Value of lactic acidosis in the assessment of the severity of acute cyanide poisoning

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Objective: **To test the hypothesis that plasma lactate concentrations could be of confirmatory value in patients with histories consistent with acute pure cyanide poisoning because immediate laboratory confirmation of suspected cyanide poisoning is rarely possible and because clinicians must rapidly decide whether to administer specific antidotes, which may have severe side effects.**

Design: **Retrospective clinical study.**

Setting: **An intensive care unit in a university-affiliated teaching hospital.**

Patients: **All acute cyanide-poisoned patients admitted to our intensive care unit, excluding fire victims, from 1988 to 1999.**

Interventions: **None.**

Measurements and Main Results: **Eleven patients were studied. Before antidotal treatment, the median plasma lactate concentration was 168 mg/dL, the median blood cyanide concentration was 4.2 mg/L. Using Spearman's test, there was a significant correlation between plasma lactate and blood cyanide concentrations ($r = .74$, $p = .017$). Before antidotal treatment, plasma lactate concentration correlated positively with anion gap and inversely with systolic blood pressure, spontaneous respiratory rate, and arterial pH. During the course of cyanide poisonings, a plasma lactate concentration of ≥72 mg/d/L (8 mmol/L) was sensitive (94%) and moderately specific (70%) for a toxic blood cyanide concentration (≥1.0 mg/L). The specificity was substantially improved in patients not receiving catecholamines (85%).**

Conclusions: **The immediate and serial measurement of plasma lactate concentrations is useful in assessing the severity of cyanide poisoning. (Crit Care Med 2002; 30:2044–2050)**

KEY WORDS: cyanides; lactic acid; acidosis; poisoning; hydroxocobalamin; thiosulfates; pharmacokinetics; sensitivity; specificity; catecholamines; cytochrome-c oxidase; antidotes

The immediate diagnosis of cyanide poisoning remains elusive despite recent improvements in blood cyanide detection methods (1–3). This poses a therapeutic dilemma for the clinician, who must rapidly decide whether to administer specific antidotes, some of which are themselves toxic (4, 5). This situation is further amplified in the case of collective intoxications, in which the clinician must also make triage decisions, as availability of antidotes to cyanide is often limited (6). These difficulties underscore the need for a rapid, readily available surrogate measure of cyanide toxicity.

Cyanide quickly binds to the ferric ion of cytochrome aa_3, inducing a noncompetitive inhibition of the mitochondrial cytochrome-c oxidase activity (7, 8). The inactivation of cytochrome-c oxidase results in a shift of aerobic to anaerobic metabolism, eventually leading to cellular adenosine triphosphate depletion and lactic acidosis (7, 9). It is now well known that the pathophysiology of cyanide poisoning is not limited to disruption of mitochondrial oxidative phosphorylation (10–14). However, due to the shift from aerobic to anaerobic metabolism, significant cyanide poisoning is invariably associated with some degree of lactic acidosis (15–17).

Lactic acidosis has been documented as an important aspect of cyanide poisoning both in rats (9, 18–21) and humans (15, 22). Various cyanide compounds, including hydrocyanic acid, cyanide salts (15, 23), sodium nitroprusside (24), and nitriles (25, 26), may induce lactic acidosis. Furthermore, in burn victims without severe burns, a plasma lactate concentration of >90 mg/dL (10 mmol/L) is a sensitive and specific indicator of cyanide intoxication (27).

However, in pure cyanide poisonings, the correlation between plasma lactate concentrations and the corresponding blood cyanide concentrations has not been addressed (22, 28). In a previous case report, we observed that plasma lactate concentrations were closely related to blood cyanide concentrations (29). Thus, we tested the hypothesis that the repeated measurement of plasma lactate concentrations could have confirmatory and therapeutic value in patients with histories consistent with acute pure cyanide poisoning.

MATERIALS AND METHODS

Patient Selection. We reviewed the charts of the 11 patients admitted to our toxicologic intensive care unit between 1988 and 1999 who had exposures to cyanide confirmed by bystanders. Victims of smoke inhalation were excluded from this study. Ten of these patients had pretreatment blood sampling for cyanide and plasma lactate. Nine of these patients had repeated blood sampling during the course of poisoning. In addition to supportive treatment

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(28, 30), including gastric lavage in cases of ingestion, specific antidotal treatment was administered. Hydroxocobalamin was the initial antidote used in these patients. Sodium thiosulfate was also administered by continuous intravenous infusion at the discretion of the attending physician.

