Enhancing Preparedness for Cyanide Terrorism

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Abstract

Although US governmental agencies consider a cyanide terrorist attack probable, the United States is ill prepared for mass-casualty incidents involving cyanide. This lack of preparedness might be attributed to the pervasive perception among health care providers and administrators of a low probability of mounting an effective response to mass cyanide poisoning. The presumed futility of a response arises in part from the assumption that intervention must occur seconds to minutes after cyanide exposure to be successful. However, data from case series and case reports suggest that a window of time for mounting an effective response to a cyanide attack or other mass-casualty disaster does exist, particularly if food or water contamination (ingestion) is the source of cyanide. To make the most of a window of time for effective intervention, preparedness efforts should entail education of emergency responders and health care professionals about cyanide as a primary or secondary toxicant risk and about the recognition and treatment of cyanide poisoning. Parallel progress needs to occur in ensuring local and regional availability of a cyanide antidote. Local and regional stockpiling of cyanide antidotes is necessary, and proactive response coordination among federal, state, and local authorities should be pursued—particularly in view of trends toward multiple concurrent terrorist attacks. The United States currently lacks an antidote with a favorable risk:benefit ratio for administration at the scene of a mass-casualty incident. However, preparedness might be enhanced with the potential introduction of hydroxocobalamin, an antidote used in France for prehospital and in-hospital empiric treatment of cyanide poisoning.

Cyanide as a Terrorist Threat

US governmental agencies including the Centers for Disease Control (CDC) and the Department of Homeland Security consider cyanide a probable chemical terrorism weapon.[1,2] Cyanide is easily obtained, lacks the requirement for special expertise to use, and is capable of causing mass casualties and disruption requiring large quantities of specific resources to address—qualities that make it a potentially effective terrorism weapon.[3] Terrorist use of cyanide could involve release of hydrogen cyanide gas into enclosed spaces such as office buildings or stadiums; liberation of hydrogen cyanide during pyrolysis in a fire or explosion; and introduction of cyanide salts into medications, the food supply, or the water supply. The exposure of several terrorist plots involving cyanide in the past five years suggests its appeal to terrorists.[3] Cyanide has also been used to commit murder, suicide, and attempted genocide and as a weapon of conventional war. In view of the possibility of a cyanide terrorism attack, the CDC, acting on recommendations from a joint Department of Health and Human Services and International Association of Fire Chiefs conference, advocated the forward deployment of cyanide antidote kits by emergency medical services (EMS) agencies in 2003.

Lack of Preparedness for a Cyanide Attack in the United States

The existence of effective cyanide antidotes differentiates cyanide from many other chemical and biological weapons that have no known effective countermeasure. The existence of antidotes and increasing concern about a potential cyanide attack notwithstanding, the United States is poorly prepared for cyanide terrorism. This point is illustrated by the results of two recent studies of stocking of cyanide antidotes in US hospitals. The first study assessed preparedness for chemical terrorist attacks in 1996 and again in 2000 by survey of 21 hospitals in a major US city of approximately 4 million people.[4] During the 5-year span of the study, the federal government markedly increased spending on bioterrorism preparedness with the passage of the 1996 Nunn-Lugar-Domenici Defense Against Weapons of Mass Destruction Act (WMD Act). Across hospitals, the number of cyanide antidote kits stocked was 276 in 1996 and 35 in 2000. The number of hospitals meeting the minimum preparedness criterion of ≥50 cyanide antidote kits in inventory was 2 in 1996 and 0 in 2000. The number of hospitals meeting criteria for decontamination preparedness was 10 in 1996 and 11 in 2000. The authors concluded that, despite an increasing threat of chemical terrorism and increased local funding for bioterrorism preparedness, hospital preparedness did not change between 1996 and 2000. Inadequacy of current preparedness was also demonstrated in a 2005 study of 1065 hospitals in the 50 largest US cities.[5] Of 806 hospitals responding to a survey, only 8 (1%) had ≥50 cyanide kits in inventory. Furthermore, only 18 of the 50 cities (36%) had collective supplies of ≥50 cyanide antidote kits across its hospitals. The authors indicated that antidote supply is insufficient to treat mass exposure in any given community in the majority of these cities.

The lack of preparedness for a cyanide attack might be attributed to the pervasive perception among US health care providers and administrators of a low probability of mounting an effective response to mass cyanide poisoning. As an effective response is presumed futile, efforts at preparedness are not undertaken.

