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.

Table 1. Intravenous N-acetylcysteine Regimens

Regimen	Loading Dose (mg/kg)	Maintenance Dose (mg/kg)
Current study	140	70/1° q4°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.

Table 2. Demographics of 74 patients with late-presenting acetaminophen poisoning

	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-acetylcysteins 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.

Table 3. Laboratory values of 74 patients with late-presenting acetaminophen (APAP) poisoning

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

Table 4. Mortality Comparison

	Number of Patients Receiving N-acetylcysteins	Time (hours) to N-acetylcysteine Median (range)	Mortality (n, %)	p-value
Current study	75	34 (24-88)	*5 (6.7%)	
Harrision 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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