

Current Awareness in Clinical Toxicology

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CURRENT AWARENESS PAPERS OF THE MONTH

Pediatric fatality review of the 2013 National Poison Database System (NPDS): focus on intent

Lowry JA, Fine JS, Calello DP, Marcus SM. Clin Toxicol 2015; online early: doi: 10.3109/15563650.2014.996292:

While rare, pediatric poisoning fatalities represent a unique group of cases with circumstances and substances that often differ significantly from adult poisonings. For the past several years, a team of pediatric toxicologists has reviewed all the fatal pediatric poisonings reported to poison centers nationwide through the National Poison Database System (NPDS) system. This is the fourth consecutive annual review presented in conjunction with the AAPCC Annual Report. The team evaluated poisoning fatality cases for children and teenagers less than 20 years of age that were reported between January and December 2013. In the past, the team only evaluated cases for those less than 18 years of age. While the total numbers we reviewed this year are included for completeness, this commentary will concentrate on those less than 18 years for consistency with prior reports.

Full text available from: <http://dx.doi.org/10.3109/15563650.2014.996292>

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Retained drugs in the gastrointestinal tracts of deceased victims of oral drug overdose

Livshits Z, Sampson BA, Howland MA, Hoffman RS, Nelson LS. Clin Toxicol 2014; online early: doi: 10.3109/15563650.2014.992528:

Context

The extent of non-absorbed drug burden in the GI tract following overdose is unknown. Patients who present with clinical signs of toxicity may not undergo decontamination due to assumption that the drug has already been completely absorbed and because of limited scientific evidence of benefit for routine GI decontamination in poisoned patients.

Objective

The goal of this study was to assess whether people who die of an oral overdose have unabsorbed drug present in the GI tract. The secondary goal was to analyze pharmacologic characteristics of retained drugs when present.

Materials and methods

Retrospective review of autopsy reports from 2008 to 2010, whose cause of death was determined as "intoxication" or "overdose," was performed at the Office of Chief Medical Examiner of the City of New York (OCME NYC). Decedents of all ages were identified via electronic OCME database. Inclusion criteria were as follows: 1) cause of death "intoxication" or "overdose" noted by forensic autopsy, 2) ingestion of a solid drug formulation.

Results

92 out of 1038 autopsies (9%) that met inclusion criteria had documentation of retained pill fragments, granules, paste, sludge, slurry, or whole pills in the GI tract. The most common drugs found were opioids and anticholinergics. Ninety-eight percent (98%) of the retained drugs were either modified-release preparations or drugs known to slow GI transit. Most decedents were dead on arrival; there were twelve in-hospital deaths and eleven patients died in the Emergency Department. Bupropion and venlafaxine were responsible for four deaths in those who received medical care. One person died in the ICU following bupropion ingestion.

Discussion and conclusion

Overdose of an oral drug that either has modified-release properties or slows GI tract motility may result in substantial unabsorbed drug burden remaining in the GI tract.

Full text available from: <http://dx.doi.org/10.3109/15563650.2014.992528>

High-dose hydroxocobalamin administered after H₂S exposure counteracts sulfide-poisoning-induced cardiac depression in sheep

Haouzi P, Chenuel B, Sonobe T. Clin Toxicol 2014; 53: 28-36.

Context

Severe H₂S poisoning leads to death by rapid respiratory and cardiac arrest, the latter can occur within seconds or minutes in severe forms of intoxication.

Objectives

To determine the time course and the nature of H₂S-induced cardiac arrest and the effects of high-dose hydroxocobalamin administered after the end of sulfide exposure.

Materials and methods

NaHS was infused in 16 sedated mechanically ventilated sheep to reach concentrations of H₂S in the blood, which was previously found to lead to cardiac arrest within minutes

following the cessation of H₂S exposure. High-dose hydroxocobalamin (5 g) or saline solution was administered intravenously, 1 min after the cessation of NaHS infusion.

Results

All animals were still alive at the cessation of H₂S exposure. Three animals (18%) presented a cardiac arrest within 90 s and were unable to receive any antidote or vehicle. In the animals that survived long enough to receive either hydroxocobalamin or saline, 71% (5/7) died in the control group by cardiac arrest within 10 min. In all instances, cardiac arrest was the result of a pulseless electrical activity (PEA). In the group that received the antidote, intravenous injection of 5 g of hydroxocobalamin provoked an abrupt increase in blood pressure and blood flow; PEA was prevented in all instances. However, we could not find any evidence for a recovery in oxidative metabolism in the group receiving hydroxocobalamin, as blood lactate remained elevated and even continued to rise after 1 h, despite restored hemodynamics. This, along with an unaltered recovery of H₂S kinetics, suggests that hydroxocobalamin did not act through a mechanism of H₂S trapping.

Conclusion

In this sheep model, there was a high risk for cardiac arrest, by PEA, persisting up to 10 min after H₂S exposure. Very high dose of hydroxocobalamin (5 g), injected very early after the cessation of H₂S exposure, improved cardiac contractility and prevented PEA.

Full text available from: <http://dx.doi.org/10.3109/15563650.2014.990976>

Early administration of isosorbide dinitrate improves survival of cyanide-poisoned rabbits

Lavon O. Clin Toxicol 2015; 53: 22-27.

