

Abuse liability of buprenorphine-naloxone tablets in untreated IV drug users.

Alho H; Sinclair D; Vuori E; Holopainen A. *Drug and Alcohol Dependence* 88(1): 75-78, 2007. (15 refs.)
Buprenorphine (Subutex (R)) is widely abused in Finland. A combination of buprenorphine plus naloxone (Suboxone (R)) has been available since late 2004, permitting a comparison of the abuse of the two products among untreated intravenous (IV) users. A survey was distributed to attendees at a Helsinki needle exchange program over 2-weeks in April, 2005. At least 30% were returned anonymously. Survey variables included: years of prior IV opioid abuse, years of buprenorphine abuse, frequency, dosage, route of administration and reasons for use, concomitant IV abuse of other substances and amount paid on the street for both buprenorphine and buprenorphine + naloxone. Buprenorphine was the most frequently used IV drug for 73% of the respondents. More than 75% said they used IV buprenorphine to self-treat addiction or withdrawal. Most (68%) had tried the buprenorphine + naloxone combination IV, but 80% said they had a "bad" experience. Its street price was less than half that of buprenorphine alone. The buprenorphine + naloxone combination appears to be a feasible tool, along with easier access to addiction treatment, for decreasing IV abuse of buprenorphine. Copyright 2007, Elsevier Science.

Caffeine induces a profound and persistent tachycardia in response to MDMA ("Ecstasy") administration.

McNamara R; Maginn M; Harkin A. *European Journal of Pharmacology* 555(2-3): 194-198, 2007. (16 refs.)

Caffeine promotes hyperthermia and lethality when co-administered with the recreational drug 3,4-methylenedioxymethamphetamine (MDMA, "Ecstasy") to rats. In the present study, co-administration of caffeine (10 mg/kg, s.c.) with MDMA (10 mg/kg, s.c.) induced a profound tachycardic response compared to rats treated with either drug alone. However, neither caffeine (30 μ M) nor MDMA, (1-30 μ M), alone or in combination, affected the electrocardiogram of the isolated heart suggesting that central and sympathomimetic actions, rather than direct actions of

these drugs on the heart, are responsible for the tachycardia. observed in vivo. This is a serious drug interaction, which could have important health consequences for recreational drug users. Copyright 2007, Elsevier Science.

Effects of alcohol and combined marijuana and alcohol use during adolescence on hippocampal volume and asymmetry. (review).

Medina KL; Schweinsburg AD; Cohen-Zion M; Nagel BJ; Tapert SF. *Neurotoxicology and Teratology* 29(1): 141-152, 2007. (129 refs.)

Background: Converging lines of evidence suggest that the hippocampus may be particularly vulnerable to deleterious effects of alcohol and marijuana use, especially during adolescence. The goal of this study was to examine hippocampal volume and asymmetry in adolescent users of alcohol and marijuana. Methods: Participants were adolescent (aged 15-18) alcohol (ALC) users (n=16), marijuana and alcohol (MJ+ALC) users (n=26), and demographically similar controls (n=21). Extensive exclusionary criteria included prenatal toxic exposure, left handedness, and psychiatric and neurologic disorders. Substance use, cognitive, and anatomical measures were collected after at least 2 days of abstinence from all substances. Results: Adolescent ALC users demonstrated a significantly different pattern of hippocampal asymmetry ($p < .05$) and reduced left hippocampal volume ($p < .05$) compared to MJ+ALC users and non-using controls. Increased alcohol abuse/dependence severity was associated with increased right > left ($R > L$) asymmetry and smaller left hippocampal volumes while marijuana abuse/dependence was associated with increased $L > R$ asymmetry and larger left hippocampal volumes. Although MJ+ALC users did not differ from controls in asymmetry, functional relationships with verbal learning were found only among controls, among whom greater right than left hippocampal volume was associated with superior performance ($p < .05$). Conclusions: Aberrations in hippocampal asymmetry and left hippocampal volumes were found for adolescent heavy drinkers. Further, the functional relationship between hippocampal asymmetry and verbal learning was abnormal among adolescent substance users compared

to healthy controls. These findings suggest differential effects of alcohol and combined marijuana and alcohol use on hippocampal morphometry and the relationship between hippocampal asymmetry and verbal learning performance among adolescents. Copyright 2007, Elsevier Science.

In heavy drinkers, fatty acid ethyl esters remain elevated for up to 99 hours.

