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Brief Report

Hydroxocobalamin for severe acute cyanide poisoning by ingestion or inhalation☆

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Abstract This chart review was undertaken to assess efficacy and safety of hydroxocobalamin for acute cyanide poisoning. Hospital records of the Fernand Widal and Lariboisière Hospitals were reviewed for intensive care unit admissions with cyanide poisoning for which hydroxocobalamin was used as first-line treatment from 1988 to 2003. Smoke inhalation cases were excluded. Hydroxocobalamin (5-20 g) was administered to 14 consecutive patients beginning a median 2.1 hours after cyanide ingestion or inhalation. Ten patients (71%) survived and were discharged. Of the 11 patients with blood cyanide exceeding the typically lethal threshold of 100 μmol/L, 7 survived. The most common hydroxocobalamin-attributed adverse events were chromaturia and pink skin discoloration. Severe cyanide poisoning of the nature observed in most patients in this study is frequently fatal. That 71% of patients survived after treatment with hydroxocobalamin suggests that hydroxocobalamin as first-line antidotal therapy is effective and safe in acute cyanide poisoning.

1. Introduction

Treatment of acute cyanide poisoning entails supportive care and administration of an antidote. Because of the rapidly progressive nature of cyanide toxicity, treatment is empiric and ideally administered immediately at the scene of the incident. Of the 4 most commonly available cyanide antidotes (hydroxocobalamin; dicobalt edetate; 4-dimethylaminophenol; and the Cyanide Antidote Kit containing amyl nitrite, sodium nitrite, and sodium thiosulfate), hydroxocobalamin appears to be unique in having a risk-benefit profile that supports its empiric use in both the prehospital and hospital settings [1-5]. The potential for serious adverse effects limits or prevents the use of the other antidotes as prehospital empiric treatment. A natural form of vitamin B_{12}, hydroxocobalamin binds cyanide to form cyanocobalamin (vitamin B_{12}), which is excreted in urine

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[1]. Hydroxocobalamin has not been associated with clinically significant adverse effects with the exception of isolated allergic reactions and transient, asymptomatic elevations in blood pressure [1-6].

The clinical properties of hydroxocobalamin as a cyanide antidote have been documented in studies in fire victims with suspected cyanide poisoning from smoke inhalation [2,3]. Because fire smoke contains numerous toxicants, these patients likely suffered poisoning of multiple concurrent etiologies. Although use of hydroxocobalamin for cases of cyanide poisoning in the absence of other concurrent toxicants has been described in case reports [7-12], its effects in pure cyanide poisoning are less well documented than in fire smoke–associated poisoning. This chart review was undertaken to enhance understanding of the effects of hydroxocobalamin as a first-line antidote in pure cyanide poisoning by assessing its efficacy and safety in patients with acute cyanide toxicity from causes other than inhalation of fire smoke.

2. Methods

This retrospective chart review was conducted at the Fernand Widal and Lariboisière Hospitals in Paris, France. Admission logs for the toxicological intensive care units of the hospitals were reviewed to identify patients with a diagnosis of cyanide poisoning from 1988 (when hydroxocobalamin was first used in these hospitals) through 2003. The Fernand Widal Hospital was the source of data from 1988 to 1998. Because the intensive care unit was transferred from Fernand Widal Hospital to Lariboisière Hospital in 1998, the latter hospital was the source of data from 1999 to 2003. Medical records of these patients were then reviewed. Cases of cyanide poisoning involving inhalation of fire smoke were excluded.

Prehospital and hospital protocols in effect during the study period specified that hydroxocobalamin be administered intravenously as soon as medically feasible at an initial dose of 5 g. The hydroxocobalamin dose could be repeated and/or a second antidote could be used in the event of incomplete or transient response. Hydroxocobalamin was prepared by the central hospital pharmacy of Assistance Publique–Hôpitaux de Paris as a sterile solution of a 5-g dose of hydroxocobalamin 100 mL from 1988 to 1996. Thereafter, the Cyanokit (hydroxocobalamin) marketed by Merck-Santé (Lyon, France) was used. Standard supportive therapy was also given.

