

Current Awareness in Clinical Toxicology

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CURRENT AWARENESS PAPERS OF THE MONTH

Acetaminophen psi parameter: a useful tool to quantify hepatotoxicity risk in acute acetaminophen overdose

Chomchai S, Chomchai C, Anusornsuwan T. Clin Toxicol 2011; online early: doi: 10.3109/15563650.2011.597031:

Context

The risk of hepatotoxicity secondary to acute acetaminophen overdose is related to serum acetaminophen concentration and lag time from ingestion to N-acetylcysteine (NAC) therapy. Psi (Greek letter ψ) is a toxicokinetic parameter that takes the acetaminophen level at 4 h post-ingestion ([APAP]4 h) and the time-to-initiation of NAC (tNAC) into account and was found to be significantly predictive of hepatotoxicity in Canadian patients with acetaminophen overdose treated with intravenous NAC.

Objective

We report the relationship of psi and hepatotoxicity in a Thai population with acute acetaminophen overdose.

Methods

This is a retrospective study of patients with acute paracetamol overdose during January 2004 to June 2009 at Siriraj Hospital. Patients were treated with the standard 21-h intravenous NAC regimen. Univariate analyses were performed with logistic regression to assess the relationships of psi, [APAP]4 h, and tNAC, and hepatotoxicity.

Results

A total of 127 patients were enrolled. The median (interquartile range; IQR) of [APAP]4 h was 267.8 (196.0-380.0) mg/L. The median (IQR) of tNAC was 8.5 (6.2-12.0) h. Thirteen patients (10.2%) developed hepatotoxicity. Univariate analysis revealed [APAP]4 h, tNAC, and psi as statistically significant predictors of hepatotoxicity

Discussion and conclusion

The psi parameter is a reliable prognostic tool to predict hepatotoxicity secondary to acute acetaminophen overdose treated with intravenous NAC. Our evidence shows that psi may be a

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more superior tool than either acetaminophen level or time-to-initiation of NAC at predicting hepatotoxicity.

Full-text available from: <http://dx.doi.org/10.3109/15563650.2011.597031>

High-dose insulin: a consecutive case series in toxin-induced cardiogenic shock

Holger JS, Stellpflug SJ, Cole JB, Harris CR, Engebretsen KM. Clin Toxicol 2011; online early: doi: 10.3109/15563650.2011.593522:

Context

Cardiovascular medication overdoses can be difficult to treat. Various treatment modalities are currently recommended. Objective. To describe patient outcomes and adverse events of high-dose insulin therapy in consecutive overdose patients in cardiogenic shock after implementation of a high-dose insulin protocol (1–10 U/kg/h, while avoiding or tapering off vasopressors).

Methods

This is an observational consecutive case series of patients identified from a registry. Data were collected by retrospective chart review of patients treated by our toxicology service with this protocol from February 2007 until March 2010.

Results

Twelve patients were treated with high-dose insulin. The mean age was 36.5 years (SD 11.7). Seven patients had pre-existing vasopressor therapy, and all were tapered off vasopressors while on insulin. Two patients experienced pulseless electrical activity cardiac arrest prior to high-dose insulin therapy. Intravenous fat emulsion was given to two patients. The mean maximum insulin infusion rate was 8.35 U/kg/h (mean = 8.35, SD 6.34). The mean duration of insulin infusion was 23.5 h (SD 19.7). The mean duration of glucose infusion post-insulin was 25.2 h (SD 17.7). The primary toxins were β -blocker in five, calcium channel blocker in two, combined β -blocker/calcium channel blocker in two, tricyclic antidepressant in one, and polydrug in 2. Clinical outcomes. Eleven of 12 patients survived. One patient expired 9 h into insulin therapy from cardiac arrest shortly after the insulin was stopped and a vasopressor re-initiated (protocol deviation). Adverse events. Six patients experienced a total of 19 hypoglycemic events. Hypokalemia (defined as < 3.0 mEq/L) developed in eight patients. Adverse sequelae. Necrotic digits occurred in one patient with known clotting disorder after receiving high-dose norepinephrine and INR reversal with fresh frozen plasma prior to insulin therapy. One patient was discharged with mild anoxic injury thought due to pulseless electrical activity arrest prior to insulin therapy. Three of these 12 patients have been previously described in published case reports.

Conclusion

High-dose insulin therapy based on a 1–10 U/kg/h dosing guideline and recommending avoidance of vasopressors appears to be effective in the treatment of toxin-induced cardiogenic shock. Hypoglycemia was the most frequent adverse event, followed by hypokalemia. Adverse events did not lead to adverse sequelae.

Full-text available from: <http://dx.doi.org/10.3109/15563650.2011.593522>

The epidemiology and type of medication errors reported to the National Poisons Information Centre of Ireland

Cassidy N, Duggan E, Williams DJP, Tracey JA. Clin Toxicol 2011; 49: 485-91.