Borucki K; Dierkes J; Wartberg J; Westphal S; Genz A; Luley C. *Alcoholism: Clinical and Experimental Research* 31(3): 423-427, 2007. (19 refs.)

Background: Both medical and forensic needs require reliable detection of earlier ethanol intake after the disappearance of ethanol from blood. The esters of ethanol with free fatty acids (FAEEs) are candidate markers of this kind. However, it is unknown whether FAEEs can serve as a marker for a single prior ethanol intake. In addition, the period for which FAEEs are elevated is unknown. Therefore, we measured FAEEs in heavy drinkers admitted to detoxification, and in healthy subjects after a drinking experiment. Methods: Blood from 30 heavy drinkers was obtained for up to 5 days during a detoxification period in a psychiatric hospital. In addition, 17 healthy subjects who participated in a drinking experiment and who were abstinent thereafter gave blood during a similar time period for analysis of FAEEs. Fatty acid ethyl esters were measured by gas chromatography-mass spectroscopy. Results: Heavy drinkers had much higher ethanol and FAEEs concentrations than healthy subjects; however, in both groups, FAEEs decreased rapidly during the first day. Only in heavy drinkers, elevated concentrations of FAEEs were observed at days 2 to 4. Concentrations of FAEEs were not associated with serum triglycerides or patients' body mass index. Conclusions: It is concluded that kinetics of FAEEs are different in heavy drinkers compared with healthy subjects and that FAEEs are of limited value for the detection of prior single ethanol intake. Copyright 2007, Research Society on Alcoholism.

Metabolic and genetic factors contributing to alcohol induced effects and fetal alcohol syndrome. (review).

Gemma S; Vichi S; Testai E. *Neuroscience and Biobehavioral Reviews* 31(2): 221-229, 2007. (53 refs.)

Alcohol-related damages on newborns and infants include a wide variety of complications from facial anomalies to neurodevelopmental delay, known as fetal alcohol syndrome (FAS). However, only less than 10% of women drinking alcohol during pregnancy have children with FAS. Understanding the risk

factors increasing the probability for newborn exposed in utero to alcohol to develop FAS is therefore a key issue. The involvement of genetics as a one risk factor in FAS has been suggested by animal models and by molecular epidemiological studies on different populations, bearing allelic variants for those enzymes, such as ADH e CYP2E1, involved in ethanol metabolism. Indeed, one of the major factors determining the peak blood alcohol exposure to the fetus is the metabolic activity of the mother, in addition to placental and fetal metabolism, explaining, at least partially, the risk of FAS. The different rates of ethanol metabolism may be the result of genetic polymorphisms, the most relevant of which have been described in the paper. Copyright 2007, Elsevier Science.

Novel approaches to the diagnosis of fetal alcohol spectrum disorder. (review).

Caprara DL; Nash K; Greenbaum R; Rovet J; Koren G. *Neuroscience and Biobehavioral Reviews* 31(2): 254-260, 2007. (47 refs.)

The diagnosis of fetal alcohol spectrum disorder is a difficult task, especially in cases where clear, physical markers of in utero alcohol exposure are not apparent. Reviewed in the following paper are some older tools for screening alcohol use in pregnancy and present novel approaches to the diagnosis of FASD, including ethanol biomarker development to behavioural phenotyping. Improving current FASD diagnostic methodology through more novel approaches may provide the possibility of earlier and wider diagnosis, allowing intervention and treatment at stages where the advanced effects of alcohol can still be mitigated. Copyright 2007, Elsevier Science.

Postoperative cognitive dysfunction in older patients with a history of alcohol abuse.

Hudetz JA; Iqbal Z; Gandhi SD; Patterson KM; Hyde TF; Reddy DM et al. *Anesthesiology* 106(3): 423-430, 2007. (64 refs.)

Background: Postoperative cognitive dysfunction (POCD) affects a significant number of patients and may have serious consequences for quality of life. Although POCD is most frequent after cardiac surgery, the prevalence of POCD after noncardiac surgery in older patients is also significant. The risk factors for POCD after noncardiac surgery include advanced age and preexisting cognitive impairment. Self-reported alcohol abuse is a risk factor for postoperative delirium, but its significance for long-term POCD has not been investigated. The goal of this study was to determine whether neurocognitive function is impaired after noncardiac surgery during general anesthesia in older patients with a history of

