactions were reported

AC, activated charcoal.
[a]Both were part of the same study protocol.
[b]Subgroup of Eddleston *et al.*[28]

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.[17,33] 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.

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References

1 Meredith TJ. Epidemiology of poisoning. *Pharmacology and Therapeutics* 1993;59:251–256.
2 Eddleston M. Patterns and problems of deliberate self-poisoning in the developing world. *Quarterly Journal of Medicine* 2000;93:715–731.
3 Nelson LS, Lewin NA, Howland MA, *et al*. Goldfrank's toxicologic emergencies. 9th ed. McGraw-Hill Medical; 2010.
4 Neuvonen PJ. Clinical pharmacokinetics of oral activated charcoal in acute intoxications. *Clinical Pharmacokinetics* 1982;7:465–489.
5 Ardagh M, Flood D, Tait C. Limiting the use of gastrointestinal decontamination does not worsen the outcome from deliberate self-poisoning. *New Zealand Medical Journal* 2001;114:423–425.
6 Chyka PA, Seger D. Position statement: single-dose activated charcoal. American Academy of Clinical Toxicology; European Association of Poisons Centres and Clinical Toxicologists. *Journal of Toxicology Clinical Toxicology* 1997;35:721–741.
7 Krenzelok EP, McGuigan M, Lheur P. Position statement: ipecac syrup. American Academy of Clinical Toxicology; European Association of Poisons Centres and Clinical Toxicologists. *Journal of Toxicology Clinical Toxicology* 1997;35:699–709.
8 Vale JA. Position statement: gastric lavage. American Academy of Clinical Toxicology; European Association of Poisons Centres and Clinical Toxicologists. *Journal of Toxicology Clinical Toxicology* 1997;35:711–719.
9 Heard K. Gastrointestinal decontamination. *Medical Clinics of North America* 2005;89:1067–1078.
10 American Academy of Clinical Toxicology; European Association of Poisons Centres and Clinical Toxicologists. Position statement and practice guidelines on the use of multi-dose activated charcoal in the treatment of acute poisoning. *Journal of Toxicology Clinical Toxicology* 1999;37:731–751.
11 Krenzelok EP, Keller R, Stewart RD. Gastrointestinal transit times of cathartics combined with charcoal. *Annals of Emergency Medicine* 1985;14:1152–1155.
12 NICE Guidelines Self Harm. http://www.nice.org.uk/nicemedia/live/10946/29424/29424.pdf. [Accessed 10 October 2010]
13 Levy G. Gastrointestinal clearance of drugs with activated charcoal. *New England Journal of Medicine* 1982;307:676–678.
14 Boehnert MT, Lewander WJ, Gaudreault P, et al. Advances in clinical toxicology. *Pediatric Clinics of North America* 1985;32:193–211.
15 Jones J, McMullen MJ, Dougherty J, et al. Repetitive doses of activated charcoal in the treatment of poisoning. *American Journal of Emergency Medicine* 1987;5:305–311.
16 Vale JA, Proudfoot AT. How useful is activated charcoal? *British Medical Journal* 1993;306:78–79.
17 Cooper GM, Buckley NA. Activated Charcoal RCT. *American Journal of Therapeutics* 2003;10:235–236.
18 Sato RL, Wong JJ, Sumida SM, et al. Adverse effects of superactivated charcoal administered to healthy volunteers. *Hawaii Medical Journal* 2002;61:251–253.
19 de Silva HA, Fonseka MM, Pathmeswaran A, et al. Multiple-dose activated charcoal for treatment of yellow oleander poisoning: a single-blind, randomised, placebo-controlled trial. *Lancet* 2003;361:1935–1938.
20 Mohamed F, Sooriyarachchi MR, Senarathna L, et al. Compliance for single and multiple dose regimens of superactivated charcoal: a prospective study of patients in a clinical trial. *Clinical Toxicology (Philadelphia)* 2007;45:132–135.
21 Cooper GM, Le Couteur DG, Richardson D, et al. A randomized clinical trial of activated charcoal for the routine management of oral drug overdose. *Quartely Journal of Medicine* 2005;98:655–660.
22 Merigian KS, Woodard M, Hedges JR, et al. Prospective evaluation of gastric emptying in the self-poisoned patient. *American Journal of Emergency Medicine* 1990;8:479–483.
23 Francis RC, Schefold JC, Bercker S, et al. Acute respiratory failure after aspiration of activated charcoal with recurrent deposition and release from an intrapulmonary cavern. *Intensive Care Med* 2009;35:360–363.
24 Sabga E, Dick A, Lertzman M, et al. Direct administration of charcoal into the lung and pleural cavity. *Annals of Emergency Medicine* 1997;30:695–697.
25 Huber M, Pohl W, Reinisch G, et al. Lung disease 35 years after aspiration of activated charcoal in combination with pulmonary lymphangioleiomyomatosis. A histological and clinicopathological study with scanning electron microscopic evaluation and element analysis. *Virchows Archiv* 2006;449:225–229.
26 Dorrington CL, Johnson DW, Brant R. The frequency of complications associated with the use of multiple-dose activated charcoal. *Annals of Emergency Medicine* 2003;41:370–377.
27 Albertson TE, Derlet RW, Foulke GE, et al. Superiority of activated charcoal alone compared with ipecac and activated charcoal in the treatment of acute toxic ingestions. *Annals of Emergency Medicine* 1989;18:56–59.
28 Eddleston M, Juszczak E, Buckley NA, et al. Multiple-dose activated charcoal in acute self-poisoning: a randomised controlled trial. *Lancet* 2008;371:579–587.
29 Goulbourne KB, Cisek JE. Small-bowel obstruction secondary to activated charcoal and adhesions. *Annals of Emergency Medicine* 1994;24:108–110.
30 Gomez HF, Brent JA, Munoz DC, et al. Charcoal stercolith with intestinal perforation in a patient treated for amitriptyline ingestion. *Journal of Emergency Medicine* 1994;12:57–60.
31 Strobel J, Zimmermann R, Eckstein R, et al. Charcoal intake and oral anticoagulation. *Journal of Travel Medicine* 2010;17:287–288.
32 Ekins BR, Ford DC, Thompson MI, et al. The effect of activated charcoal on *N*-acetylcysteine absorption in normal subjects. *American Journal of Emergency Medicine* 1987;5:483–487.
33 Merigian KS, Blaho KE. Single-dose oral activated charcoal in the treatment of the self-poisoned patient: a prospective, randomized, controlled trial. *American Journal of Therapeutics* 2002;9:301–308.
34 Pond SM, Lewis-Driver DJ, Williams GM, et al. Gastric emptying in acute overdose: a prospective randomised controlled trial. *Medical Journal of Australia* 1995;163:345–349.

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