Hospital records pertaining to prehospital intervention, the stay in the intensive care unit, and the ensuing hospital stay were reviewed for patients meeting eligibility criteria. Information extracted from hospital records included demographics; circumstances of poisoning; clinical presentation; pretreatment vital signs; antidotal and supportive treatments; and critical laboratory values including blood cyanide concentrations, survival, and pretreatment and posttreatment neurologic status.

Neurologic status was summarized as the Glasgow Coma Scale (GCS) score, which reflects degree of neurologic impairment on the basis of ocular, verbal, and motor responses [13]. Glasgow Coma Scale scores range from 3 to 15, and scores of $\geq$13 to <15, 9 to 12, and $\leq$8 reflect mild, moderate, and severe neurologic impairment, respectively. In cases in which a coma stage instead of a GCS score was reported, the following approximation was used to convert coma stage to a GCS score: coma stage absent or normal consciousness = GCS score 15; coma stage I = GCS 12; coma stage II = GCS score 7; coma stage III = GCS score 5; and coma stage IV = GCS score 3.

Adverse events, defined as any untoward medical occurrences observed within 7 days after hydroxocobalamin administration, were retrospectively collected based on review of the medical files from the intensive care unit (including fire and emergency medical services reports), detailed patient progress notes, and discharge summaries from the intensive care unit. Causality assessments as reported in these documents were summarized. If a causality assessment was missing, the authors retrospectively assigned causality (ie, possibly related or not related to hydroxocobalamin) based on the description of the adverse event.

Data were summarized by patient and, for some variables, for the sample as a whole. No hypothesis testing was undertaken.

The relation of plasma lactate to cyanide concentrations in a subset of this sample was previously described [14]. In the previously described subset [14], clinical and laboratory data were collected before hydroxocobalamin administration and at the same time that a blood specimen was collected for measurement of plasma lactate. In contrast, in the present study, initial clinical and laboratory data were collected at the time of presentation.

3. Results

3.1. Sample

The sample included 14 consecutive patients poisoned with cyanide (12 men, 2 women; median age, 35.2 years) (Table 1). The cause of acute cyanide poisoning was ingestion of a potassium cyanide salt in 10 cases, ingestion of mercuric cyanide in 1 case, ingestion of acetonitrile in 1 case, inhalation of cyanogen bromide in 1 case, and exposure to cyanide from unknown origin in 1 case. Of the 14 poisonings, 12 involved suicide attempts. Six patients reported (at some time during their hospital stay) a medical history of depression. All patients were treated with hydroxocobalamin as first-line antidotal therapy. During the study period, no cyanide-poisoned patient received an antidote other than hydroxocobalamin as first-line treatment.

Table 1 Summary of characteristics of cyanide poisoning at the time of presentation

Patient no.	Age (y)	Sex	Type of cyanide	Circumstances of poisoning	Blood cyanide concentration (μmol/L)	SBP (n = 14)/DBP (n = 11) (mm Hg)	Heart rate (beats per minute)	Respiratory rate, breaths per minute	GCS score
1	25.0	Male	KCN	Ingestion/suicide attempt	125	150/90	100	–	15
2	28.3	Female	KCN	Ingestion/suicide attempt	154	110/60	120	8	12
3	50.9	Male	Suspected cyanide salt	Unknown circumstances	103	0/0	0	0	3
4	26.9	Male	KCN	Ingestion/suicide attempt	150	95/50	110	3	3
5	32.0	Male	KCN	Ingestion/suicide attempt	125	65/–	80	–	15
6	51.6	Male	KCN	Ingestion/suicide attempt	158	200/120	110	25	15
7	38.7	Male	KCN	Ingestion/suicide attempt	238	120/70	90	14	12
8	31.7	Female	KCN	Ingestion/suicide attempt	196	0/0	0	0	3
9	64.0	Male	KCN	Ingestion/suicide attempt	260	50/0	30	–	3
10	38.3	Male	Cyanogen bromide	Inhalation/occupational accident	13	130/80	72	18	15
11	14.8	Male	Mercuric cyanide	Ingestion/suicide attempt	217	100/–	120	–	15
12	43.7	Male	KCN	Ingestion/suicide attempt	–	80/–	120	0	3
13	39.9	Male	Acetonitrile	Ingestion/suicide attempt	170	90/60	80	–	15
14	22.3	Male	KCN	Ingestion/suicide attempt	–	115/80	140	20	15
				Mean (SD)	159 (66.3)	93.2 (53.9)/55.5 (40.1)	83.7 (44.6)	9.8 (9.7)	10 (6)
				Median (range)	156 (13-260)	97.5/60 (0-200/0-120)	95 (0-140)	8 (0-25)	12 (3-15)

