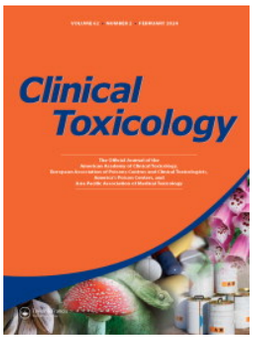

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ARTICLES

Activated Charcoal Reduces the Need for *N*-Acetylcysteine Treatment After Acetaminophen (Paracetamol) Overdose

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ABSTRACT

Background: The evidence for efficacy of gastric lavage and activated charcoal for gastrointestinal decontamination in poisoning has relied entirely on volunteer studies and/or pharmacokinetic studies and evidence for any clinical benefits or resource savings is lacking. Aim of Study: To investigate the value of gastrointestinal decontamination using gastric lavage and/or activated charcoal in acetaminophen (paracetamol) poisoning. Patients and Methods: We analyzed a series of 981 consecutive acetaminophen poisonings. These patients were treated with gastric lavage and activated charcoal, activated charcoal alone, or no gastrointestinal decontamination. The decision as to which treatment was received was determined by patient cooperation, the treating physician, coingested drugs, and time to presentation after the overdose. Results: Of 981 patients admitted over 10 years, 10% (100) had serum concentrations of acetaminophen that indicated a probable or high risk of hepatotoxicity. The risk of toxic concentrations for patients ingesting less than 10 g of acetaminophen was very low. In patients presenting within 24 hours, who had ingested 10 g or more, those who had been given activated charcoal were significantly less likely to have probable or high risk concentrations (Odds ratio 0.36, 95% CI 0.23–0.58, $p < 0.0001$). Gastric lavage, in addition to activated charcoal, did not further decrease the risk (Odds ratio 1.12, 95% CI 0.57–2.20, $p = 0.86$). Conclusions:

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Toxic concentrations of serum acetaminophen (paracetamol) are uncommon in patients ingesting less than 10 g. In those ingesting more, activated charcoal appears to reduce the number of patients who achieve toxic acetaminophen concentrations and thus may reduce the need for treatment and hospital stay.

INTRODUCTION

The evidence in favor of the use of gastrointestinal decontamination in poisoning in general, and acetaminophen (paracetmol) poisoning in particular, has relied entirely on volunteer studies and/or pharmacokinetic studies.[1–5] Controlled trials of gastric emptying in unselected patients with poisoning have shown no benefits.[6–8] Thus the use of activated charcoal (AC) alone (without gastric emptying) has been recommended in most poisonings.[5–8] However, despite the wealth of volunteer studies demonstrating reduced absorption of a large number of drugs when AC is administered, evidence that the use of AC leads to any clinical benefits or resource savings is lacking.[1–5] The lack of obvious benefits may be due to the outcome of most poisonings being generally favorable with supportive treatment alone. Thus there is not general acceptance that charcoal has clinical efficacy in even the most severe poisonings.[9]

Acetaminophen is moderately well adsorbed by charcoal *in vitro* and in volunteer studies.[5,10,11] However, in many centers in the US, the use of charcoal has been avoided because it may also reduce absorption of orally administered *N*-acetylcysteine (NAC).[12] The aim of this study was to assess the impact of gastrointestinal decontamination on the clinical outcome of acetaminophen poisoning, in particular the need for treatment with NAC.

PATIENTS AND METHODS

All presentations to our unit who ingested acetaminophen between January 1987 and September 1996 were analyzed. A general description of the unit, data collection, and some other details of the treatment and outcomes of these patients have been reported elsewhere.[13,14] Our usual management of patients presenting within 4 hours who have taken >125 mg/kg of acetaminophen is to give AC (1–2 g/kg) and intravenous fluids. Gastric lavage is performed if indicated by coingested substances or sometimes due to decisions taken by the emergency physician. However, if patients refuse to cooperate and if no more toxic substance has been ingested, gastrointestinal decontamination will not be performed. Serum acetaminophen concentrations are taken at 4 hours or on presentation (if this is later than 4 hours). We compared the likelihood of having a concentration of acetaminophen that indicated the need for treatment (based on the 2 main nomograms used;[12,13] Figure 1) and other characteristics in those who received AC and in those with no gastrointestinal decontamination. We also compared those who received gastric lavage and charcoal with those who received charcoal alone. The possible, probable, and high risk lines shown in Figure 1 were defined by Prescott *et al*. and Rumack *et al*.[1,2] They are parallel lines with an origin at 4 hours of serum concentration of 150 mg/L, 200 mg/L, and 300 mg/L, respectively, declining with a half-life of 4 hours. The probable risk line is generally used in the UK while the possible risk line is generally used in the US.

