

Current Awareness in Clinical Toxicology

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CURRENT AWARENESS PAPERS OF THE MONTH

Efficiency of acidemia correction on intermittent versus continuous hemodialysis in acute methanol poisoning

Zakharov S, Pelclova D, Navratil T, Belacek J, Latta J, Pisar M, Rulisek J, Leps J, Zidek P, Kucera C, Bocek R, Mazur M, Belik Z, Chalupa J, Talafa V, Kodras K, Nalos D, Sedlak C, Senkyrik M, Smid J, Salek T, Roberts DM, Hovda KE. *Clin Toxicol* 2016; online early:

doi: [10.1080/15563650.2016.1250901](https://doi.org/10.1080/15563650.2016.1250901):

Context

Acidemia is a marker of prognosis in methanol poisoning, as well as compounding formate-induced cytotoxicity. Prompt correction of acidemia is a key treatment of methanol toxicity and methods to optimize this are poorly defined.

Objective

We studied the efficiency of acidemia correction by intermittent hemodialysis (IHD) and continuous renal replacement therapy (CRRT) in a mass outbreak of methanol poisoning.

Methods

The study was designed as observational cohort study. The mean time for an increase of 1 mmol/L HCO_3^- , 0.01 unit arterial blood pH, and the total time for correction of HCO_3^- were determined in IHD- and CRRT-treated patients.

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Results

Data were obtained from 18 patients treated with IHD and 13 patients treated with CRRT. At baseline, CRRT group was more acidemic than IHD group (mean arterial pH 6.79 ± 0.10 versus 7.05 ± 0.10 ; $p = 0.001$). No association was found between the rate of acidemia correction and age, weight, serum methanol, lactate, formate, and glucose on admission. The time to HCO_3^- correction correlated with arterial blood pH ($r = -0.511$; $p = 0.003$) and creatinine ($r = 0.415$; $p = 0.020$). There was association between the time to HCO_3^- correction and dialysate/effluent and blood flow rates ($r = -0.738$; $p < 0.001$ and $r = -0.602$; $p < 0.001$, correspondingly).

The mean time for HCO_3^- to increase by 1 mmol/L was 12 ± 2 min for IHD versus 34 ± 8 min for CRRT ($p < 0.001$), and the mean time for arterial blood pH to increase 0.01 was 7 ± 1 mins for IHD versus 11 ± 4 min for CRRT ($p = 0.024$). The mean increase in HCO_3^- was 5.67 ± 0.90 mmol/L/h for IHD versus 2.17 ± 0.74 mmol/L/h for CRRT ($p < 0.001$).

Conclusions

Our study supports the superiority of IHD over CRRT in terms of the rate of acidemia correction.

Full text available from: <http://dx.doi.org/10.1080/15563650.2016.1250901>

Adverse events associated with pediatric exposures to dextromethorphan

Paul IM, Reynolds KM, Kauffman RE, Banner W, Bond GR, Palmer RB, Burnham RI, Green JL. Clin Toxicol 2016; online early:

doi: 10.1080/15563650.2016.1240803:

Study objective

Dextromethorphan is the most common over-the-counter (OTC) antitussive medication. We sought to characterize adverse events associated with dextromethorphan in children <12 years old from a surveillance program of OTC cough/cold medication exposures.

Methods

This is a retrospective case series of oral exposures to dextromethorphan with ≥ 1 adverse event from multiple U.S. sources (National Poison Data System, FDA Adverse Event Reporting System, manufacturer safety reports, news/media, medical literature) reported between 2008 and 2014. An expert panel determined the relationship between exposure and adverse events, estimated dose ingested, intent of exposure, and identified contributing factors to exposure.

Results

1716 cases contained ≥ 1 adverse event deemed at least potentially related to dextromethorphan; 1417 were single product exposures. 773/1417 (55%) involved only one single-ingredient dextromethorphan product (dextromethorphan-only). Among dextromethorphan-only cases, 3% followed ingestion of a therapeutic dose; 78% followed an overdose. 69% involved unsupervised self-administration and 60% occurred in children <4 years old. No deaths or pathologic dysrhythmias occurred. Central nervous system [e.g., ataxia ($N = 420$)] and autonomic symptoms [e.g., tachycardia ($N = 224$)] were the most common adverse events. Flushing and/or urticarial rash occurred in 18.1% of patients. Dystonia occurred in 5.4%.