KCN indicates potassium cyanide; SBP, systolic blood pressure; DBP, diastolic blood pressure; –, data not available.

3.2. Initial clinical status

Individual values for pretreatment vital signs, respiratory rate, and GCS scores are shown in Table 1. Two patients were found in cardiac arrest; 4, in shock; and 5, with severe neurological impairment (GCS score ≤8). An additional 2 patients went into cardiac arrest during transport (n = 1) or at the hospital (n = 1), and 1 patient went into respiratory arrest at the scene after being found with a respiratory rate of 3 breaths per minute. Mean (SD) blood cyanide concentration among the 12 patients having evaluable pretreatment blood samples was 159 μmol/L (66.3) (median, 156 μmol/L) (Table 1). Blood cyanide concentrations before administration of hydroxocobalamin exceeded the typically lethal threshold of 100 μmol/L (2.6 mg/L) [15] in 11 of the 12 patients with available blood cyanide concentrations.

3.3. Antidotal and supportive therapy

Hydroxocobalamin (total dose, 5 to 20 g) was administered as first-line antidotal therapy beginning a mean of 3.1 hours (SD, 3.2) (median, 2.1 hours [range, 0.3-12]) after cyanide exposure (Table 2). Hydroxocobalamin was administered in both the prehospital setting and at the hospital intensive care unit in 5 patients, only in the prehospital setting in 2 patients, and only in the hospital intensive care unit in 7 patients. Hydroxocobalamin was administered as the only cyanide antidote in 9 patients; other cyanide antidotes were administered in 5 patients (sodium thiosulfate in 4 and both sodium thiosulfate and dicobalt edetate in 1). The patient who had ingested mercuric cyanide was administered dimercaprol (British anti-Lewisite) 200 mg and dimethylsuccinic acid 400 mg for associated mercury poisoning.

Supportive therapy included normobaric oxygen in 11 patients, cardiopulmonary resuscitation in the 2 patients found in cardiac arrest, catecholamines at the scene or upon hospital admission in 8 patients, and mechanical ventilation in 7 patients (Table 2). The most common concomitant medications given on the day of poisoning were plasma substitutes and crystalloid infusion solutions (n = 13), benzodiazepines (ie, diazepam, flunitrazepam, midazolam, oxazepam; n = 8), anesthetics (n = 7), and cardiac therapy (n = 6). The most common concomitant medications given during hospitalization in the intensive care unit (beginning the day after the poisoning) were plasma substitutes and infusion solutions (n = 7), antidiabetes therapy (n = 5), and mineral supplements (n = 5).

3.4. Survival outcomes

Of the 14 patients, 10 (71%) survived and were discharged, and 4 (29%) died in the intensive care unit because of postanoxic injury (Table 3). The mean (SD) time to death was 6.3 days (3.9) (range, 4-12 days). All patients who died were in cardiac or respiratory arrest before they were treated with hydroxocobalamin. Of the 10 surviving patients, 9 had no clinically evident neurologic sequelae, and 1 had postanoxic encephalopathy with memory impairment. This patient first received hydroxocobalamin 12 hours after he was discovered and after he had suffered cardiac arrest leading to anoxic brain damage.

Of the 9 patients administered hydroxocobalamin as sole antidote, 7 survived (1 with neurological sequelae). Pretreatment blood cyanide concentrations in these 7 survivors ranged from 13 to 217 μmol/L (median, 125 μmol/L), and time between initial cyanide exposure and treatment ranged from 1 to 12 hours. Of the 7 patients administered hydroxocobalamin as sole antidote and having a documented blood cyanide concentration greater than 100 μmol/L, 5 survived.