Context

More effective, rapidly delivered, safer antidotes are needed for cyanide poisoning. Previous study has demonstrated a beneficial effect of isosorbide dinitrate on the survival of cyanide-poisoned mice.

Objective

To evaluate the effectiveness of isosorbide dinitrate compared with that of sodium nitrite in cyanide poisoning.

Materials and methods

A comparative animal study was performed using 18 rabbits, randomized into 3 study groups. Animals were poisoned intravenously with potassium cyanide (1 mg/kg). The first group was not given any further treatment. The second and third groups were treated intravenously 1 min after poisoning with sodium nitrite (6 mg/kg) and isosorbide dinitrate (50 µg/kg), respectively. The primary outcome was short-term survival of up to 30 min. Secondary outcomes included time to death, a clinical score, mean blood pressure, pulse, blood pH, and lactate and methemoglobin levels.

Results

Rabbits treated with isosorbide dinitrate or sodium nitrite survived while only one untreated rabbit survived. Median time to death of the 5 poisoned and untreated animals was 10 min. All the animals collapsed soon after poisoning, exhibiting rapidly disturbed vital signs and developed lactic metabolic acidosis; average peak blood lactate levels were 15.5–19.1 mmol/L at 10 min after poisoning. The treated animals improved gradually with practically full recovery of the clinical scores, vital signs, and blood gas levels. Sodium nitrite administration raised methemoglobin to an average peak of 7.9%, while isosorbide dinitrate did not change methemoglobin levels.

Conclusion

Early administration of isosorbide dinitrate improved the short-term survival of cyanide-poisoned rabbits. Isosorbide dinitrate shows potential as an antidote for cyanide poisoning and may exert its effect using a nitric-oxide-dependent mechanism.

Full text available from: <http://dx.doi.org/10.3109/15563650.2014.990564>

Use of multi-dose activated charcoal in phenytoin toxicity secondary to genetic polymorphism

Chan BSH, Sellors K, Chiew AL, Buckley NA. Clin Toxicol 2015; online early: doi: 10.3109/15563650.2014.998338:

Introduction

Phenytoin is metabolised in the liver by cytochrome (CYP)2C9 and 2C19 enzymes. Due to saturation of enzyme capacity, the elimination half-life is prolonged at supratherapeutic levels. Genetic polymorphisms of CYP2C9 and 2C19 are reasonably common and further prolong the elimination of phenytoin. There are conflicting reports regarding whether multiple-dose activated charcoal (MDAC) significantly increases the clearance of phenytoin in poisoning.

Case report

We present 3 patients with phenytoin toxicity and very slow elimination secondary to reduced CYP enzyme function from genetic polymorphisms. MDAC was used in two patients and led to rapid and large reductions in the measured elimination half-lives. This is contrasted with very prolonged elimination in a third patient who did not receive MDAC.

Conclusion

MDAC may play a role in the management of chronic phenytoin toxicity, especially in those with very slow endogenous elimination secondary to genetic polymorphisms.

Full text available from: <http://dx.doi.org/10.3109/15563650.2014.998338>

Effect of single-dose *Ginkgo biloba* and *Panax ginseng* on driving performance

LaSala GS, McKeever RG, Patel U, Okaneku J, Vearrier D, Greenberg MI. Clin Toxicol 2015; online early: doi: 10.3109/15563650.2014.999159:

Context

Panax ginseng and *Ginkgo biloba* are commonly used herbal supplements in the United States that have been reported to increase alertness and cognitive function.

Objective

The objective of this study was to investigate the effects of these specific herbals on driving performance.

Materials and methods

30 volunteers were tested using the STISIM3[®] Driving Simulator (Systems Technology Inc., Hawthorne, CA, USA) in this double-blind, placebo-controlled study. The subjects were randomized into 3 groups of 10 subjects per group. After 10-min of simulated driving, subjects received either *ginseng* (1200 mg), *Ginkgo* (240 mg), or placebo administered orally. The test herbals and placebo were randomized and administered by a research assistant outside of the study to maintain blinding. One hour following administration of the herbals or placebo, the subjects completed an additional 10-min of simulated driving. Standard driving parameters were studied including reaction time, standard deviation of

lateral positioning, and divided attention. Data collected for the divided attention parameter included time to response and number of correct responses. The data was analyzed with repeated-measures analysis of variance (ANOVA) and Kruskal-Wallis test using SPSS 22 (IBM, Armonk, NY, USA).

Results

There was no difference in reaction time or standard deviation of lateral positioning for both the *ginseng* and *Ginkgo* arms. For the divided attention parameter, the response time in the *Ginkgo* arm decreased from 2.9 to 2.5 s. The *ginseng* arm also decreased from 3.2 to 2.4 s. None of these values were statistically significant when between group differences were analyzed.

Discussion and conclusion

The data suggests there was no statistically significant difference between *ginseng*, *Ginkgo* or placebo on driving performance. We postulate this is due to the relatively small numbers in our study. Further study with a larger sample size may be needed in order to elucidate more fully the effects of *Ginkgo* and *ginseng* on driving ability.

Full text available from: <http://dx.doi.org/10.3109/15563650.2014.999159>

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Carbamate insecticides

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CHEMICAL WARFARE, BIOLOGICAL WARFARE AND RIOT CONTROL AGENTS

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