Prevalence of use and acute toxicity associated with the use of NBOMe drugs

Introduction
The 25X-NBOMe series are N-2-methoxybenzyl analogues of the respective 2C-X substituted phenethylamine and include 25B-(N(BOMe)2, 25B-NBOMe, 25C-NBOMe, 25D-NBOMe, 25E-NBOMe, 25G-NBOMe, 25H-NBOMe, 25I-NBOMe, 25N-NBOMe and 25iP-NBOMe. There are reports of their use as novel psychoactive substances and associated acute toxicity from Europe, the United States and elsewhere over the last five years. This review will discuss the epidemiology of use and pattern of acute toxicity associated with use of these compounds.

Methods
A PubMed search was performed using the search terms 'NBOMe', '25B-N(BOMe)2', '25B-NBOMe', '25C-NBOMe', '25D-NBOMe', '25E-NBOMe', '25G-NBOMe', '25H-NBOMe', '25I-NBOMe', '25N-NBOMe' and '25iP-NBOMe' covering the years 1966–2014. In addition, abstracts from the 2010–2013 congresses of the European Association of Poisons Centres and Clinical Toxicologists and the 2010–2013 North American Congress of Clinical Toxicology were reviewed using these search terms. Further information was obtained from the European Information System and Database on New Drugs co-ordinated by the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA).
Prevalence of use

There are no national or international surveys collecting data on the prevalence of use of NBOMe drugs. The only information on prevalence of use is from two sub-population surveys of individuals who frequent nightclubs. Of 22,289 respondents of the 2013 Global Drugs Survey, 582 (2.6%) had previously used an NBOMe; the most commonly used NBOMe was 25I-NBOMe (442 respondents, 2.0% of whole cohort and 75.9% of those who had used an NBOMe). In a survey of 397 clubbers in London nightclubs in 2013, 11.8% had heard of the NBOMe drugs (compared with 96.0% for mephedrone), and 4.8% had ever used an NBOMe (compared with 76.6% for mephedrone).

Acute toxicity

There were 29 published cases in the literature of acute toxicity associated with the use of an NBOMe: 25I-NBOMe – 23 cases; 25B-NBOMe – 3 cases; 25C-NBOMe – 3 cases. Commonly reported features include tachycardia (96.6%), hypertension (62.0%), agitation/aggression (48.2%), seizures (37.9%) and hyperthermia (27.6%). Five patients were reported to have developed acute kidney injury. There were an additional 25 reports of acute toxicity related to the use of 25I-NBOMe reported to the EMCDDA. The pattern of toxicity in these cases is similar to that seen in the published cases.

NBOMe-related deaths

25I-NBOMe has been detected in eight fatalities; in one of these, 25C-NBOMe was also detected. The role of the NBOMe drugs in these deaths has not been determined in all cases.

Conclusions

Currently, there is evidence suggesting limited use of the NBOMe class of drugs as novel psychoactive substances compared with that of classical recreational drugs and other novel psychoactive substances such as mephedrone.

Full text available from: http://dx.doi.org/10.3109/15563650.2015.1004179

Methylphenidate intoxications in children and adults: exposure circumstances and evidence-based dose threshold for pre-hospital triage


Context

Methylphenidate intoxications mostly have a relatively mild course, although serious complications can occur.

Objective

We aimed to characterize methylphenidate exposures and reassess our current dose threshold for hospital referral (2 mg/kg).

Methods

In a prospective follow-up study, we analysed 364 consecutive methylphenidate exposures that were reported to the Dutch Poisons Information Center. Patients and/or physicians were surveyed by telephone using standardized questionnaires. Three physicians independently scored the observed severity of the intoxication of each patient as 'no/mild' (observation at home) or 'moderate/severe' (hospital referral necessary).

Results

Unintentional exposures (40%) mostly occurred at home involving the patients' own medication or those from a family member. Compared to unintentionally exposed patients,
intentionally exposed patients were exposed to relatively high methylphenidate doses (3.1 vs 1.6 mg/kg), more often used immediate release methylphenidate formulations (62 vs 34%) and more frequently had concomitant exposures (71 vs 17%). Severe symptoms like convulsions or coma were reported only in patients with concomitant exposures. Following exposure to methylphenidate only (i.e. no concomitant exposures), the most commonly reported symptoms were dry mucosa, headache, agitation, sleepiness and tachycardia. Our results show that the reported methylphenidate dose is predictive of the observed severity of the intoxication and can therefore aid in pre-hospital triage.

**Conclusion**

We increased our current dose threshold for hospital referral from 2 to 3 mg/kg. In addition, we will refer patients at lower doses when clinical symptoms indicate the need for hospital referral. Application of this new dose threshold optimizes triage, thereby reducing unnecessary hospital referral and thus costs, without jeopardising patient safety.

Full text available from: [http://dx.doi.org/10.3109/15563650.2015.1004579](http://dx.doi.org/10.3109/15563650.2015.1004579)

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**The epidemiology and characteristics of carbon monoxide poisoning among recreational boaters**


**Introduction**

Carbon monoxide (CO) poisoning has been reported in the setting of recreational boating however, previous research addressing the epidemiology of carbon monoxide-related injury and death in recreational boaters has been limited.

**Materials and methods**

The United States Coast Guard (USCG) Recreational Boating Statistics annual reports for the 10-year period 2002 – 2011 were analyzed to determine the epidemiology and characteristics of carbon monoxide poisoning among recreational boaters in the United States. Regression analysis was performed to determine statistical significance for trend.