3.5. Adverse events

Adverse events considered possibly to be caused by hydroxocobalamin were reported in 8 of the 14 patients (57%). Adverse events attributed to hydroxocobalamin were chromaturia (red-colored urine; Fig. 1) (n = 5), pink-to-red skin discoloration (n = 3), increase in heart rate (n = 1), and elevated blood pressure (n = 1). (The number of adverse events exceeds the number of patients with adverse events because some patients had multiple adverse events.)

The increase in blood pressure occurred in a patient with very labile blood pressure, ranging from severe hypotension to severe hypertension, during resuscitation. The severe increase in blood pressure reported as an adverse event occurred after the second infusion of hydroxocobalamin. This patient had previously received intravenous atropine, isoproterenol, epinephrine, and a fluid bolus at the scene of the incident.

3.6. Laboratory values

No obvious trends in changes in hematology, coagulation, or clinical chemistry parameters were observed during the 3 days after hospital admission with the exception of a gradual decrease in platelet counts and prothrombin index (Table 4). Changes in clinical laboratory values were consistent with the clinical condition of the patients.

4. Discussion

Efficacy of a cyanide antidote is influenced by numerous factors including the time between cyanide exposure and antidote administration, the environment and context in which cyanide poisoning occurs, the health and medical status of the patient, and the adequacy of supportive measures. In this retrospective chart review, use of hydroxocobalamin as a first-line antidote was associated with survival in 10 of 14 patients (71%), most of whom had severe poisoning from attempted suicide by cyanide ingestion. Blood cyanide concentrations exceeded the typically lethal threshold in 11 of 12 patients with available

Table 2 Summary of cases of cyanide poisoning treated with hydroxocobalamin

Patient no.	Hydroxocobalamin total dose (g)	Time between ingestion/ inhalation and hydroxocobalamin administration (h)	Other antidotes	Supportive therapy			
				Cardiopulmonary resuscitation	Isobaric oxygen	Duration of mechanical ventilation (d)	Catecholamine
1	5	[a]	None	No	No	Not required	Not required
2	10	0.25	Sodium thiosulfate	No	Yes	0.7	Not required
3	10	12	None	Yes	Yes	6	Dobutamine, dopamine, epinephrine
4	20	0.5	None	No	Yes	5	Dopamine, epinephrine on day 2
5	10	3	None	No	Yes	Not required	Dobutamine
6	5	5.5	None	No	No	Not required	Not required
7	10	2.17	Sodium thiosulfate	No	Yes	Not required	Dobutamine, dopamine, epinephrine
8	15	[a]	Sodium thiosulfate, dicobalt edetate	Yes	Yes	4	Dobutamine, epinephrine, norepinephrine
9	10	4[b]	None	No	Yes	12	Epinephrine, isoproterenol hydrochloride
10	5	1.58	None	No	Yes	Not required	Not required
11	5	2[b]	Dimercaprol, dimethylsuccinic acid	No	Yes	Not required	Not required
12	9	1.5	Sodium thiosulfate	No	Yes	2	Dopamine, dobutamine
13	10	4	Sodium thiosulfate	No	Yes	8	Dopamine on day 1
14	5	1	None	No	No	Not required	Not required
Median (range)	10 (5-20)	2.1 (0.25-5.5)					

[a] Data not available.
[b] Estimated time.