alcohol abuse. Methods: Subjects aged 55 yr and older with self-reported alcohol abuse (n = 28) and age-, sex-, education-matched non-alcoholic controls (n = 28) were tested using a neurocognitive battery before and 2 weeks after elective surgery (n = 28) or a corresponding time interval without surgery (n = 28). Verbal memory, visuospatial memory, and executive functions were assessed. A neurologic examination was performed to exclude subjects with potential cerebrovascular damage. Results: Significant three-way interactions (analysis of variance) for Visual Immediate Recall, Visual Delayed Recall, Semantic Fluency, Phonemic Fluency, and the Color-Word Stroop Test implied that cognitive performance in the alcoholic group decreased after surgery more than it did in the other three groups. Conclusions: The results suggest that a history of alcohol abuse in older patients presents a risk for postoperative cognitive impairment in the domains of visuospatial abilities and executive functions that may have important implications for quality of life and health risks. Copyright 2007, Lippincott, Williams & Wilkins.

Psychotropic analgesic nitrous oxide for alcoholic withdrawal states. (review).

Gillman MA; Lichtigfeld FJ; Young TN. *Cochrane Database of Systemic Reviews* 2: CD005190, 2007. (54 refs.)

Background: Alcoholism is a global problem with 5-10% of the world's population demonstrating alcohol-related diseases. One of the most severe consequences of alcohol dependence is the withdrawal syndrome, for which benzodiazepines are the most popular current treatment. An alternative method to benzodiazepine employs psychotropic analgesic nitrous oxide (PAN). Objectives: To assess the effects of PAN for treating alcohol withdrawal states Search strategy We searched the Cochrane Central Register of Controlled Trials (The Cochrane Library Issue 2, 2005), MEDLINE, EMBASE, CINAHL (all to May 2005). We scanned internet websites, reference lists of relevant articles and abstracts of the international Conferences on Alcoholism. We contacted researchers in the field and industry to identify unpublished trials. No language and publication restrictions. Selection criteria Randomised controlled trials including voluntary participants dependent on alcohol. PAN was compared to oxygen and/or benzodiazepine regimens. Data collection and analysis Two authors independently assessed the methodological quality of the trials and extracted data. Main results Five studies, 212 participants, were included. PAN showed improvement of symptoms (RR 1.35; 95% CI 1.01 to 1.79), of the amount and duration of sedative

medication and of psychomotor function (WMD -8.71; 95% CI -13.71 to -3.71). At one hour post intervention, no significant differences were found for depression (WMD -2.40; 95% CI -8.70 to 3.89) and anxiety (WMD -3.70; 95% CI -10.53 to 3.12). None of the included studies reported any significant adverse effects of any treatment. Authors' conclusions: Results indicate that PAN may be an effective treatment of the mild to moderate alcoholic withdrawal state. The rapidity of the therapeutic effect of PAN therapy coupled with the minimal sedative requirements, may enable patients to enter the psychological treatment phase more quickly than those on sedative regimens, accelerating the patients recovery. Our review does not provide strong evidence due to the small sample sizes of the included trials. Neither does the review indicate any causes for concern that PAN is more harmful than the benzodiazepines. Clinicians wishing to use PAN may initially wish to do so within trial settings. Further high quality trials should be done to confirm these findings and to investigate whether the PAN therapy has fewer adverse effects than other treatments for the alcohol withdrawal states. Studies to investigate the possible cost-effectiveness of PAN by reducing costly hospital admissions and decreasing post administration supervision also need to be performed. Copyright 2007, John Wiley & Sons.

Another 'soberade' on the market: does Outox keep its promise?

Pavlic M; Libiseller K; Grubwieser P; Ulmer H; Sauper T; Rabl W. *Wiener Klinische Wochenschrift* 119(3-4): 104-111, 2007. (33 refs.)

Objective: Several products are being widely promoted for reduction of the concentration of alcohol in the human body. One of these preparations, the fructose soft drink Outox, claims to noticeably increase the alcohol elimination rate (beta 60). Theories to explain this 'fructose effect' are based on the assumption that NAD⁺, the coenzyme for alcohol dehydrogenase, is regenerated faster in the presence of fructose. Method: A randomized double-blind, placebo-controlled cross-over study was performed with 30 volunteers in two drinking sessions each. Under strictly identical conditions, the same amount of alcohol was consumed, followed by the consumption of either 250 ml Outox or 250 ml placebo. Periodical measurements of blood (BAC), breath (BrAC) and urine alcohol concentration (UAC) were performed. Results: Analyses revealed a significant difference (P < 0.0001) between the mean alcohol levels of the Outox and the placebo drinking sessions. The overall mean BAC difference was 0.077 g/l (BAC 0.748 g/l without vs 0.671 g/l with Outox), equivalent to 10.3%.