Conclusions

No fatalities were identified in this multifaceted surveillance program following a dextromethorphan-only ingestion. Adverse events were predominantly associated with overdose, most commonly affecting the central nervous and autonomic systems.

Full text available from: <http://dx.doi.org/10.1080/15563650.2016.1240803>

Clinical effects of unintentional pediatric buprenorphine exposures: experience at a single tertiary care center

Toce MS, Burns MM, O'Donnell KA. Clin Toxicol 2016; online early: doi: 10.1080/15563650.2016.1244337:

Context

Exploratory buprenorphine ingestions in young children have been associated with clinically significant toxicity. However, detailed data on the clinical presentation and management of these patients are lacking. In an attempt to obtain more comprehensive data, we sought to examine a single center cohort of patients with report of buprenorphine exposure and provide descriptive analysis of rates of respiratory depression, time to respiratory depression, interventions, disposition, and outcomes.

Study design

We performed a retrospective cohort study at a single pediatric tertiary care center of children between the age of 6 months and 7 years of age hospitalized between 1 January 2006 and 1 September 2014 with report of buprenorphine or buprenorphine/naloxone exposure. Patients with possible exposure to more than one agent were excluded. We extracted clinical findings, including time to respiratory depression, interventions, and disposition from the medical record.

Results

Eighty-eight patients met the inclusion criteria. Seven patients were excluded. The median age was 24 months [IQR 18–30]. 20 patients (23%) received activated charcoal while 48 (55%) were treated with naloxone. 36 (41%) patients were admitted to the ICU. Observed clinical effects included respiratory depression (83%), oxygen saturation by pulse oximetry (SpO₂) < 93% (28%), depressed mental status (80%), miosis (77%), and emesis (45%). Median time from exposure to respiratory depression was 263 min [IQR 105–486]. The median hospital length of stay was 22 h [IQR 20–26] and was positively associated with estimated exposure dose ($p = 0.002$).

Conclusion

Pediatric patients exposed to buprenorphine are likely to exhibit signs and symptoms of opioid toxicity, including respiratory depression, altered mental status and miosis. Although the majority of patients developed signs of clinical toxicity within 8 h of reported exposure, the optimum duration of monitoring remains unclear.

Full text available from: <http://dx.doi.org/10.1080/15563650.2016.1244337>

Coagulation parameters in copperhead compared to other *Crotalinae* envenomation: secondary analysis of the F(ab')₂ versus Fab antivenom trial

Gerardo CJ, Vissoci JRN, Brown MWJ, Bush SP. Clin Toxicol 2016; online early: doi: 10.1080/15563650.2016.1250275:

Context

Coagulation derangements in copperhead envenomation are considered less severe than other crotaline envenomations, resulting in recommendations to limit both coagulation testing and antivenom treatment. A prospective, blinded, multicenter, randomized clinical trial comparing the effectiveness of F(ab')₂ versus Fab antivenom in crotaline envenomation patients was completed in 2011. We determined the difference between coagulation parameters in copperhead compared to other crotaline envenomations.

Methods

We performed a post hoc analysis comparing the coagulation parameters (platelets and

fibrinogen) prospectively obtained in the aforementioned trial. All the patients received antivenom in one of three treatment arms [$F(ab')_2$ with maintenance, $F(ab')_2$ with placebo maintenance, or Fab with maintenance]. Coagulation parameters were measured at pretreatment baseline, during acute hospitalization, day 5, day 8, and day 15 post-enuvenomation. Mean platelet count and fibrinogen levels for the copperhead and other crotaline groups were compared. The platelet and fibrinogen point estimates with distribution are presented graphically over time.