Table 3 Survival outcomes in patients with acute cyanide poisoning treated with hydroxocobalamin

Patient no.	Blood cyanide concentration (μmol/L)	Outcome
1	125	Survival
2	154	Survival
3	103	Survival with persistent post-anoxic encephalopathy
4	150	Death (day 5): coma, hemodynamic failure
5	125	Survival
6	158	Survival
7	238	Death (day 4): decerebration
8	196	Death (day 12): refractory shock, coma
9	260	Death (day 12): decerebration
10	13	Survival
11	217	Survival
12	[a]	Survival
13	170	Survival
14	[a]	Survival

[a] Data not available.

cyanide concentrations. Of the 11 patients with blood cyanide exceeding the typically lethal threshold, 7 (64%) survived, and only 1 of these 7 patients had clinically evident neurologic sequelae. These results extend previous case reports of successful use of hydroxocobalamin to treat acute cyanide poisoning [7-12]. The latter reports involved single cases. The current investigation differs from those reports in describing the efficacy and safety of hydroxocobalamin as first-line treatment in 14 consecutive cases of cyanide poisoning that was documented by measurements of blood cyanide concentration in 12 of the 14 patients.

Survival outcomes in this sample, in which 13 of 14 patients had pure cyanide poisoning, are consistent with those in 2 studies of hydroxocobalamin administered to smoke inhalation victims with poisoning by multiple toxicants including cyanide [2,3]. Prehospital administration of hydroxocobalamin for suspected smoke inhalation–associated cyanide poisoning was associated with survival rates of 72% among 69 patients (or 67% among the 42 patients with cyanide poisoning confirmed by blood cyanide concentrations) in a prospective, open-label study conducted in Paris from 1989 to 1994 [2] and 42% among 72 patients with known survival status in a retrospective study of 8 years of experience of the Paris Fire Brigade [3]. Results of the latter study should be interpreted cautiously because cyanide poisoning was not confirmed by measurement of blood cyanide.

Although hydroxocobalamin was developed as antidotal monotherapy, it is sometimes used in conjunction with other cyanide antidotes in the critically ill patient. Administration of multiple antidotes can make it difficult to ascertain the impact of the individual concurrently administered antidotes on clinical status. In the current sample, hydroxocobalamin was administered without another cyanide antidote in 9 patients, 7 of whom survived (1 with neurological sequelae). Median pretreatment blood cyanide concentration in these 7 survivors was 125 μmol/L, and time between initial cyanide exposure and treatment ranged from 1 to 12 hours.

Hydroxocobalamin appears to have been particularly useful in patients treated before the onset of cardiac arrest leading to anoxic brain damage. All 4 patients who died were in cardiac or cardiorespiratory arrest before hydroxocobalamin was administered. This finding underscores the need for rapid intervention. At the same time, however, results of this study support the existence of a window of time for effective intervention for acute cyanide poisoning, particularly in cases of ingestion of cyanide salts. The median time between ingestion or inhalation of cyanide and administration of hydroxocobalamin was 2.1 hours in the sample as a whole, in which 71% of patients survived. One patient with preintervention blood cyanide concentration of 170 μmol/L, a value substantially exceeding the typically lethal threshold, survived when treated with hydroxocobalamin 4 hours after cyanide ingestion. This patient ingested acetonitrile, which causes delayed onset of cyanide poisoning. Delayed onset of cyanide poisoning might explain the lag between ingestion and antidotal treatment in this case. Among the 11 patients with blood cyanide concentrations exceeding 100 μmol/L before antidotal treatment, time

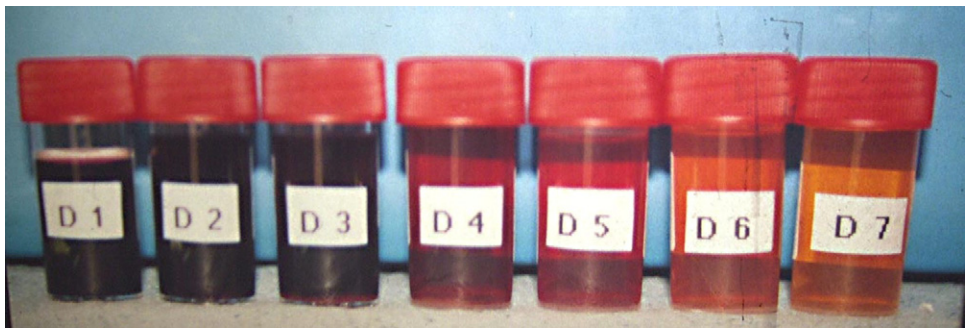

Fig. 1 Discoloration of urine induced by a 10-g dose of hydroxocobalamin in a patient with normal renal function (patient 13). Urine samples from 7 days (day 1 [D1] through 7 [D7]) are shown.