Statistical Methods

Due to the nonnormality of the continuous variables, medians are presented and the Wilcoxon two-sample test was used to compare groups. For dichotomous variables,

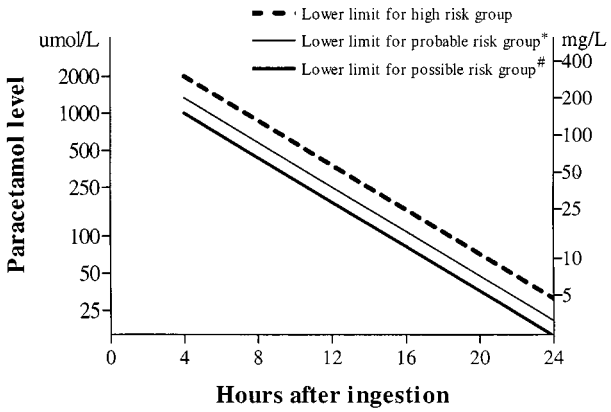

Figure 1. Nomogram used to define patients at possible, probable, or high risk of hepatotoxicity on the basis of serum concentrations between 4 and 24 hours postingestion of acetaminophen (paracetamol).
* Treatment line used in the US nomogram.[2]
# Treatment line used in the Prescott (UK) nomogram.[1]

Yates' continuity corrected chi-square or Fisher's exact test were performed.

RESULTS

Nine-hundred eighty-one patients were admitted with suspected or confirmed acetaminophen poisoning. There were 748 patients with nontoxic serum concentrations, 62 possibly toxic, 51 probably toxic, 49 high risk, and 40 presented >24 hours after ingestion (Figure 1). For 31 patients, the time of ingestion was either unknown or ingestion was over many hours. Twenty-five percent of patients had gastric lavage followed by AC, 36% had charcoal alone, and 39% had no gastrointestinal decontamination.

The risk of toxic concentrations for patients ingesting less than 10 g was very low (Figure 2). Thus, a cut-off of 10 g was used to compare methods of gastrointestinal decontamination. Table 1 compares patients ingesting ≥10 g of acetaminophen and presenting within 24 hours who received none or two different methods of decontamination. Patients who received AC (with or without gastric lavage) were significantly less likely to have probable or high risk concentrations (Odds ratio 0.36, 95% CI 0.23–0.58, $p < 0.0001$) or concentrations above the US nomogram treatment line (Odds ratio 0.50, 95% CI 0.33–0.75, $p = 0.0007$). There were 50 patients whose gastrointestinal decontamination had preceded the measurement of acetaminophen by less than 1 hour. However, excluding these from the analysis did not significantly alter the proportion with at-risk concentrations (Odds ratios for probable or high risk concentration: 0.35 95% CI 0.21–0.57, $p < 0.0001$, and for concentration above the US nomogram treatment line: 0.52, 95% CI 0.34–0.79, $p = 0.003$). Gastric lavage conferred no additional benefit over charcoal alone (Odds ratios for probable or high risk concentration: 1.12, 95% CI 0.57–2.20, $p = 0.86$, and for concentration above the US nomogram treatment line: 0.76, 95% CI 0.44–1.31, $p = 0.33$).

As would be expected from our treatment guidelines, those who received decontamination generally presented earlier ($p = 0.0001$). They also had a slightly younger median age and were more commonly female (Table 1). The effectiveness of charcoal was evident in those presenting within 2 hours with perhaps minor benefits up to 4 hours (Figure 3).

DISCUSSION

This study suggests a substantial clinical benefit and some resource savings from the use of AC in acetaminophen poisonings greater than 10 g in patients who present within 2 to 4 hours. Only 15% of those presenting within 2 hours who were given charcoal were above the possible risk line compared to 41% of those who did not receive gastrointestinal decontamination. Since treatment in our study was not randomly determined, and a number of baseline factors (age, gender, time to presentation) were unequally distributed, it is possible that these may also have influenced the concentrations obtained. It is possible that being younger or of female gender would reduce the acetaminophen concentrations obtained, although this is unlikely as these people weigh less and might receive a larger dose in mg/kg (body weight was not routinely measured). In our series, the general trend for those who had repeat serum concentrations was for the initially toxic concentrations to become nontoxic.[13] Thus, late sampling of concentrations, *per se*, when comparing