Blood Specimen Collections. Samples were simultaneously collected for blood cyanide and plasma lactate in accordance with our intensive care unit's cyanide treatment guideline. Blood cyanide samples were collected in dry heparin and maintained at 4°C until measurements were made. Plasma lactate specimens were collected in dry heparin, immediately placed on ice, and centrifuged during 4 mins at 3000 rpm at ambient temperature, then immediately measured. Blood specimens were collected before antidotal treatment in ten patients. In four patients (patients 4, 6, 7, and 8), the blood specimens were collected by the first medical team to reach the scene and were brought at ambient temperature to the hospital. The delays between blood sampling and admission to the hospital were 120, 90, 108, and 45 mins, respectively. In the six remaining patients, specimens were collected at hospital admission. Repeat blood samples were collected during the course of poisoning, the frequency depending on the gravity of the intoxication.

Toxicologic Analyses. Blood cyanide concentrations were measured by one of two methods. The colorimetric assay using microdiffusion as previously described by Rieders (31) was employed in patients 1–5 and 8–10. The detection threshold of this method was 0.06 mg/L. Another colorimetric assay using microdiffusion, as described by Laforge et al. (2), was used in patients 6, 7, and 11. The detection threshold of this method was 0.10 mg/L. We assigned a value of zero to samples that had blood cyanide concentrations below the threshold of detection.

Biological Analyses. Plasma lactate concentrations were determined by an enzymatic method (32). The normal range is 9–18 mg/dL (1–2 mmol/L). Arterial blood gases were measured by means of a blood gas analyzer (Radiometer, Copenhagen, Denmark). The anion gap was calculated as $(Na^+ + K^+) - (Cl^- + HCO_3^-)$. The normal range of our laboratory is ≤16 mmol/L.

Data Analysis on Admission. In the ten patients who did not receive hydroxocobalamin before blood collection, we studied the correlations between plasma lactate concentrations and the following variables: blood cyanide concentrations, pulse rate, systolic blood pressure, spontaneous respiratory rate, Glasgow Coma Scale score, arterial pH, $Paco_2$, Pao_2, anion gap, and blood glucose concentration. We also studied the correlations between blood cyanide concentrations and the following variables: pulse rate, systolic blood pressure, spontaneous respiratory rate, Glasgow Coma Scale score, arterial pH, $Paco_2$, Pao_2, anion gap, and blood glucose concentration. The Spearman's rank correlation test was employed. All tests were two-tailed and p values of ≤.05 were considered significant. The results are expressed as median (number of patients, range).

Analysis of Time-Course of Blood Cyanide and Plasma Lactate Concentrations. The kinetics of cyanide and lactate were calculated using Kinetica software (Version 1.1, InnaPhase, Champs-sur-Marne, France). The kinetics of cyanide could be reasonably determined in five patients (patients 1, 3, 4, 6, and 7) and those of plasma lactate in six patients (patients 1, 2, 3, 6, 7, and 11). As we did not know the baseline values of plasma lactate concentrations, we studied only their early decay.

Determination of Toxicodynamic-Toxicokinetic (TK-TD) Relationships of Plasma Lactate and Blood Cyanide Concentrations. The TK-TD relationships were studied using a sigmoidal Emax model according to the following equation (33): $E = Emax \times C^n/[C_{50}^n + C^n] + E_0$, where E denotes the plasma lactate concentration, C the corresponding blood cyanide concentration, E_0 the baseline value of plasma lactate concentration, Emax the difference between the maximal value of plasma lactate concentration reached during the plateau phase and E_0, C_{50} the blood cyanide concentration corresponding to half the Emax, and n the Hill factor. We used Prism 2 software (GraphPad Software, San Diego, CA) for modeling the TK-TD relationship.

Analysis of the Supportive Value of Plasma Lactate Concentrations in Cyanide Poisoning. We evaluated the sensitivity and specificity of the plasma lactate concentrations in relation to potentially toxic blood cyanide concentrations, defined as blood cyanide of ≥1.0 mg/L (27, 34). The sensitivity and specificity of plasma lactate concentrations were calculated step by step from 45 to 90 mg/dL (5 to 10 mmol/L) in each patient, and then the mean sensitivity and specificity were calculated at each value of plasma lactate concentration. The positive and negative predictive values were then calculated for the value of plasma lactate concentration offering the best compromise between sensitivity and specificity. Because it is well known that exogenous catecholamines can increase lactate production (35, 36), we calculated these values after excluding patients who had received a sustained infusion of catecholamines.