Table 4 Median (range) hematology, clinical chemistry, and coagulation parameters in patients with acute cyanide poisoning treated with hydroxocobalamin

Hospital admission day	0	1	2	3
Hematology and coagulation parameters				
Red blood cell count $\times 10^{12}$/L	n = 10; 4.4 (3.5-5.5)	n = 11; 4.2 (3.6-5.5)	n = 6; 4.0 (3.7-5.5)	n = 2; 4.2 (3.5-4.8)
Hemoglobin (g/dL)	n = 10; 13.3 (10.6-16.8)	n = 11; 12.5 (11.2-16.7)	n = 6; 12.9 (11.5-16.8)	n = 2; 13.2 (11.5-14.8)
Hematocrit (%)	n = 10; 39.6 (33.3-48.6)	n = 11; 36.8 (32.1-47.5)	n = 6; 37.4 (34.1-49.1)	n = 2; 37.7 (33.2-42.1)
Platelets $\times 10^9$/L	n = 10; 259.5 (177.0-311.0)	n = 11; 222.0 (165.0-287.0)	n = 6; 199.0 (145.0-252.0)	n = 2; 174.0 (161.0-187.0)
White blood cell count $\times 10^9$/L	n = 10; 15.4 (3.9-27.1)	n = 11; 15.7 (6.7-29.0)	n = 6; 16.2 (7.0-22.7)	n = 3; 11.5 (9.7-17.2)
Neutrophils (%)	n = 5; 83.4 (60.0-92.3)	n = 7; 86.8 (72.5-93.0)	n = 3; 78.8 (69.4-87.8)	n = 2; 85.6 (85.3-85.8)
Eosinophils (%)	n = 5; 0.0 (0.0-7.0)	n = 7; 0.0 (0.0-0.9)	n = 3; 0.0 (0.0-0.3)	n = 2; 1.2 (0.9-1.4)
Basophils (%)	n = 5; 0.0 (0.0-0.1)	n = 7; 0.0 (0.0-0.2)	n = 3; 0.0 (0.0-0.1)	n = 2; 0.3 (0.0-0.5)
Lymphocytes (%)	n = 5; 10.1 (4.0-20.0)	n = 7; 8.7 (2.0-24.3)	n = 3; 16.1 (5.7-23.1)	n = 2; 8.2 (7.7-8.6)
Monocytes (%)	n = 5; 5.0 (3.6-11.0)	n = 7; 4.4 (2.1-10.0)	n = 3; 6.1 (5.1-7.5)	n = 2; 4.9 (4.6-5.2)
Prothrombin index (%)	n = 12; 81.0 (44.0-100.0)	n = 9; 71.0 (54.0-88.0)	n = 5; 61.0 (48.0-100,0)	n = 4; 61.5 (51.0-74.0)
Clinical chemistry parameters				
Creatinine (μmol/L)	n = 14; 104.0 (49.0-181.0)	n = 11; 82.0 (44.0-171.0)	n = 8; 108.0 (46.0-300.0)	n = 7; 104.0 (62.0-229.0)
Glucose (mmol/L)	n = 12;17.4 (4.7-61.1)	n = 9; 8.5 (5.3-51.5)	n = 7; 9.7 (7.9-11.3)	n = 6; 9.2 (8.1-17.4)
Bilirubin (μmol/L)	n = 10; 9.8 (1.6-94.0)	n = 5; 15.0 (3.0-64.0)	n = 8; 13.3 (4.7-48.0)	n = 2; 27.4 (16.8-38.0)
Alkaline phosphatase (IU/L)	n = 11; 56.0 (31.0-94.0)	n = 7; 55.0 (38.0-73.0)	n = 8; 48.0 (21.0-70.0)	n = 3; 49.0 (42.0-68.0)
Aspartate aminotransferase (IU/L)	n = 12; 23.0 (6.0-274.0)	n = 8; 43.5 (8.0-481.0)	n = 8; 52.0 (13.0-395.0)	n = 3; 42.0 (23.0-53.0)
Alanine aminotransferase (IU/L)	n = 12; 16.5 (5.0-281.0)	n = 8; 25.0 (10.0-217.0)	n = 8; 32.0 (11.0-165.0)	n = 3; 24.0 (14.0-75.0)
Creatine phosphokinase (IU/L)	n = 9; 64.0 (27.0-273.0)	n = 9; 407.0 (153.0-6149.0)	n = 5; 718.0 (245.0-1587.0)	n = 2; 880.0 (648.0-1112.0)
Urea (mmol/L)	n = 14; 4.7 (2.7-7.7)	n = 11; 4.5 (1.3-7.4)	n = 9; 4.3 (2.0-11.0)	n = 6; 9.1 (3.0-13.6)
Total protein (mmol/L)	n = 12; 63.0 (30.0-92.0)	n = 11; 61.0 (55.0-76.0)	n = 9; 59.0 (52.0-69.0)	n = 7; 54.0 (45.0-61.0)
Sodium (mmol/L)	n = 13; 141.0 (133.0-145.0)	n = 11; 140.0 (135.0-147.0)	n = 9; 138.0 (123.0-144.0)	n = 7; 136.0 (119.0-141.0)
Potassium (mmol/L)	n = 13; 3.4 (1.7-4.4)	n = 11; 3.6 (2.8-4.6)	n = 9; 3.8 (2.8-6.2)	n = 7; 3.9 (2.5-7.1)
Chloride (mmol/L)	n = 12; 98.0 (86.0-120.0)	n = 11; 103.0 (95.0-112.0)	n = 9; 101.0 (94.0-113.0)	n = 7; 99.0 (89.0-117.0)
Calcium (mmol/L)	n = 10; 2.0 (0.9-2.4)	n = 10; 2.1 (2.0-2.4)	n = 8; 2.2 (1.7-2.4)	n = 6; 2.0 (1.6-2.2)

