Response to Letter to the Editor on Article: Stellpflug SJ, Fritzlar SJ, Cole JB, Engebretsen KM, Holger JS. Cardiotoxic Overdose Treated with Intravenous Fat Emulsion and High-dose Insulin in the Setting of Hypertrophic Cardiomyopathy. *J Med Toxicol* 2011; 7(2):151–3

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Thank you for reading our case report and discussion with interest, and for the constructive comments. We agree that in this patient, the lack of clinical improvement during the high-dose insulin (HDI) therapy and the improvement following the intravenous fat emulsion (IFE) therapy makes it likely that this was indeed another case of a patient improving primarily because of the IFE. The conclusion was stated in an intentionally nonspecific way with “The treatment combination...was successful for this patient...” because there were several treatments used simultaneously. This wording was used in an effort to comply with the slight uncertainty of the cause for clinical improvement and also the reviewers' comments during the editing. Although the conclusion is technically correct, we understand that the nonspecific nature of it likely underestimates the effect of the IFE treatment for the reader. The comments elsewhere in the manuscript certainly do not contradict the conclusion; they are just more specific.

It is true that many, if not all, IFE case reports demonstrate the effect only following conventional treatments. IFE has historically (in its brief history) been used following conventional treatments, so this is not a surprise. Conventional therapies for

beta blocker and calcium channel blocker overdoses may currently include pressors for some providers, as indicated in your letter to the editor, but we need to clarify that point. Casually mentioning pressors as “conventional” may be interpreted by readers as “correct,” and they should not necessarily be so interpreted. Peripheral vasopressors should likely only be used in the treatment of calcium channel blocker and beta blocker overdoses if other primary therapies (intravenous fluid boluses, calcium, and appropriately dosed high-dose insulin) are unsuccessful. Even at that point, pressors should only be used if there is concern about less than optimal perfusion, especially to the brain, at that point in clinical decision making. The best animal studies available on this topic all indicate that pressors are less effective than high-dose insulin and may actually increase mortality (Kline et al. *J Pharmacol Exp Ther*, 1993; Kerns et al. *Ann Emerg Med*, 1997; Holger et al. *Clin Toxicol*, 2007).

A head-to-head HDI vs. IFE study would be interesting to see, but there are a couple of notable items from your comments on this topic. The first note is that although it would be an interesting study to read, I am not sure that it would be very clinically applicable right now because of how these two treatments are used. HDI is typically used early on in patients such as the one in our case report in an effort to avoid further decline in the clinical status. IFE, on the other hand, is typically used in the setting of cardiac arrest or at a stage of severe clinical decline (this pre-arrest usage is supported by the recent ACMT position statement and a few case reports such as ours). The head-to-head comparison

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would thus be of two different modalities typically used at different points in the treatment course. The second note is that even if a potential head-to-head HDI/IFE study would be clinically useful, this case does not make an argument to complete such a study. As stated in the case discussion, this patient was highly unique in that she had hypertrophic cardiomyopathy (HCM). Based on the clinical status and the

real-time echocardiography, the HDI (or the combination of treatments) likely induced obstructive cardiac pathophysiology. The ineffectiveness of the HDI likely had as much to do with the HCM as anything else in this case. An argument for a head-to-head study should be made based on a patient with normal baseline cardiac function, not a patient such as the one in our report.