Results

122 patients were enrolled in the study. There were 22 patients with copperhead envenomation, 93 with other crotaline envenomations, and 7 that could not be definitively determined. The mean age was 42 (SD 20) years. There was a minor pretreatment difference in mean baseline platelet count between the copperhead group ($246 \times 10^9/L$ 95% CI 215, 277) compared to other crotaline envenomation patients ($184 \times 10^9/L$ 95% CI 167, 202). There was a modest pretreatment difference in mean fibrinogen level between copperhead patients (345 mg/dL 95% CI 277, 415) and other crotaline patients (261mg/dL 95% CI 241, 281). Pretreatment coagulation parameter means were normal and converged post treatment.

Conclusion

On average, copperhead envenomations have less severe initial coagulation derangements. However, in mild envenomations, differences in laboratory values are minimal and there is substantial variation in individual patients regardless of species. Species alone should not be used to determine the need for laboratory testing or treatment in crotaline snakebite.

Full text available from: <http://dx.doi.org/10.1080/15563650.2016.1250275>

Can a serum acetaminophen concentration obtained less than 4 hours post-ingestion determine which patients do not require treatment with acetylcysteine?

Yarema MC, Green JP, Sivilotti ML, Johnson DW, Nettel-Aguirre A, Victorino C, Spyker DA, Rumack BH. Clin Toxicol 2016; online early: doi: 10.1080/15563650.2016.1247959:

Context

The interpretation of acetaminophen concentrations obtained prior to 4 hours after an acute, single overdose remains unclear. Patient care decisions in the Emergency Department could be accelerated if such concentrations could reliably exclude the need for treatment.

Objective

To determine the agreement between a serum acetaminophen concentration obtained less than 4 hours after an acute ingestion and the subsequent 4 + hour concentration, and the predictive accuracy of early concentrations for identifying patients with potentially toxic exposures.

Methods

A secondary analysis of patients admitted for acetaminophen poisoning at one of the 34 hospitals in eight Canadian cities from 1980 to 2005. We examined serum acetaminophen concentrations obtained less than 4 hours post-ingestion, and again 4 or more hours post-ingestion. For the diagnostic accuracy analysis, we specified a cutpoint of 100 $\mu g/mL$ ($662 \mu mol/L$) obtained between 2 and 4 hours and a subsequent 4 to 20 hour acetaminophen concentration above the nomogram treatment line of 150 $\mu g/mL$ ($993 \mu mol/L$).

Results

Of 2454 patients identified, 879 (36%) had a subsequent acetaminophen concentration

above the nomogram treatment line. The 2-4 hour concentration demonstrated a sensitivity of 0.96 [95% CI; 0.94, 0.97] and a negative likelihood ratio of 0.070 [0.048, 0.10]. Coingested opioids reduced this sensitivity to 0.91 [0.83, 0.95], and antimuscarinics to 0.86 [0.72, 0.94]. Only very low to undetectable acetaminophen concentrations prior to 4 hours reliably excluded a subsequent concentration over the treatment line.

Conclusions

Applying an acetaminophen concentration cutpoint of 100 µg/mL (662 µmol/L) at 2–4 hours after an acute ingestion as a threshold for repeat testing and/or treatment would occasionally miss potentially toxic exposures. Absorption of acetaminophen is only slightly delayed by coingested opioids or antimuscarinics. Our analysis validates the practice of not retesting when the first post-ingestion acetaminophen concentration is below the lower limit of quantification.

Full text available from: <http://dx.doi.org/10.1080/15563650.2016.1247959>

Circulating acetaminophen metabolites are toxicokinetic biomarkers of acute liver injury

Vliegenthart ADB, Kimmitt RA, Seymour JH, Homer NZ, Clarke JI, Eddleston M, Gray A, Wood DM, Dargan PI, Cooper JG, Antoine DJ, Webb DJ, Lewis SC, Bateman DN, Dear JW. Clin Pharmacol Ther 2016; online early: doi: 10.1002/cpt.541:

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Incidence and clinical course of left ventricular systolic dysfunction in patients with carbon monoxide poisoning

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A review of the carcinogenic potential of glyphosate by four independent expert panels and comparison to the IARC assessment

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