Journal Club Synopsis Block 6, Dec 9, 2014 Discussion Leader: Christopher Smelley Mentors: Dr. Denis Mann and Dr. James Olson

### "Activated Charcoal: to give or not to give, that is the question?

#### Scenario:

You are working at the Region's Leader, near the end of your shift. A 54 yo male brought in by EMS. CC: overdose, suicide attempt. He took this "large mug with blue goo in the bottom", not sure how long ago. Patient is awake but confused, grabbing at things that aren't there. Initial Vitals: T 99 HR 143 BP 155/99 Sa  $O_2$  97%. When questioned, patient has a vacuous expression and does not acknowledge your existence. Physical Exam findings are consistent with anticholinergic OD. ie. Large pupils, tachycardia, confusion, decreased bowel sounds. You are concerned that this represents a massive ingestion. The patient is not capable of voluntarily drinking activated charcoal. Does he even need activated charcoal? What are the risks of charcoal treatment? Should you consider intubating patient in order to administer charcoal? Does this completely protect his airway and prevent aspiration? You find the ingestion occurred about 1 hour ago. Does this affect the utility of charcoal?

# Introduction:

Drug overdose can present in many different ways, from mild to massive and has various treatment modalities to include the use of activated charcoal (AC), which is a highly controversial treatment option because of its questionable efficacy and safety. The rationale for using AC is that it works by adsorbing poisons in the gastrointestinal tract, decreasing the extent of absorption of the poison, thereby reducing or preventing systemic toxicity. After reviewing the literature, there are very few recent publications about AC. I performed a PubMed search specifically pertaining to time to administration of AC and aspiration risk for AC to explore evidence to justify the use of AC for a situation as in our clinical scenario above. Ultimately, the articles below were chosen for discussion.

# Article 1:

Incidence of Aspiration Pneumonia in Intubated Patients Receiving Activated Charcoal. Moll J, et al. *The Journal of Emergency Medicine*, Vol. 17, No. 2, pp. 279–283, 1999.

This article was a small retrospective review of intubated patients who then received AC. Objective evidence of infiltrate on chest radiograph during initial 48 h of hospitalization was used to determine the incidence of aspiration pneumonia. Patients with known preexisting pneumonia or with administration of AC before intubation were excluded. There were 64 patients identified. Of those, 50 patients included in the study, overdosed on a large variety of substances, required acute intubation and then received AC. Only two patients of these 50 (4%) with initial negative radiographs developed a new infiltrate after intubation and AC. In our discussions, we did point out that aspiration may not be immediately apparent on chest x-ray and it is difficult to determine with certainty if the two patients that developed infiltrates did not aspirate before being intubated. Overall, even though it was a small study, it did show a low incidence of aspiration pneumonia in the intubated patient, therefore its use should be considered in this patient population.

# Article 2:

Efficacy of Activated Charcoal Administered More Than Four Hours After Acetaminophen Overdose. Spiller HA, et al. *The Journal of Emergency Medicine*, Vol. 30, No. 1, pp. 1–5, 2006.

The objective of this article was to evaluate whether late administration of AC (> 4h postingestion), in addition to standard N-acetylcysteine (NAC) therapy, after acetaminophen overdose provides additional patient benefit over NAC therapy alone. This was a 1-year nonrandomized prospective, multi-center, observational case series, performed at three poison centers and one poison center system. Entrance criteria were all acute acetaminophen overdoses with: 1) an acetaminophen blood concentration determined to be in the toxic range by the Rumack-Matthew nomogram; and 2) all therapies, including NAC and activated charcoal, initiated between 4 and 16 h post-ingestion. There were 145 patients meeting entrance criteria, of whom 58 patients (40%) received NAC only and 87 patients (60%) received NAC and activated charcoal. Overall, 23 patients had elevations of AST or ALT greater than 1000 IU/L, of which 21 patients received NAC only (38% of total NAC only group) and 2 patients received NAC and activated charcoal (2% of total NAC + AC group). Administration of activated charcoal in this series of patients with toxic acetaminophen concentrations treated with NAC was associated with reduced incidence of liver injury. We did discuss that although there was lower incidence of injury, this was not found to be statistically significant. The study also didn't prove any patient benefit vs NAC therapy alone.

#### Article 3:

The Effect of Activated Charcoal on Drug Exposure in Healthy Volunteers: A Meta-Analysis. Jurgens G, et al. *Clinical Pharmacology & Therapeutics* Vol 85; 5. May 2009. 501-505.

The objective of the study was to estimate the effect of AC administered during the first 6 h after drug intake and the effect of drug properties on drug exposure. 64 controlled studies were integrated in a meta-analysis. AC administered 0-5 min after administration of a drug reduced median drug exposure by 88.4%. The effect of AC continued to be statistically significant when administered up to >4 h after drug intake (median reduction in drug exposure 27.4%). The reduction in drug exposure was correlated with the AC/drug ratio, the volume of distribution (Vd) and time to peak concentration. The authors pointed out that in one quarter of the comparisons, a 1 h delay to AC still reduced drug uptake by nearly 62% and in a quarter of the comparisons, a 4 h delay to AC still reduced drug uptake by over 31%. A very interesting feature of their study was an analysis of the reduction in drug absorption plotted against the AC/ drug ratio, which suggested that the optimal dose of AC may be much greater than the conventional 10:1 ratio currently used. As we discussed, earlier administration of AC is more effective at eliminating the drug in question, but this study did demonstrate that AC can still be considered effective up to 4 h after drug ingestion. Our question was "does this clinically matter?"; a question that this study was unable to address. However, are we underdosing AC in our patients? It would be interesting to see a future study using larger doses of AC to correlate a better clinical effect.

#### **Bottom Line:**

We will probably never have all of the evidence we need from prospective randomized controlled trials to definitively guide use of AC for the overdose patient. The latest Position Statement from the American Academy of Clinical Toxicology on single dose AC advises that we not use AC routinely, but does not provide much specific guidance for when it should be considered. We as clinicians must incorporate the risk of aspiration, the potential toxicity of the drug and time of ingestion into our clinical decision. However after reviewing the above articles, there is evidence to administer AC up to 4 h after ingestion or possible later than 4 h in certain circumstances. The literature also indicated that we may need to give more than the traditional 10:1 ratio, even up to 40:1 ratio, charcoal to drug. The patient's mental status and aspiration risk will always be a concern. However this one small study in intubated patients showed a low incidence of aspiration. Overall, I do believe there is enough evidence to justify the use of AC in select overdoses.