Commentary

Hyperinsulinemia-euglycemia therapy: a useful tool in treating calcium channel blocker poisoning

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See related review by Lheureux *et al*., http://ccforum.com/content/10/3/212

Abstract

Hyperinsulinemia-euglycemia (HIE) therapy, when initiated promptly and aggressively, may offer considerable advantages in the treatment of calcium channel blocker poisoning. Although its mechanism of action is uncertain, HIE improves the efficiency with which the poisoned myocardium uses metabolic fuel, the end result of which is improvements in inotropy and other cardiovascular parameters. Although HIE is not universally accepted, the reports included in the previous issue of *Critical Care* should prompt clinicians to consider HIE an appropriate therapy specifically for calcium channel blocker poisoning.

Interest in a bizarre treatment for calcium channel blocker poisoning, namely hyperinsulinemia-euglycemia (HIE), continues to grow. In the previous issue of *Critical Care*, Lheureux and coworkers [1] review this unusual therapy that was first proposed by medical toxicologists approximately 1 decade ago [2-4]. Clinicians unfamiliar with this treatment modality have been apprehensive about starting patients on HIE, with good reason. A considerable amount of clinical advice on the management of intoxicated patients is delivered via poison control centers; to administer enormous doses of insulin to a hypotensive, bradycardic, hyperglycemic, acidotic patient based on the telephone recommendation of an unknown poison control staff member requires much faith. Hopefully, this review will help critical care clinicians to evaluate HIE therapy on the basis of scientific evidence and eliminate the role of blind faith in the treatment of critically ill patients poisoned with calcium channel blockers.

Why does HIE work? Mechanistic studies have identified, in shock states, a transition from myocardial usage of free fatty acids to glucose as metabolic fuel. Administration of insulin may improve the efficiency of glucose utilization, probably via an indirect mechanism that involves disrupting enzyme kinetics at pyruvate dehydrogenase or possibly another enzyme. The inhibition of lipolysis in lieu of the more efficient substrate glucose may result in improved inotropy, along with enhancement of other cardiovascular parameters, the summation of which is reflected in an improvement in the patient's condition. Irrespective of the mechanism that produces these beneficial changes, it does so rapidly, often within a matter of minutes.

Pitfalls of the therapy nonetheless exist. Currently, most nontoxicologists do not adequately perceive that HIE is directed toward calcium channel poisoning, a clinical entity distinct from diabetic ketoacidosis. Consequently, one major mistake made by clinicians is to titrate from doses used to treat diabetic ketoacidosis to the 1.0 IU/kg per hour needed for calcium channel poisoning. This timid approach is fraught with danger because of the natural history of calcium channel blocker poisoning. Patients may be hypotensive yet appear well perfused, awake, and apparently stable. These findings can mislead physicians to a false sense of security because severely intoxicated patients can suddenly descend into cardiovascular collapse, the abruptness of which the uninitiated simply would not believe. HIE therapy is necessarily aggressive because of the dramatic changes observed in severely intoxicated patients. An additional pitfall is that HIE improves only inotropy, blood pressure, and other hemodynamic parameters. For clinicians intending to treat complete heart block, HIE will produce disappointing results.

For these and other reasons, HIE has not met with universal acceptance, even among medical toxicologists. Some clinicians correctly point out that its efficacy has never been rigorously established; they cite nearly as many cases of HIE failure published in the literature as reported successes. A closer examination may reveal that HIE was simply started too late to be effective, and it may be unfair to deride HIE as

HIE = hyperinsulinemia-euglycemia.

failing if the therapy was administered, for example, at the end of cardiopulmonary resuscitation. After all, when the myocardium dies, along with the body surrounding it, few if any therapies are likely to satisfy any true measure of effectiveness. It may also be that some patients are simply beyond recovery for any combination of therapies, even those that include HIE. Unfortunately, these questions are answered best by comparative clinical studies.

So, are we likely to ever see a clinical trial to ascertain the effectiveness of HIE therapy for the treatment of calcium channel blocker poisoning in humans? It may be difficult. Although calcium channel blocker poisoning is a common cause of pharmaceutical overdose death in the USA, the numbers are still nonetheless low. Clinical trials would necessarily be multicenter, unfunded, and unlikely. Until then, Lheureux and colleagues [1] have done us a considerable service with this well conceived and thoroughly researched review. Although medical toxicologists have championed HIE for some time, they have been largely unable to get this unique therapy accepted clinically. Perhaps this excellent review will popularize it.

Competing interests

The authors declare that they have no competing interests.

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