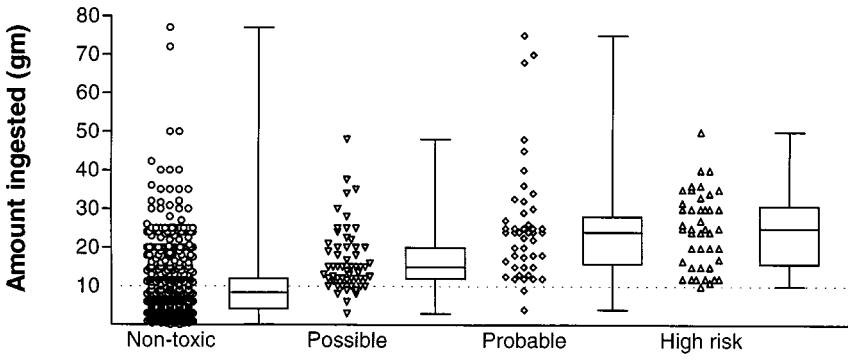

Figure 2. The effect of reported dose of acetaminophen (paracetamol) ingested (median, quartiles, and range), on the expected risk of hepatotoxicity determined from subsequent serum concentrations (from Figure 1).

Table 1

Proportion of Patients, Ingesting ≥10 g of Acetaminophen and Presenting Within 24 Hours, with Probable or High Risk Concentrations and the Method of Gastrointestinal Decontamination Used

	No GI Decontamination (n = 167)	Charcoal Alone (n = 163)	Lavage & Charcoal (n = 120)	p Value (combined charcoal v none)
Median age (range)	24 (13–89)	23 (14–78)	20 (13–64)	0.02
Female	99 (59.3%)	111 (68.1%)	80 (66.7%)	0.09
Stupor/coma	13 (7.8%)	6 (3.7%)	17 (14.2%)	0.9
Median amount ingested, g (range)	15 (10–75)	12.5 (10–77)	15 (10–70)	0.65
Median time to presentation, min (range)	385 (10–1380)	135 (5–885)	120 (14–840)	0.0001
Concentration above the possible risk line	68 (40.7%)	45 (27.6%)	27 (22.5%)	0.0007
Probable or high risk concentration	50 (29.9%)	21 (12.9%)	17 (14.2%)	<0.0001
Median length of stay, hours (range)	22.3 (1–170)	19.2 (2–285)	18.8 (2.7–154)	0.04

Odds ratio need for NAC treatment if charcoal received: Probable or high risk concentration: OR 0.36 (95% CI 0.23–0.58); Possible risk concentration: OR 0.50 (95% CI 0.33–0.75).

those not given charcoal to those who received charcoal, would not account for the higher proportion of toxic concentrations in late presentations. However, this does not exclude the possibility that the late presenters had ingested larger doses. Our sample was not sufficiently large to compare subgroups with significant power in such *post hoc* analysis. However, we believe the results are valid as:

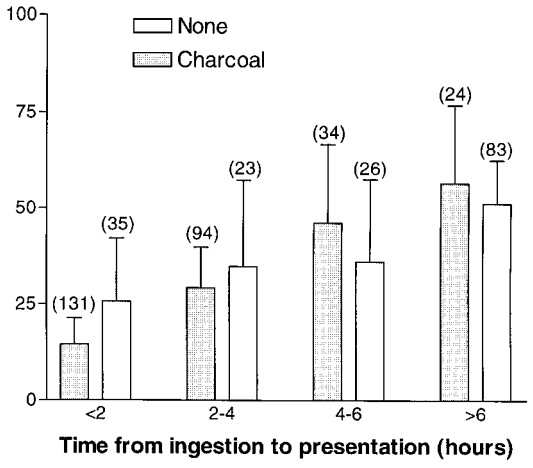

Figure 3. Percent of overdoses (95% CI) with concentrations in the possible risk range (total n in group) stratified by time from ingestion and treatment with charcoal.

1. The effect within the group who received charcoal was largely confined to the first 2 hours after ingestion (Figure 3) and that the groups were similar after this time.
2. The results are in agreement with *in vitro* and volunteer studies.[5,10,11]
3. The results make biological sense based on the pharmacokinetics of acetaminophen.[15]
4. The proportion of patients developing potentially toxic concentrations from the total cohort of 981 patients is lower than that reported where charcoal has been withheld as part of a protocol testing oral NAC.[12]

In Australia (and many other countries), this largely supports current clinical practice.[16] However, the use of charcoal is not routine in acetaminophen poisoning in the US where there appears to be some controversy largely related to the restriction on the use of intravenous (IV) preparations of NAC. This has lead to some recommendations to avoid charcoal as it reduces oral NAC absorption, although this position has come under recent criticism. It has been proposed that charcoal could be given followed by either the usual or an increased dose of oral NAC.[17,18] This seems more reasonable than to withhold charcoal as has been recommended previously, but the clinical consequences of such changes in the established NAC protocol have not been determined. The use of NAC IV avoids these concerns.[19] Our study supports the

routine use of AC up to 2 hours after overdose. Beyond this time, selected patients who may have delayed gastric emptying due to opioids or anticholinergic drug ingestion may still benefit, as may those ingesting sustained or delayed release preparations.[20–22]

