High-dose, intravenous, 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 APAP 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 APAP poisoning described as a 140 mg/kg loading dose followed by 70 mg/kg every 4 hrs until the transaminases decline.

Objective

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

Methods

A retrospective, observational chart review of an institutionally approved HINAC protocol from 1998 to 2013 at 2 toxicology centers. Inclusion criteria included HINAC administration >24 hrs post-ingestion and/or initial transaminases twice the upper limit of normal with history of >8 gms of ingested APAP. Patients were excluded by inadequate data, dosing deviation from HINAC protocol >25%, and chronic ingestion (>2 ingestions, separated by >8 hrs). Our primary outcome was death; secondary outcomes included liver failure (defined by transaminases >1000 IU/L), King's College laboratory criteria for poor prognosis and anaphylactoid reactions. Outcomes were compared to previously published NAC regimens.

Results

There were 74 patients who presented after 24 hours with median age 31 years (range 1-71). 49 (66%) were female, 18 (24%) had history of chronic ethanol abuse and 4 had history of hepatic disease. 65 (88%) of the ingestions were suicidal and the mean time from ingestion to presentation was 34 hours (range 24-88) with median initial APAP concentration 80.5 mcg/ml (range 2-516). The median number of doses of HINAC received was 7 (range 2-26). 14 patients met at least 1 King's College criteria. There were 5 deaths (2 non-APAP). 4 (0.5%) patients had anaphylactoid reactions. The median number of doses of HINAC received was 7 (range 2-26).

Table 1: Laboratory values

Description	N (%)	Median (Range)
Initial serum APAP (mcg/ml)	47 (3.1)	80.5 (2-516)
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)	51 (22-68)
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		

Discussion

Despite more than half of our patients experiencing hepatotoxicity and presenting later than one of the other studies (Harrison 1990), our patients had significantly decreased mortality. Limitations include retrospective design, potential reviewer bias, multiple chart reviewers and some missing data.

Table 2: NAC Regimens

		Load. dose (mg/kg)	Maint. dose (mg/kg)	Total (mg/kg)	Rx Length (hrs)
Current study	IV	140	70 q4°	420-2030	20-112
Prescott 1979	IV	150	50/4°, then 100/16°	300	20

Table 3: Mortality Comparison

Study	Patients Receiving NAC (N)	Time (hrs) to NAC 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

*2 patients were determined to have non-APAP related mortality secondary to complications from prolonged opioid induced hypotension; one with extensive ischemic bowel noted during laparotomy and the second with hypoxic brain injury

Conclusion

Patients with late-presenting APAP poisoning who are treated with HINAC have decreased mortality compared to previous studies.