Activated Charcoal in Resource Poor Settings: Reviewing the Evidence

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- No commercial disclosures

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Intro

- Activated Charcoal
  - Used for 1,000s years
    - 1550 BC (Cooney)
  - Cheap sources - wood, coconut, petroleum
  - Porous, high internal surface area
    - 10 tsp = Wembley Stadium Pitch
  - GI elimination (“gut dialysis”)
Resource Poor Setting

- “Environment where the use of routine antidotes is unavailable or prohibitively expensive” *
  - Example: Digifab for oleander

- Poisonings in RPS
  - Pesticides and plants
  - Higher mortality (10-20%)
  - Limited access to care
  - Limited resources

* Howland MA, GTE9 2010
Consensus “Lag”...

- Consensus Guidelines:
  - 2005: AACT/EAPCCT

- Best evidence/research:
  - 2005: Cooper GM, et al - QJM (MDAC)

- High-quality meta-analyses/opinion papers:
  - 2009: Jurgens G - Clin Pharm Ther
Consensus “Lag”...

- **Consensus Guidelines:**
  - 2005: AACT/EAPCCT

- **Best evidence/research:**

- **High-quality meta-analyses/opinion papers:**
  - 2009: Jurgens G – Clin Pharm Ther
Hypothesis

- Activated Charcoal in RPS
  - Favorable risk-benefit ratio
    - High safety profile
    - Theoretical mechanism
    - Ease of use

- OBJECTIVES
  - To identify poisonings in RPS in which the use of AC is supported by sound clinical evidence
Methods

- Review of English-language literature in last 20yrs by 2 independent reviewers of clinical evidence supporting use of SDAC and MDAC in suspected poisonings
  - EMEDLINE, PubMed, Clinicaltrials.gov, Cochrane Databases and Google Scholar
- Terms:
  - “Activated Charcoal” and “poison” or “overdose” or “ingestion” or “gastric decontamination” or “intestinal dialysis”
- Expanded search:
  - “SDAC” “single dose activated charcoal” “MDAC” “multi-dose activated charcoal” “multiple dose activated charcoal”
Methods

- **Exclusion:**
  - Non-English language
  - Animal studies
  - Healthy human volunteer trials
  - Case reports
  - Studies that incorporated the use of hemodialysis
  - Lack of AC decontamination (efficacy) data
SDAC

45 Trials

14 Human Trials
- 7 Excluded
  - Lack of efficacy data

31 Excluded
- 10 Reviews,
  - 7 Human volunteers,
  - 9 Animal reports,
  - 3 Case reports/series

7 Trials,
- 5 Prospective
- 2 Retrospective
### Efficacy Studies of SDAC

<table>
<thead>
<tr>
<th>Author/Yr</th>
<th>Study type</th>
<th>Study vs. Control</th>
<th>N</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spiller</td>
<td>Retrospective APAP</td>
<td>AC+NAC NAC</td>
<td>97,960</td>
<td>0.5% vs. 0.8%</td>
</tr>
<tr>
<td>Spiller</td>
<td>Prospective APAP + time to NAC</td>
<td>AC+NAC NAC</td>
<td>145</td>
<td>None</td>
</tr>
<tr>
<td>Cooper</td>
<td>Prospective All ODs</td>
<td>AC No AC</td>
<td>327</td>
<td>0.3%</td>
</tr>
<tr>
<td>Merigian</td>
<td>Prospective All OD</td>
<td>AC No AC</td>
<td>1479</td>
<td>None</td>
</tr>
<tr>
<td>Buckley</td>
<td>Retrospective APAP</td>
<td>AC GL+AC Control</td>
<td>981</td>
<td>None</td>
</tr>
<tr>
<td>Kornberg</td>
<td>Prospective Children</td>
<td>AC SOI+AC</td>
<td>70</td>
<td>None</td>
</tr>
<tr>
<td>Underhill</td>
<td>Prospective APAP</td>
<td>AC GL SOI</td>
<td>60</td>
<td>None</td>
</tr>
</tbody>
</table>