The mean BrAC difference was 0.045 mg/l (BrAC 0.314 mg/l without vs 0.269 mg/l with Outox), equivalent to 14.3%. Differences were lower for women than for men. A significant difference between the alcohol elimination rates (beta 60) was not found. Conclusions: The results show that the soft drink Outox may decrease the alcohol concentration by about 10%. However, BAC and BrAC differences are rather a consequence of slower gastric absorption of alcohol, because Outox does not increase the alcohol elimination rate. Our study demonstrates that the claim of Outox or other fructose drinks to work as a 'soberade' cannot be proven from a scientific point of view. It should be the task of physicians to warn potential consumers, especially in connection with drinking and driving. Copyright 2007, Springer Wien.

Pharmacologic treatment of acute pediatric methamphetamine toxicity.

Ruha AM; Yarema MC. *Pediatric Emergency Care* 22(12): 782-785, 2006. (12 refs.)

Objective: To report our experience with the use of benzodiazepines and haloperidol for sedation of pediatric patients with acute methamphetamine poisoning. Methods: We performed a retrospective chart review of 18 pediatric patients who were admitted to an intensive care unit for methamphetamine toxicity from January 1997 to October 2004 and treated with benzodiazepines or haloperidol. Clinical features, dose of drug received, and laboratory test results were noted. Adverse effects from the use of haloperidol such as prolonged QTc, dystonic reactions, and torsades de pointes were recorded. Results: Eighteen patients received a benzodiazepine, the dose of which varied depending on the agent used. Twelve patients also received parenteral haloperidol. No complications developed from the use of either haloperidol or benzodiazepines. Conclusions: In this case series of pediatric patients poisoned with methamphetamine, parenteral benzodiazepines and haloperidol were used to control agitation. No serious adverse effects were observed from the use of these agents. Copyright 2006, Lippincott, Williams & Wilkins.

Primary care quality and addiction severity: A prospective cohort study.

Kim TW; Samet JH; Cheng DM; Winter MR; Safran DG; Saitz R. *Health Services Research* 42(2): 755-772, 2007. (45 refs.)

Background. Alcohol and drug use disorders are chronic diseases that require ongoing management of physical, psychiatric, and social consequences. While

specific addiction-focused interventions in primary care are efficacious, the influence of overall primary care quality on addiction outcomes has not been studied. The aim of this study was to prospectively examine if higher primary care quality is associated with lower addiction severity among patients with substance use disorders. Study Population. Subjects with alcohol, cocaine, and/or heroin use disorders who initiated primary care after being discharged from an urban residential detoxification program. Measurements. We used the Primary Care Assessment Survey (PCAS), a well-validated, patient-completed survey that measures defining attributes of primary care named by the Institute of Medicine. Nine summary scales cover two broad areas of primary care quality: the patient-physician relationship (communication, interpersonal treatment, thoroughness of the physical exam, whole-person knowledge, preventive counseling, and trust) and structural/organizational features of care (organizational access, financial access, and visit-based continuity). Each of the three addiction outcomes (alcohol addiction severity (ASI-alc), drug addiction severity (ASI-drug), and any drug or heavy alcohol use) were derived from the Addiction Severity Index and assessed 6-18 months after PCAS administration. Separate longitudinal regression models included a single PCAS scale as the main predictor variable as well as variables known to be associated with addiction outcomes. Main Results. Eight of the nine PCAS scales were associated with lower alcohol addiction severity at follow-up ($p \leq .05$). Two measures of relationship quality (communication and whole-person knowledge of the patient) were associated with the largest decreases in ASI-alc (-0.06). More whole-person knowledge, organizational access, and visit-based continuity predicted lower drug addiction severity (ASI-drug: -0.02). Two PCAS scales (trust and whole-person knowledge of the patient) were associated with lower likelihood of subsequent substance use (adjusted odds ratio, [AOR]=0.76, 95 percent confidence interval [95% CI]=0.60, 0.96 and AOR=0.66, 95 percent CI=0.52, 0.85, respectively). Conclusion. Core features of primary care quality, particularly those reflecting the quality of the physician-patient relationship, were associated with positive addiction outcomes. Our findings suggest that the provision of patient-centered, comprehensive care from a primary care clinician may be an important treatment component for substance use disorders. Copyright 2007, Health Administration Press.