Patrick Ng, MD
University of Colorado Denver
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"Oral Sodium Thiosulfate for Severe Acute Oral Cyanide Exposure"

Cyanide is a readily available and deadly poison, particularly with oral exposure where larger doses can occur before any symptoms develop. Multiple governmental agencies consider oral cyanide poisoning a top chemical threat. When ingested, the cyanide ion is exposed to the acidic conditions of the stomach and is rapidly converted to hydrogen cyanide gas which then enters the systemic circulation and causes toxicity. In significant exposures, the mechanism of detoxifying cyanide in vivo gets overwhelmed. This system requires sulfur and forms the relatively nontoxic byproduct, thiocyanate.

Currently there are no FDA approved antidotes specifically for oral cyanide. An ideal antidote would be one that can be easily administered, safe, stable and be applicable in a mass casualty setting. Further, it would be one that can be given to individuals who may have been exposed and not yet manifesting signs of toxicity or are unsure of exposure. Intravenous antidotes require more resources compared to an oral antidote and are expensive. Previously, we found the combination of oral glycine/oral sodium thiosulfate was effective in improving survival in swine poisoned with oral cyanide. Glycine serves to alkalinize the gastric pH, thus decreasing the formation of HCN. Thiosulfate serves as a sulfur donor to rhodanese; the enzyme involved in the formation of thiocyanate. Though effective, oral glycine is not readily available in the medical setting. Furthermore, a more practical intervention would be a single agent vs a combination product. The efficacy of oral sodium thiosulfate alone has not been thoroughly evaluated. Understanding the efficacy of oral sodium thiosulfate, a more readily available xenobiotic that has been demonstrated to be safe for human use, will build upon the data from our prior experiments and be useful in the development of an oral antidote for oral cyanide poisoning.

We hypothesize oral sodium thiosulfate will safely reduce mortality from oral cyanide exposure in swine and propose to develop this treatment as an oral cyanide countermeasure.

Using an established swine model of oral cyanide poisoning, animals will be given a lethal dose of potassium cyanide via NG tube. Animals will be randomized to receive oral sodium thiosulfate or no treatment. Animals in the treatment group will receive oral sodium thiosulfate via orogastric tube after oral potassium cyanide. Survival at 60 minutes and time to return to spontaneous ventilation will be compared between the two groups.