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High Dose, Variable Length, N-acetylcysteine (HINAC) Therapy for Late-presenting Acetaminophen Poisoning

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Introduction:

Two previous studies have demonstrated a decreased mortality from 58-80% to 37-52% for patients with late-presenting acetaminophen poisoning who were treated with Prescott's N-acetylcysteine protocol. Since 1998, we have utilized a high dose, intravenous, variable length, N-acetylcysteine (HINAC) regimen for patients with acetaminophen poisoning.

| Regimen | Loading Dose (mg/kg) | Maintenance Dose (mg/kg) |
|---------------|----------------------|--|
| Current study | 140 | 70/1* q4 ^h until AST/ALT decrease |
| Prescott 1979 | 150 | 50/4*, then 100/16* or until recovery from encephalopathy or death |

Objective:

To describe our clinical experience of HINAC therapy for the treatment of late-presenting acetaminophen-poisoned patients.

Methods:

A retrospective, observational chart review of an institutionally approved HINAC protocol from 1998 to 2003 at two toxicology centers for patients with late-presenting acetaminophen poisoning. Inclusion criteria included HINAC administration >24 hours post-ingestion with detectable acetaminophen levels at >24 hours and/or initial transaminases twice the upper limit of normal with history of >8gms of ingested acetaminophen. Patients were excluded by inadequate data, dosing deviation from HINAC protocol >25%, and chronic ingestion (>2 ingestions, separated by >8 hours). Our primary outcome was death; secondary outcomes included liver failure (defined by transaminases >1000 IU/L), King's College criteria for poor prognosis and anaphylactoid reactions. Outcomes were compared to previously published NAC regimens.

| | Median (Range) | n (%) |
|----------------------------------|----------------|----------|
| Age (years) | 31 (1-71) | |
| Pediatric (age <18) | | 15 (20%) |
| Gender, female | | 49 (66%) |
| History of hepatic disease | | 4 (5%) |
| Chronic ethanol abuse | | 18 (24%) |
| Suicidal intent | | 65 (88%) |
| Time to N-acetylcysteine (hours) | 34 (24-88) | |
| N-acetylcysteine doses received | 7 (2-26) | |

Results:

Seventy-four patients met inclusion criteria. Forty-seven had detectable acetaminophen levels with median 80.5 and range 2-516 mcg/ml. Forty-five patients had peak AST >1000 U/L. Median peak AST was 2756 U/L and range 18-23470 U/L. Fourteen patients met at least 1 King's College criteria and there were 5 deaths (2 non-acetaminophen). Four patients had anaphylactoid reactions.

| Description | n (%) | Median (Range) |
|-------------------------------------|-----------|-----------------|
| Initial serum alcohol (mg/dl) | 17 (23%) | 20 (1-592) |
| Peak AST >1000 (U/L) | 45 (61%) | 2756 (15-23470) |
| Peak ALT >1000 (U/L) | 43 (58%) | 3184 (11-17658) |
| *Peak protime >100 (secs) | 2 (2.7%) | 17.7 (11-148) |
| *Peak creatinine >3.3 (mg/dl) | 16 (22%) | 1.1 (0.4-13.7) |
| *Low pH <7.3 | 9 (12.1%) | 7.36 (7.1-7.5) |
| Hypoglycemia during hospitalization | 7 (9.4%) | |
| Peak phosphorus >3.7 (mg/dl) | 16 (22%) | 3.3 (1-8.8) |
| Peak lactate >3.0 (mmol/L) | 19 (26%) | 3.2 (0.9-15.7) |

*King's College criteria for poor prognosis

| | Number of Patients Receiving N-acetylcysteine | Time (hours) to N-acetylcysteine Median (range) | Mortality (n, %) | p-value |
|---------------|---|---|------------------|----------|
| Current study | 75 | 34 (24-88) | *5 (6.7%) | |
| Harrison 1990 | 41 | 17 (10-36) | 15 (36.5%) | p<0.0001 |
| Keays 1991 | 25 | 53 (36-80) | 13 (52%) | p<0.0001 |

*Two of these patients were determined to have non-acetaminophen related mortality secondary to complications from prolonged opioid induced hypotension; one case with extensive ischemic bowel noted during laparotomy, and the second with hypoxic brain injury.

Conclusions:

Patients with late-presenting acetaminophen poisoning who are treated with HINAC have decreased mortality compared to previous studies (p<0.0001).

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