Abbreviations: AC=activated charcoal; APAP=acetaminophen/paracetamol; AST/ALT=transaminases; g=grams; GL=gastric lavage; h=hours; ICU=intensive care unit; kg=kilograms; LOS=length of stay; N=number of patients; NAC=N-acetylcysteine; OD=overdose; SOI=syrup of ipecac; ↑=increase; ↓=decrease

* Not limited to RPS
# Efficacy Studies of SDAC

<table>
<thead>
<tr>
<th>Author/Yr</th>
<th>Mortality</th>
<th>Secondary Endpoint(s)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spiller 2007</td>
<td>0.5% vs. 0.8%</td>
<td>↓ AST/ALT&gt;1000</td>
<td>AC 2.9% vs. 12% SDAC benefit, ↓ liver damage</td>
</tr>
<tr>
<td>Spiller 2006</td>
<td>None</td>
<td>↓ AST or ALT &gt;1,000 8h 0% vs. 11.7% 2.7% vs. 52% 13-16h 10% vs. 45%</td>
<td>4-9-12h ↑ Effect of AC when NAC started later</td>
</tr>
<tr>
<td>Cooper 2005</td>
<td>0.3%</td>
<td>1° LOS, no dif 2° vomit/aspiration/ICU no dif</td>
<td>Low acuity, severe ODs and &lt;1hr excluded</td>
</tr>
<tr>
<td>Merigian 2002</td>
<td>None</td>
<td>1° LOS, no dif 2° clinical worse/emesis ↓ Emesis- AC 25% v no AC 14%</td>
<td>Subjective endpt. Low acuity 86% discharged,</td>
</tr>
<tr>
<td>Buckley 1999</td>
<td>None</td>
<td>↓ risk of hepatotoxicity AC 12.9% AC+GL 14.2% control 29.9%</td>
<td>AC ↓ serum toxicity</td>
</tr>
<tr>
<td>Kornberg 1991</td>
<td>None</td>
<td>Less emesis and shorter LOS w AC</td>
<td>SOI ↑ side effects, delays AC</td>
</tr>
<tr>
<td>Underhill 1990</td>
<td>None</td>
<td>% fall in serum [APAP] AC 52 GL39 SOI 41</td>
<td>AC &gt; GL or SOI if &lt;2hrs</td>
</tr>
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</table>

**Abbreviations:** AC=activated charcoal; g=grams; h=hours; ICU=intensive care unit; LOS=length of stay; MRT=mean residence time; N=number of patients; NAC=N-acetylcysteine; OD=overdose; SDAC=single dose activated charcoal; Tx= treatment; ↑=increase; ↓=decrease
MDAC

7 Trials
Human, non-volunteer

3 Excluded
Case Series/Reports

4 Trials
All with Efficacy Data
<table>
<thead>
<tr>
<th>Author/Yr</th>
<th>Study type</th>
<th>Intervention</th>
<th>Patient pop.</th>
<th>Mortality</th>
</tr>
</thead>
</table>
| Eddleston 2008 | Prospective | No AC  SDAC 50g  MDAC 50g q4h x6   | 4632 Sri Lanka all ODs      | MDAC 6.3%  
SDAC 7.1%  
No AC 6.8%     |
| Roberts 2006  | Prospective | SDAC 50g  MDAC 50g q4h x6           | 254 Sri Lanka cardioactive steroids | None               |
| De Silva 2003 | Prospective | SDAC 50g  MDAC q6h x72h              | 401 Sri Lanka cardioactive steroids | SDAC 8%  
MDAC 2.5%     |
| Ibanez 1995   | Retrospective | MDAC vs. no AC                      | 39 Digoxin                  | None               |