Introduction

Medication errors are widely reported for hospitalised patients, but limited data are available for medication errors that occur in community-based and clinical settings. Epidemiological data from

poisons information centres enable characterisation of trends in medication errors occurring across the healthcare spectrum.

Aim

The objective of this study was to characterise the epidemiology and type of medication errors reported to the National Poisons Information Centre (NPIC) of Ireland.

Methods

A 3-year prospective study on medication errors reported to the NPIC was conducted from 1 January 2007 to 31 December 2009 inclusive. Data on patient demographics, enquiry source, location, pharmaceutical agent(s), type of medication error, and treatment advice were collated from standardised call report forms. Medication errors were categorised as (I) prescribing error (i.e. physician error), (ii) dispensing error (i.e. pharmacy error), and (iii) administration error involving the wrong medication, the wrong dose, wrong route, or the wrong time.

Results

Medication errors were reported for 2348 individuals, representing 9.56% of total enquiries to the NPIC over 3 years. In total, 1220 children and adolescents under 18 years of age and 1128 adults (= 18 years old) experienced a medication error. The majority of enquiries were received from healthcare professionals, but members of the public accounted for 31.3% (n = 736) of enquiries. Most medication errors occurred in a domestic setting (n = 2135), but a small number occurred in healthcare facilities: nursing homes (n = 110, 4.68%), hospitals (n = 53, 2.26%), and general practitioner surgeries (n = 32, 1.36%). In children, medication errors with non-prescription pharmaceuticals predominated (n = 722) and anti-pyretics and non-opioid analgesics, anti-bacterials, and cough and cold preparations were the main pharmaceutical classes involved. Medication errors with prescription medication predominated for adults (n = 866) and the major medication classes included anti-pyretics and non-opioid analgesics, psychoanaleptics, and psychleptic agents. Approximately 97% (n = 2279) of medication errors were as a result of drug administration errors (comprising a double dose [n = 1040], wrong dose [n = 395], wrong medication [n = 597], wrong route [n = 133], and wrong time [n = 110]). Prescribing and dispensing errors accounted for 0.68% (n = 16) and 2.26% (n = 53) of errors, respectively.

Conclusion

Empirical data from poisons information centres facilitate the characterisation of medication errors occurring in the community and across the healthcare spectrum. Poison centre data facilitate the detection of subtle trends in medication errors and can contribute to pharmacovigilance. Collaboration between pharmaceutical manufacturers, consumers, medical, and regulatory communities is needed to advance patient safety and reduce medication errors.

Full-text available from: <http://dx.doi.org/10.3109/15563650.2011.587193>

Acute plant poisoning: analysis of clinical features and circumstances of exposure

Fuchs J, Rauber-Lüthy C, Kupferschmidt H, Kupper J, Kullak-Ublick GA, Ceschi A. Clin Toxicol 2011; online early: doi: 10.3109/15563650.2011.597034:

Introduction

Human contact with potentially toxic plants, which may occur through abuse or by accident or attempted suicide, is frequent and sometimes results in clinically significant toxicity.

Objective

The aim of the present study was to identify which plants may lead to severe poisoning, and to define the clinical relevance of plant toxicity for humans in Switzerland.

Methods

We analyzed 42 193 cases of human plant exposure and 255 acute moderate, severe, and lethal

poisonings, which were reported to the Swiss Toxicological Information Centre between January 1995 and December 2009.

Results

Plant contact was rarely responsible for serious poisonings. Lethal intoxications were extremely rare and were caused by plants with cardiotoxic (*Taxus baccata*) or mitosis-inhibiting (*Colchicum autumnale*) properties.

Conclusions

Most often, plant contact was accidental and patients remained asymptomatic or developed mild symptoms, which fully resolved within a short time.

Full-text available from: <http://dx.doi.org/10.3109/15563650.2011.597034>

Studies on ethylene glycol poisoning: one patient — 154 admissions **Hovda KE, Julsrud J, Øvrebø S, Brørs O, Jacobsen D. Clin Toxicol 2011; 49: 478-84.**

Objective

Fomepizole is the antidote of choice in toxic alcohol poisonings. Potential side effects from frequent use of fomepizole were studied in a patient admitted 154 times with ethylene glycol (EG) poisoning. The intra-individual correlation between the serum-ethylene glycol (serum-EG) and the osmolal gap (OG) EG-kinetics, and other laboratory parameters were also studied.

Methods

Combined pro- and retrospective collection of material from three different hospitals, and results from autopsy.