Time to Treatment of Cyanide Poisoning: Implications for Emergency Response and for Stockpiling

The presumed futility of an effective response to mass cyanide poisoning arises in part from the assumption that intervention must occur seconds to minutes after cyanide exposure to be successful. Cyanide can in fact incapacitate and kill very quickly, at a rate dependent on the form, concentration, and route of exposure, by impairing the body's ability to use oxygen to produce energy for sustaining cellular function. Because it progresses quickly and because no diagnostic test can confirm cyanide poisoning in the time required for initiating intervention, cyanide poisoning must be diagnosed presumptively if intervention is to be effective. Rapid recognition and empiric intervention by first responders to the scene of a cyanide attack are crucial to saving lives and reducing morbidity.

While rapid recognition and intervention are paramount, data from case series and case reports suggest that—contrary to widespread belief—a window of time for mounting an effective response to a cyanide attack or other mass-casualty disaster does exist, particularly if poisoning occurs by ingestion.[6-9] In one study, patients with a diagnosis of cyanide poisoning (excluding that arising from smoke inhalation) from 1988 to 1999 in the Fernand Widal and Lariboisiere Hospitals in France were identified through review of medical records.[6] Eleven patients with pure cyanide poisoning, including 10 poisonings by ingestion and 1 by inhalation, were identified (Table 1).[6] All patients received the cyanide antidote hydroxocobalamin and supportive therapy. Seven (7) of the 11 patients survived despite severe poisoning in all cases. Among the 7 who survived, initial blood cyanide concentration ranged from 0.3 to 5.9 mg/L (≥1 mg/L=toxic concentration), and time between cyanide ingestion/inhalation and antidote treatment ranged from 0.7 to 3 hours. Among the 4 who died, initial blood cyanide concentration ranged from 4.0 to 6.9 mg/L, and time between cyanide ingestion/inhalation and antidote treatment ranged from 1.8 to 3 hours.

Successful intervention for cyanide poisoning has also been documented in other cases in which exposure and antidotal intervention were separated by hours.[7-9] For example, a 4-year-old girl who became comatose 9 hours after exposure to cyanide from ingestion of boiled cassava was treated with the cyanide antidotes sodium thiosulfate and sodium nitrite 19 hours after ingestion.[7] The patient recovered normal breathing the day after antidotal treatment and survived with no sequelae. Similar cases have been reported in adults given antidotal treatment ≥1 hour after cyanide ingestion.[8,9] Although these observations do not support definitive conclusions about the window of time for effective intervention, the findings are consistent with the presence of such a window: survival was documented in patients treated with an antidote and supportive care up to 3 hours after ingestion of cyanide.

To make the most of a window of time for effective intervention, preparedness efforts should entail education of emergency responders and health care professionals about cyanide as a primary or secondary toxicant risk and about the recognition of cyanide poisoning. Signs and symptoms of poisoning, while nonspecific, are often manifested instantaneously and dramatically after exposure to moderate to high levels of cyanide, and they can thereby elicit the immediate attention of medical personnel and emergency responders trained to recognize chemical poisoning.

The Need for an Antidote Well-Suited for Prehospital Empiric Use

To capitalize on a window of time for effective intervention for cyanide poisoning, parallel progress needs to occur in ensuring local and regional availability of a cyanide antidote and educating emergency responders and health care providers in the use of the antidote. Local and regional stockpiling of cyanide antidotes is necessary, and proactive response coordination among federal, state, and local authorities should be pursued—particularly in view of trends toward multiple concurrent terrorist attacks. The need for better preparedness on these fronts is considerable. The United States currently lacks an antidote with a favorable risk:benefit ratio for administration on an empiric basis at the scene of a mass-casualty incident. Of several cyanide antidotes available around the world, the Cyanide Antidote Kit is the only one presently sold in the United States.[10] The Cyanide Antidote Kit includes sodium nitrite and thiosulfate, which are administered intravenously, and amyl nitrite (available as pearls), which is administered via a mechanical ventilation device or by gauze sponge for inhalation to stabilize the victim until an intravenous line can be established. Potent vasodilators, sodium nitrite and amyl nitrite can cause severe hypotension leading to shock.[11] In addition, the therapeutic mechanism of the nitrites—neutralization of cyanide by forming methemoglobin—can be dangerous because methemoglobinemia reduces the ability of the blood to carry oxygen.[12-14] Methemoglobinemia is particularly dangerous in the presence of a pre-existing blood oxygenation deficit such as that in smoke-inhalation victims, who often have concurrent carboxyhemoglobinemia because of exposure to carbon monoxide. The additive effects of carboxyhemoglobinemia and methemoglobinemia, both of which reduce the oxygen-carrying capacity of the blood, can be lethal. The Cyanide Antidote Kit is therefore not recommended for smoke-inhalation victims, who often have concurrent cyanide poisoning and carbon monoxide poisoning. The other cyanide antidotes, dicobalt edetate (dicobalt-EDTA) and 4-dimethylaminophenol (4-DMAP), are not used in the United States because of their toxicity. Dicobalt-EDTA can cause severe hypotension, particularly in patients without cyanide poisoning.[10,15] 4-DMAP is associated with severe methemoglobinemia, reticulocytosis, nephrotoxicity, and hemolysis.[10,15]

