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Articles You Might Have Missed

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Wright R, Anderson J, Adams C, et al. 2011 ACCF/AHA focused update incorporated into the ACC/AHA 2007 guidelines for the management of patients with unstable angina/non-ST-elevation myocardial infarction. Circulation 2011;123:e426-579 (CACP:e535–e537).

Background: Acute chest pain in patients following cocaine use remains an epidemic problem. Cocaine-associated chest pain (CACP) warrants special consideration because cocaine can induce myocardial injury via different pathophysiological mechanisms than coronary artery disease. These new guidelines evaluated existing studies and were developed to update those of McCord et al. (Circulation 2008;117:1897–1907).

Research Question: What guidelines does the literature support for the diagnosis, management, and treatment of unstable angina/non-ST-elevation myocardial infarction related to cocaine abuse?

Methods: Panelists from the American College of Cardiology and American Heart Association reviewed preclinical studies and clinical trials involving cocaine cardiovascular effects prior to and following the 2008 publication in an effort to revise and incorporate relevant new data into existing guidelines. Evidence and recommendations were classified by strength and potential to impact outcome.

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Results: The panelists recommend nitroglycerin and IV or oral calcium channel blockers as first-line therapy for CACP with or without acute coronary syndrome. For patients with CACP and ST elevation that does not resolve with these therapies, the authors recommend acute coronary intervention or systemic fibrinolytic therapy when angiography is not possible. Coronary angiography is recommended in patients with continued chest pain or new ECG changes suggestive of ischemia. Combined alpha- and beta-blocker agents are recommended for hypertension unresponsive to nitroglycerin or a calcium channel blocker. Other recommendations include 24-h observation for CACP patients not requiring acute intervention and calcium channel blocker therapy (verapamil) for tachycardia.

Critique: Why did the guidelines change so much from 2007 AHA position statement? This "update" presents a significant departure from the 2007 management strategy without explanation or substantial new evidence to support this change.

The most glaring change is the omission of benzodiazepines as first-line therapy. In several studies, benzodiazepines have been shown to safely and effectively alleviate chest pain similar to NTG and may have other system benefits as well in cocaine intoxication. The authors also failed to consider phentolamine as treatment for hypertension despite existing clinical trials demonstrating benefit.

The elevation of calcium channel blocking drugs to first line therapy was not substantially supported by the authors. For example, their only clinical reference in support of calcium channel blockers (883) is a study showing benefit of phentolamine. The use of verapamil for tachycardia is unreferenced. Pharmacokinetics were apparently neglected in selecting therapies. Why use long-acting agents like diltiazem/verapamil when there are shorter-acting alternatives that have duration of activity closer to that of cocaine? Finally, the guidelines were

less than comprehensive: omitting important aspects of CACP management such as dysrhythmia management and drug abuse counseling (probably the most important element of long term outcome).
Implications for Toxicologist: This current version of guidelines for treatment of CACP was written with a narrow focus, is poorly referenced, and does not follow the standard of care that most toxicologists would employ. This reiterates the importance of having broad input, such as the inclusion of toxicologists, when crafting guidelines that will affect practitioners across many disciplines.

Larkin G, Beautrais A. A preliminary naturalistic study of low-dose ketamine for depression and suicide ideation in the emergency department. International Journal of Neuropsychopharmacology. 2011;14:1127–1131.

Background: Antidepressant medications have a slow onset of action and do not provide immediate relief of depression and suicidal ideation (SI). Recent reports suggest that ketamine may rapidly (within hours) improve acute depressive symptoms in multiple psychiatric diagnoses.
Research question: What are the effects of low-dose ketamine on depression and suicidality in Emergency Department (ED) patients?
Methods: This was an open-label trial of intravenous ketamine (0.2 mg/kg over 1–2 min) to patients who presented to the ED with a primary complaint of depression with SI and who met DSM-IV criteria for major depressive disorder. Drug effect was assessed by repeated administration of the Montgomery–Asberg Depression Rating Scale (MADRS), which was administered at baseline, several times during the ED observation period (4 h), and daily over the following 10 days. Safety and tolerability were also assessed using the Young Mania Rating Scale and Brief Psychiatric Rating Scale. Primary outcome measures included changes in depression and SI using MADRS assessed with box-plot analysis and repeated measures ANOVA. Time to remission was analyzed using Kaplan–Meier survival analysis.
Results: Volunteers (n=14) had immediate improvement in their depression scores and relief of suicidal ideations during the initial observation period that was sustained for the 10-day follow-up period. The authors report the treatment was tolerated without any ill-effects and only one patient was lost to follow-up.
Conclusion: Administration of ketamine to ED patients experiencing depression and suicidal ideation may be beneficial and warrants further investigation.
Critique: The authors delineated their inclusion and exclusion criteria, treatment protocol, and outcome measures well. Additionally, they included a comprehensive discussion of several limitations. Although methodologically sound, this was not a comparative trial. This preliminary research sets the stage for a future randomized controlled trial of ketamine in a similar subgroup of patients.
Implications for the Toxicologist: Ketamine is a promising acute pharmacologic intervention for depression and suicidal ideation that may serve as a bridge between acute intervention and the onset of action of standard antidepressants. Given the limited psychiatric resources and frequency of suicidal patients evaluated in the ED, this therapy may ultimately lend itself to decreasing SI, hospital length of stay, and return ED visits for SI or overdose.