Abbreviations: AC=activated charcoal; g=grams; h=hours; ICU=intensive care unit; LOS=length of stay; MRT=mean residence time; N=number of patients; NAC=N-acetylcysteine; OD=overdose; SDAC=single dose activated charcoal; Tx=treatment; ↑=increase; ↓=decrease
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</table>
| Eddleston 2008 | MDAC 6.3%  
SDAC 7.1%  
No AC 6.8% | ↓ Adverse events | ↓ Trend mortality: early AC  
↓ Trend need for Tx |
| Roberts 2006 | None | ↓ MRT and $t_{1/2}$ | Small study no deaths. |
| De Silva 2003 | SDAC 8%  
MDAC 2.5% | ↓ Arrhythmia, atropine, pacing  
↓ ICU admits | ↓ Mortality  
↓ Need for Tx |
| Ibanez 1995 | None | ↑ $t_{1/2}$  
↑ Cl $98$ vs. $55$ | Small study, benefit in renal failure,  
78% ↑ elimination |

**Abbreviations**: AC=activated charcoal; g=grams; h=hours; ICU=intensive care unit; LOS=length of stay; MRT=mean residence time; N=number of patients; NAC=N-acetylcysteine; OD=overdose; SDAC=single dose activated charcoal; Tx=treatment; ↑=increase; ↓=decrease
## Mortality Benefit of AC for Pesticide Poisoning

<table>
<thead>
<tr>
<th>Author/year</th>
<th>Study type</th>
<th>Study vs. control</th>
<th>Patient population</th>
<th>Mortality Rate</th>
<th>Point Estimate</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eddleston 2008</td>
<td>Prospective subset Pesticides</td>
<td>MDAC vs. SDAC vs. No AC</td>
<td>2037</td>
<td>10% vs. 13.7%</td>
<td>ARR 3.7% NNT 27</td>
<td>↓ Trend mortality with MDAC</td>
</tr>
</tbody>
</table>

**Abbreviations:** ARR=absolute risk reduction; MDAC=multiple dose activated charcoal; NNT=number needed to treat; SDAC=single dose activated charcoal.
Limitations

- Sick patients excluded, just given AC
- Transport times typically in excess of 2 hours
  - Eddleston
    - Trend for decreased mortality in early subgroup
    - Enhanced monitoring, vigilance, new protocols
    - Paraquat excluded
- Underpowered for consensus “window” of 1 hr
  - Clinically, but not statistically, significant
  - Failure to show benefit ≠ Absence of benefit
Adverse Events

- Isbister 2004 (4,562 toxic ingestions)
  - Aspiration overall (1.6%)
  - Risk Factors for Aspiration
    - TCAs, Seizures, >24hrs to present, spontaneous emesis and decreased GCS score
Adverse Events

- Dorrington 2003 (878 MDAC pts)
  - Most common ↑Mg and Na
  - No SBO
  - Aspiration Pnuemonitis (0.6%)  
  - No further sequelae
Adverse Events

- Eddleston 2008
  - 2,957 pts w AC and atropine
    - No SBOs, 2 referred for possible acute abdomen
    - All deaths had autopsy
      - No charcoal found in lungs
Conclusion

- No adequately powered trial looking at AC given within AACT/EAPCCT approved “window”
  - Failure to find benefit doesn’t mean there isn’t one
  - Consider as early as possible if no contraindications
    - Opportunity for pre-hospital research ???

- Adverse events are extremely rare even in RPS

- MDAC-Benefit for Select Poisonings in RPS
  - Enhanced Elimination
  - Cardiac Glycosides
  - Organophosphorus Poisonings
THANKS FOR YOUR ATTENTION
REFERENCES


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34. Roberts DM. Pharmacokinetics of digoxin cross-reacting substances in patients with acute yellow oleander (Thevetia peruviana) poisoning, including the effect of activated charcoal. Ther Drug Monit 2006;28: 784–792.

REFERENCES