To help address the need for a cyanide antidote with potential use in terrorist incidents and other situations requiring rapid out-of-hospital intervention, the cyanide antidote hydroxocobalamin is being evaluated for possible introduction in the United States. Hydroxocobalamin was licensed in 1996 in France for the treatment of cyanide poisoning, and it has been administered as empiric prehospital treatment and for the in-hospital treatment of cyanide poisoning from inhalation and ingestion.[9,16-21] A precursor of vitamin B12, hydroxocobalamin neutralizes cyanide by binding it to form vitamin B12.[10] Hydroxocobalamin does not induce methemoglobinemia or cause hemodynamic instability. Its most common side effects are discoloration of urine and mucous membranes and abnormalities in specific laboratory tests.[22-24] These effects, attributed to the red color of the hydroxocobalamin molecule, are transient (lasting 1 to 3 days) and do not appear to reflect clinically meaningful changes. Isolated allergic reactions have been reported after administration of hydroxocobalamin.[25,26] With a risk:benefit ratio offering the potential for prehospital empiric treatment, hydroxocobalamin may help to enhance preparedness for a cyanide attack if it is introduced in the United States.

Conclusions

A cyanide terrorist attack involving mass casualties is not unlikely in the United States. Several issues impinge on efforts to achieve cyanide preparedness (Table 2). While cyanide can kill quickly, cyanide poisoning has been effectively treated with antidotal therapy and supportive care even when hours elapse between cyanide exposure and intervention. Rapid recognition and empiric treatment by first responders are necessary for reducing individual and public health impacts of a cyanide attack.

While adequate preparedness for such an attack appears to be feasible, it has not been achieved. Adequate preparedness would entail making available an antidote that is effective and safe for empiric prehospital use, stockpiling antidotes locally and regionally in hospitals and emergency vehicles, developing plans for rapid distribution and mass dispensing, educating emergency responders and health care professionals in the recognition and management of cyanide poisoning, and raising public awareness of the potential for a cyanide attack and of how to respond.

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Table 1. Summary of Cases of Cyanide Poisoning Treated with Hydroxocobalamin[6]

Patient #	Type of cyanide	Age, y/ sex	Time (h) between ingestion and antidote administration	Blood cyanide concentration, mg/l	Systolic blood pressure, mmHg	Heart rate, bpm	Respiratory rate, breaths per minute	Glasgow Coma Scale score	Outcome
1	KCN	63/ Male	3	6.9	40	72	0	3	Died
2	KCN	38/ Male	2	6.4	40	80	0	3	Died
3	Hg(CN)2	14/ Male	2	5.9	60	140	Not documented	15	Survived
4	CN salt	30/ Female	2	5.3	0	0	0	3	Died
5	KCN	52/ Male	1.7	4.3	160	112	25	15	Survived
6	KCN	28/ Female	1.5	4.2	110	120	8	12	Survived
7	KCN	26/ Male	1.8	4.0	95	110	0	3	Died
8	KCN	32/ Male	0.8	3.4	70	80	Not documented	15	Survived
9	Au(CN)2 -KCN	53/ Female	Unknown	1.2	120	96	Not documented	15	Survived
10	Br-CN	39/ Male	0.7	0.3	130	66	8	15	Survived
11	KCN	44/ Male	3	Not documented	80	120	0	3	Survived

Table 2. Issues Impinging on Efforts at Cyanide Preparedness

▪ Cyanide can kill quickly by impairing the body's ability to utilize oxygen for energy production. ▪ Unlike illness or toxicity caused by many other biological or chemical agents, cyanide poisoning can be effectively treated. ▪ A treatment window for antidotal therapy exists. ▪ Rapid recognition and empiric treatment by first responders are necessary for reducing individual and public health impacts of a cyanide attack. ▪ The United States currently lacks an antidote with a favorable risk:benefit ratio for administration on an empiric basis at the scene of a mass-casualty incident.