REFERENCES

1. Vale JA. Position statement: Gastric lavage. American Academy of Clinical Toxicology; European Association of Poisons Centres and Clinical Toxicologists. *J Toxicol Clin Toxicol* 1997;**35**:711–719.
2. Chyka PA. Multiple-dose activated charcoal and enhancement of systemic drug clearance: Summary of studies in animals and human volunteers. *J Toxicol Clin Toxicol* 1995;**33**:399–405.
3. Vale JA, Proudfoot AT. How useful is activated charcoal? *BMJ* 1993;**306**:78–79.
4. Palatnick W, Tenenbein M. Activated charcoal in the treatment of drug overdose. An update. *Drug Saf* 1992; **7**:3–7.
5. Chyka PA, Seger D. Position statement: Single-dose activated charcoal. American Academy of Clinical Toxicology; European Association of Poisons Centres and Clinical Toxicologists. *J Toxicol Clin Toxicol* 1997;**35**:721–741.
6. Kulig K, Bar-Or D, Cantrill SV, Rosen P, Rumack BH. Management of acutely poisoned patients without gastric emptying. *Ann Emerg Med* 1985;**14**:562–567.
7. Merigian KS, Woodard M, Hedges JR, *et al*. Prospective evaluation of gastric emptying in the self-poisoned patient. *Am J Emerg Med* 1990;**8**:479–483.
8. Pond SM, Lewis-Driver DJ, Williams GM, Green AC, Stevenson NW. Gastric emptying in acute overdose: A prospective randomised controlled trial. *Med J Aust* 1995; **163**:345–349.
9. Demaziere J, Saissy JM, Vitris M, *et al*. Effets du diazepam sur la mortalite des intoxications aigues par la chloroquine. *Ann Fr d Anesth Reanim* 1992;**11**:164–167.
10. Rose SR, Gorman RL, Oderda GM, Klein-Schwartz W, Watson WA. Simulated acetaminophen overdose: Pharmacokinetics and effectiveness of activated charcoal. *Ann Emerg Med* 1991;**20**:29–33.
11. Chamberlain JM, Gorman RL, Oderda GM, Klein-Schwartz W, Klein BL. Use of activated charcoal in a simulated poisoning with acetaminophen: A new loading dose for *N*-acetycysteine. *Ann Emerg Med* 1993;**22**:45–49.
12. Smilkstein MJ, Knapp GL, Kulig KW, Rumack BH. Efficacy of oral *N*-acetylcysteine in the treatment of acetaminophen overdose: Analysis of the national multicenter study (1976 to 1985). *N Engl J Med* 1988; **319**:1557–1562.
13. Buckley NA, Whyte IM, O'Connell D, Dawson AH. Oral or intravenous *N*-acetylcysteine: Which is the treatment of choice for early paracetamol (acetaminophen) poisoning? *J Toxicol Clin Toxico*l 1999;**37**:759–767.
14. Buckley NA, Dawson AH, Whyte IM, McManus P, Ferguson N. Six years of self poisoning in Newcastle 1987–1992. *Med J Aust* 1995;**162**:190–193.
15. Slattery JT, Levy G. Acetaminophen kinetics in acutely poisoned patients. *Clin Pharmacol Ther* 1979;**25**:184–195.
16. Vale JA, Proudfoot AT. Paracetamol (acetaminophen) poisoning. *Lancet* 1995;**346**:547–552.
17. Brent J. Are activated charcoal-*N*-acetylcysteine interactions of clinical significance? *Ann Emerg Med* 1993;**22**: 84–86.
18. Spiller HA, Krenzelok EP, Grande GA, Safir EF, Diamond JJ. A prospective evaluation of the effect of activated charcoal before oral *N*-acetylcysteine in acetaminophen overdose. *Ann Emerg Med* 1994;**23**:519–523.
19. Dhawan A, Sorrell MF. Acetaminophen overdose: Need to consider intravenous preparation of *N*-acetylcysteine in the United States. *Am J Gastroenterol* 1996;**91**: 1476.
20. Heading RC, Nimmo J, Prescott LF, Tothill P. The dependence of paracetamol absorption on the rate of gastric emptying. *Br J Pharmacol* 1973;**47**:415–421.
21. Nimmo WS, Heading RC, Wilson J, Tothill P, Prescott LF. Inhibition of gastric emptying and drug absorption by narcotic analgesics. *Br J Clin Pharmacol* 1975;**2**:509–513.
22. Tighe TV, Walter FG. Delayed toxic acetaminophen level after initial four hour nontoxic level. *J Toxicol Clin Toxicol* 1994;**32**:431–434.

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