Results

A 26-year-old female with a dissociative disorder was admitted with EG poisoning a total of 154 times. Her admission data revealed a median pH of 7.31 (range 6.87-7.49), pCO₂: 4.2 kPa (1.2-6.7) (32 mmHg [9-50]), HCO₃⁻: 15 mmol/L (4-26) (15 mEq/L [4-26]), base deficit (BD): 10 mmol/L (-4 to 27) (10 mEq/L [-4 to 27]), serum-creatinine 65 µmol/L (40-133) (0.74 mg/dL [0.45-1.51]), OG 81 mOsm/kgH₂O (25-132), and serum-EG 44 mmol/L (4-112) (250 mg/dL [25-700]). She was treated with fomepizole 99 times, ethanol 60 times (with a combination of both six times), and dialysis 73 times. The correlation between serum-EG and OG was good (r² = 0.76). She was finally found dead outside hospital with an EG blood concentration of 81 mmol/L (506 mg/dL). An autopsy revealed calcium oxalate crystals in the kidneys, slight liver steatosis, and slight edema of the lungs.

Discussion

The frequent use of fomepizole in this young patient was not associated with any detectable side effects; neither on clinical examination and lab screening, nor on the later autopsy. Regarding the sequelae from the repetitive EG-poisoning episodes, her kidney function seemed to normalize after each overdose. She was treated with buffer and antidote without hemodialysis 81 times without complications, supporting the safety of this approach in selected cases.

Full-text available from: <http://dx.doi.org/10.3109/15563650.2011.590140>

Intentional ethylene glycol poisoning increase after media coverage of antifreeze murders

Morgan BW, Geller RJ, Kazzi ZN. West J Med 2011; 12: 296-9.

Abstract and full-text available from: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3117604/>

The pharmacology and toxicology of the synthetic cathinone mephedrone (4-methylmethcathinone)

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Current awareness of piperazines: pharmacology and toxicology

Elliott S. Drug Test Anal 2011; 3: 430-38.

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Clinical experience with and analytical confirmation of "bath salts" and "legal highs" (synthetic cathinones) in the United States

Spiller HA, Ryan ML, Weston RG, Jansen J. Clin Toxicol 2011; 49: 499-505.

Recently, there has been a worldwide rise in the popularity and abuse of synthetic cathinones. In 2009 and 2010, a significant rise in the abuse of a new group of synthetic cathinones was reported in Western Europe. In 2010, the rapid emergence of a new drug of abuse, referred to as bath salts or "legal high," occurred in the USA. The growing number of cases along with the alarming severity of the effects caused by the abuse of these substances prompted significant concern from both healthcare providers and legal authorities. We report the experience of the first 8 months of two regional poison centers after the emergence of a new group of substances of abuse.

Method

This was a retrospective case series of patients reported to two poison centers with exposures to bath salts. Additionally, 15 "product samples" were obtained and analyzed for drug content using GC/MS.

Results

There were 236 patients of which 184 (78%) were male. Age range was 16–64 years (mean 29 years, SD 9.4). All cases were intentional abuse. There were 37 separate "brand" names identified. Clinical effects were primarily neurological and cardiovascular and included: agitation (n = 194), combative behavior (n = 134), tachycardia (n = 132), hallucinations (n = 94), paranoia (n = 86), confusion (n = 83), chest pain (n = 40), myoclonus (n = 45), hypertension (n = 41), mydriasis (n = 31), CPK elevations (n = 22), hypokalemia (n = 10), and blurred vision (n = 7). Severe medical outcomes included death (n = 1), major (n = 8), and moderate (n = 130). Therapies included benzodiazepines (n = 125), antipsychotics (n = 47), and propofol (n = 10). Primary dispositions of patients were: 116 (49%) treated and released from ED, 50 (21%) admitted to critical care, 29 (12%) admitted to psych, and 28 (12%) lost to follow up. Nineteen patients had blood and/or urine analyzed using GC/MS. MDPV was detected in 13 of 17 live patients (range 24–241 ng/mL, mean 58 ng/mL). The four samples with no drug detected, reported last use of bath salts >20 h prior to presentation. Three of five patients had MDPV detected in urine (range 34–1386 ng/mL, mean 856 ng/mL). No mephedrone or methylone was detected in any sample. Quantitative analysis performed on postmortem samples detected MDPV in blood at 170 ng/mL and in urine at 1400 ng/mL. No other synthetic cathinones were detected.

Discussion

This is the first report of MDPV exposures with quantitative blood level confirmation. Clinical effects displayed a sympathomimetic syndrome, including psychotic episodes often requiring sedation, movement disorders, and tachycardia. Within 8 months of their appearance, 16 states had added synthetic cathinones to the controlled substances list as a Schedule I drug.

Conclusion

We report the emergence of a new group of substances of abuse in the USA, known as bath salts,

with quantitative results in 18 patients. State and federal authorities used timely information from poison centers on the bath salt outbreak during investigations to help track the extent of use and the effects occurring from these new drugs. Close collaboration between state authorities and poison centers enhanced a rapid response, including legislation.

Full-text available from: <http://dx.doi.org/10.3109/15563650.2011.590812>

Methadone, cocaine, opiates, and metabolite disposition in umbilical cord and correlations to maternal methadone dose and neonatal outcomes

de Castro A, Jones HE, Johnson RE, Gray TR, Shakleya DM, Huestis MA. *Ther Drug Monit* 2011; 33: 443-52.

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