Hydroxocobalamin and Sodium Thiosulfate versus Sodium Nitrite and Sodium Thiosulfate in Acute Cyanide Toxicity

To the Editor:

We read with interest the recent study comparing sodium nitrite and hydroxocobalamin with sodium thiosulfate given to both groups. While we commend the authors for performing a comparison between hydroxocobalamin and sodium nitrite, we had a few questions regarding the study design and implementation.

An important consideration with the use of hydroxocobalamin, which is red in color, is its light absorption characteristics. This is especially relevant for laboratory tests that rely on colorimetric measurements. In vivo and in vitro studies have established inferences from hydroxocobalamin with many common assays such as chemistries, hematology, and cooximetry. Therefore, it is unclear that the laboratory results in the hydroxocobalamin group are accurate. While pH, lactate, and bicarbonate were similar in both groups, it is difficult to determine the effect hydroxocobalamin had on these assays.

We also question whether the primary outcome of improvement in mean arterial blood pressure is of appropriate clinical relevance in the setting of cyanide toxicity. While hydroxocobalamin is able to raise the blood pressure in part due to scavenging of nitric oxide, it is unclear what prognostic function an improvement in blood pressure has in cyanide poisoning. Thus, although the hydroxocobalamin group had an earlier improvement in their mean arterial pressure, this may have been due to scavenging of nitric oxide rather than reversal of cyanide poisoning and did not change in outcome when compared to the sodium nitrate group.

Most cases of suspected cyanide poisoning are typically in the setting of fires where the use of nitrites would be contraindicated. Of greater civilian or non-military interest is the comparison between sodium thiosulfate alone and hydroxocobalamin with sodium thiosulfate.

David H. Jang, MD
Lewis S. Nelson, MD
Robert S. Hoffman, MD
New York University
New York City Poison Control Center
New York, NY

Funding and support: By Annals policy, all authors are required to disclose any and all commercial, financial, and other relationships in any way related to the subject of this article that might create any potential conflict of interest. The author has stated that no such relationships exist. See the Manuscript Submission Agreement in this issue for examples of specific conflicts covered by this statement.


In reply:

We appreciate Dr. Jang and his colleagues’ interest and comments on our study. As evidenced by our study that consisted of laboratory values before and after administration of hydroxocobalamin, and in comparison with a control, the addition of hydroxocobalamin did not appear to affect the results. In addition, our measurements for pH, lactate, and bicarbonate are not colorimetric tests. Finally, the references cited by Dr. Jang have also shown that these values are not known to have interference from hydroxocobalamin.

The goal of the study was to demonstrate equivalence of the study drugs for the treatment of cyanide poisoning in our model. As noted in the manuscript, we not only found hydroxocobalamin and sodium thiosulfate to be equivalent to sodium nitrite and sodium thiosulfate in survival, but also demonstrated a significant increase in mean arterial pressure, which may impart a clinical benefit. There are still many theories as to how hydroxocobalamin exerts its effects on mean arterial pressure and we discussed nitric oxide scavenging as a potential positive side effect in the manuscript.

Finally, we feel that given its efficacy in animal models and human case reports/series coupled with its purported lack of side effects, hydroxocobalamin would be an appropriate antidote for all situations of possible cyanide poisoning: military or non-military. Whether it imparts a greater therapeutic advantage than sodium thiosulfate alone is currently being investigated in our lab. In addition, we have also completed a study evaluating hydroxocobalamin alone in cyanide-induced cardiac arrest and found it performed well.