**Results**

The mean number of accidents, injuries and deaths per year due to CO exposure on recreational watercrafts was 14.5 (95% CI 12.1-16.9), 30.9 (95% CI 22.4-39.4) and 6.7 (95% CI 4.5-9.0) respectively. Cabin motorboats accounted for 49 accidents, 123 injuries and 29 deaths. California had 24 carbon monoxide-related accidents over the 10-year study period. Regression analysis showed no overall linear trend in the number of carbon monoxide-related boating accidents, injuries, or deaths as an absolute number or as a percent of all boating accidents, injuries or deaths over the study period.

**Discussion**

The majority of carbon monoxide-related boating accidents, injuries and deaths occurred with cabin motorboats. The state with the largest number of carbon monoxide-related accidents over the 10-year study period was California.

**Conclusions**

Carbon monoxide-related accidents involving recreational boating constitute an important and under recognized cause of injury and death in the United States.

Full text available from: [http://dx.doi.org/10.3109/15563650.2014.996571](http://dx.doi.org/10.3109/15563650.2014.996571)
Can AST/ALT ratio indicate recovery after acute paracetamol poisoning?


Context
Paracetamol (acetaminophen or APAP) is the most common pharmaceutical exposure in the US. Elevations in aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels indicate hepatic toxicity. AST and ALT levels rise in similar proportions but later decline at different rates, with AST falling more rapidly than ALT.

Objective
To determine whether the AST/ALT ratio can indicate that a patient has passed the time of peak AST concentration.

Methods
We retrospectively identified cases of patients hospitalized for acute APAP poisoning by querying the pharmacy database of all patients treated with acetylcysteine (NAC) from January 1, 2001 to March 19, 2013. We included all patients with severe APAP poisoning, defined as AST or ALT greater than 1000 IU/L. Patients who were given NAC for other indications, those without APAP poisoning, and those receiving liver transplantation were excluded. We then recorded paired AST and ALT concentrations from each patient's hospital course. We classified each pair as clearly post-peak or not, and calculated the AST/ALT ratio for each pair of values. We compared different thresholds of AST/ALT ratio in increments of 0.1 to find the optimal value that reliably indicated resolving transaminases.

Results
We identified 1820 patients who received NAC during the study period. Of these, 333 received NAC for suspected poisoning by APAP. After excluding patients without severe APAP poisoning, other diagnoses explaining transaminase elevations, and patients who underwent liver transplantation, we had 37 evaluable patients with 343 evaluable pairs of AST and ALT concentrations. An AST/ALT ratio less than or equal to 0.4 was 99% sensitive for identifying patients with resolving transaminases.

Conclusion
An AST/ALT ratio less than or equal to 0.4 following severe hepatoxicity from paracetamol poisoning appears to be highly predictive of recovery in patients treated with NAC. This has potential to be an indicator of safe discontinuation of NAC treatment.

Full text available from: http://dx.doi.org/10.3109/15563650.2015.1006399

Comparison of intermittent and continuous extracorporeal treatments for the enhanced elimination of dabigatran


Context
Severe bleeding associated with dabigatran frequently requires intensive care management. An antidote is currently unavailable and data reporting the effect of dialysis on elimination of dabigatran are encouraging, but limited.

Objective
To report the effect of intermittent hemodialysis (IHD) and continuous renal replacement therapy (CRRT) at enhancing elimination of dabigatran.
**Materials and methods**

Patients were identified by existing collaborative networks. Pre-filter dabigatran plasma concentrations were measured in all patients, and in dialysate of three patients.

**Results**

Seven patients received dialysis, five with active bleeding and two requiring emergent surgery. Five received IHD and two received CRRT. The plasma elimination half-life of dabigatran was 1.5–4.9 h during IHD, and 14.0–27.5 h during CRRT. Mean dabigatran plasma clearance during IHD was 85–169 mL/min in three patients. Time to obtain a subtherapeutic dabigatran concentration depended on the initial concentration, being 8–18 h for IHD in three patients while 4 h was insufficient in a supratherapeutic case. A 38% rebound in dabigatran levels occurred after one case during IHD, and thrombin time increased after IHD in another, but not after 144 h CRRT or 17 h IHD in two others; data were incomplete in three cases. The amount removed during IHD was proportional to the pre-IHD concentration and clearance, but was consistently low at 3.3–17.4 mg in three patients where this was determined. Moderate bleeding occurred while obtaining vascular access in one patient. Two patients died from intracerebral bleeding, and the influence of treatments could not be determined in these cases.

**Discussion and conclusions**

IHD enhanced elimination of dabigatran more efficiently than CRRT, but their net effect remains poorly defined. Dialysis decisions, including modality and duration, must be individualized based on a risk–benefit assessment.

Full text available from: [http://dx.doi.org/10.3109/15563650.2015.1004580](http://dx.doi.org/10.3109/15563650.2015.1004580)

**The pharmacokinetics of sertraline in overdose and the effect of activated charcoal**


Abstract and full text available from: [http://dx.doi.org/10.1111/bcp.12500](http://dx.doi.org/10.1111/bcp.12500)

**Extracorporeal treatment for lithium poisoning: systematic review and recommendations from the EXTRIP Workgroup**


Abstract and full text available from: [http://dx.doi.org/10.2215/CJN.10021014](http://dx.doi.org/10.2215/CJN.10021014)

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**Plastics**


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**Polycyclic aromatic hydrocarbons**


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Propylene glycol


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