Buckley N, Juurlink D, Ibister G, Bennett M, Lavonas E. Hyperbaric oxygen for carbon monoxide poisoning. Cochrane Database of Systematic Reviews. 2011;4:1–42.

Background: Carbon monoxide poisoning is a common toxicologic problem worldwide. Mainstays of treatment are focused on prevention of delayed neurologic sequelae. Hyperbaric oxygen remains a highly debated treatment modality.
Research Question: Do randomized control trials demonstrate that hyperbaric oxygen prevents the development of neurologic sequelae from acute carbon monoxide exposure 1 month after treatment?
Methods: This Cochrane review searched multiple electronic databases to identify all randomized control trials involving hyperbaric oxygen (HBO) in nonpregnant adults following CO exposure. Two reviewers extracted data for demographics, treatment received, and presence of neurologic sequelae at follow-up.
Results: Six trials were systematically critiqued for evidence supporting use of HBO. Due to patient heterogeneity, differences in HBO protocols, and varying outcome measures, no clear treatment recommendation could be determined.
Conclusion: There is currently not enough evidence to support the use of HBO as a standard of care for patients poisoned with carbon monoxide.
Critique: Reviews of each study were thorough and objective. The authors appeared to go to great lengths to contact some of the primary authors with questions that arose during their dissection of the studies.
Implications for the Toxicologist: This review provides an excellent summary of the existing clinical research. The conclusion allows for toxicologists to determine local standards of care in the approach to treating carbon monoxide poisoning.

Bebarta V, Maddry J, Borys D, Morgan D. Incidence of tricyclic antidepressant-like complications after cyclobenzaprine overdose. Am J Emerg Med 2011;29(6):645–649.

Background: Cyclobenzaprine has a chemical structure similar to tricyclic antidepressants (TCAs) suggesting a

potential for similar clinical effects as TCAs following overdose.

Research Question: What is the incidence of tricyclic antidepressant-like effects following cyclobenzaprine overdose?

Methods: A retrospective chart review of Texas poison center data from 2005 to 2006 was performed for cyclobenzaprine and amitriptyline overdose in patients 12 years and older, and clinical effects of the two groups compared. Clinical notes were reviewed by a trained abstractor for symptoms, signs, and treatments not coded by the poison information specialist. Ten percent of the charts were then audited by one of the authors for accuracy of data extraction.

Results: Two hundred nine cases of isolated cyclobenzaprine overdoses were evaluated. Of these cases, there were no cases of widened QRS (>100 ms), ventricular dysrhythmia or death. Two patients had seizures unrelated to cyclobenzaprine; one patient with hyponatremia and one with a brain mass. There were 262 amitriptyline overdoses with 11 % having widened QRS or ventricular dysrhythmia and 0.02 % experiencing seizures. Sodium bicarbonate was given to 31 % of patients with amitriptyline overdose but only 0.01 % of the cyclobenzaprine overdoses. Amitriptyline overdose was associated with higher incidence of coma, tachycardia, and need for intubation when compared to the cyclobenzaprine.

Conclusion: Patients with acute intentional cyclobenzaprine overdoses in this case review did not experience QRS widening, ventricular dysrhythmia, seizures or death.

Critique: Overall, this is a well-done study with case and coding review to allow for capture of the most data and a comparison between cyclobenzaprine and amitriptyline overdoses. This is a poison center-based study and limitations include those associated with such studies, such as reporting bias and lack of confirmation of the alleged ingestion.

Implications for the Toxicologist: This study provides evidence that patients with cyclobenzaprine overdoses are likely to experience anticholinergic effects from the medication but do not experience the cardiotoxic or neurotoxic effects traditionally associated with TCAs.

Conflicts of Interest There are no conflicts to declare.