between ingestion or inhalation of cyanide and administration of hydroxocobalamin ranged from 0.25 to 12 hours. Seven of these patients survived, 1 with neurologic sequelae. The patient surviving with neurologic sequelae received hydroxocobalamin 12 hours after initial cyanide exposure. Therefore, while cyanide poisoning can rapidly

progress to severe toxicity and death, these cases suggest that even delayed intervention may be helpful in severely poisoned patients. This consideration may be particularly relevant for planning and implementing responses to cyanide terrorist attacks or other mass-casualty disasters.

Given the retrospective nature of the chart review, the safety and tolerability data should be interpreted cautiously. Review of hospital records showed that hydroxocobalamin administration was associated with few clinically significant adverse events. The most common adverse events attributed to hydroxocobalamin were chromaturia and red skin discoloration. These latter events, which were anticipated based on previous experience with hydroxocobalamin [2-4], are attributed to the red color of the compound and are reversible. The chromaturia and skin discoloration typically resolve within 2 to 3 days of hydroxocobalamin administration (Figure 1 for chromaturia). Transient and generally asymptomatic elevations in blood pressure have likewise been reported after hydroxocobalamin administration [4,16].

The clinical laboratory data show no evidence of hydroxocobalamin toxicity. Laboratory findings were compatible with the clinical condition of the patients. The clinical laboratory results should be interpreted carefully: hydroxocobalamin can interfere with some laboratory tests because it has maximum absorption at wavelengths used in many colorimetric assays [17,18]. Hydroxocobalamin-associated interference with clinical laboratory tests generally lasts 2 to 3 days although longer periods of interference have been observed. Urinalysis parameters are also affected [4].

Limitations of this study include its retrospective nature, the lack of a comparison group, and the relatively small, heterogeneous sample. These shortcomings limit the ability to draw definitive conclusions about the data. However, the finding that 71% of patients in this sample survived potentially lethal cyanide poisoning after treatment with hydroxocobalamin suggests that hydroxocobalamin is effective and safe in patients with acute cyanide poisoning from ingestion or inhalation.

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