RESULTS

Clinical Status at the Time of Presentation. Eleven patients were hospitalized with a history consistent with acute cyanide poisoning. There were eight male patients and three female patients with a median age of 38 yrs (n = 11, 14–63 yrs). Cyanide poisoning resulted from ingestion in ten cases and inhalation in one case (patient 10). Ten of these patients had pretreatment blood sampling for cyanide and plasma lactate. Nine of these patients had repeated blood sampling during the course of poisoning. Table 1 shows the type of poison, the blood cyanide and plasma lactate concentrations, the clinical status at the time of presentation, and the final outcome. Transient seizures were witnessed in two patients (patients 8 and 11). Table 2 shows the arterial blood gases on admission. Table 3 shows the supportive and specific treatments used in these patients.

Plasma Lactate Concentrations at the Time of Presentation Before Antidotal Treatment. A blood specimen was collected before antidotal treatment in ten patients. The median plasma lactate concentration was 168 mg/dL (n = 10, 43–477 mg/dL), and the median blood cyanide concentration was 4.2 mg/L (n = 10, 0.34–6.9 mg/L). The initial blood cyanide concentration in these patients was uniformly the highest value obtained. There was a significant correlation between plasma lactate and blood cyanide concentrations ($r = .74$, $p = .017$) (Fig. 1).

There were significant inverse correlations between plasma lactate concentrations and systolic blood pressure ($r = -.87$, $p < .002$) (Fig. 2), spontaneous respiratory rate ($r = -.87$, $p = .012$), and arterial pH ($r = -.87$, $p < .005$) (Fig. 2). There was a significant positive correlation between plasma lactate concentrations and anion gap ($r = .83$, $p = .008$) (Fig. 2). The correlation with blood glucose concentration did not reach the level of statistical significance ($p = .059$). There was no significant correlation of plasma lactate concentrations with heart rate, Glasgow Coma Scale score, $Paco_2$, or Pao_2.

There were significant inverse correlations of blood cyanide concentrations with systolic blood pressure ($r = -.72$, $p = .023$) (Fig. 3) and arterial pH ($r = -.91$, $p < .002$) (Fig. 3). There was a significant positive correlation with anion gap ($r = .77$, $p = .021$) (Fig. 3) and blood glucose concentration ($r = .78$, $p = .017$). There was no significant correlation of blood cyanide concentration with pulse rate, respiratory rate, Glasgow Coma Scale score, Pao_2, or $Paco_2$.

Time Course of Blood Cyanide and Plasma Lactate Concentrations. Repeat blood samples were collected in nine cases. The median number of measurements per patient was seven (range, 4–10). The median time interval was 2 hrs (range, 0.25–25 hrs). The kinetics of

Table 1. Type of poison, blood cyanide and plasma lactate concentrations, and clinical status at time of presentation and final outcome in 11 cases of acute cyanide poisoning

No.	Type of Cyanide	Sex	Age	Delay, Hrs[a]	Blood Cyanide, mg/L	Plasma Lactate, mg/dL	Systolic Blood Pressure, mm Hg	Heart Rate, beats/min	Respiratory Rate, breaths/min	Glasgow Coma Scale Score	Outcome
1	KCN	M	63	3	6.9	477	40	72	0	3	Fatal
2	KCN	M	38	2	6.4	430	40	80	0	3	Fatal
3	$Hg(CN)_2$	M	14	2	5.9	177	60	140	ND	15	Survival
4	CN salt	F	30	2	5.3	189	0	0	0	3	Fatal
5	KCN	M	52	1.7	4.3	77	160	112	25	15	Survival
6	KCN	F	28	1.5	4.2	122	110	120	8	12	Survival
7	KCN	M	26	1.8	4.0	159	95	110	0	3	Fatal
8	KCN	M	32	0.8	3.4	222	70	80	ND	15	Survival
9	$Au(CN)_2$-KCN	F	53	UK	1.2	43	120	96	ND	15	Survival
10	BrCN[b]	M	39	0.7	0.3	46	130	66	18	15	Survival
11	KCN	M	44	3	ND[c]	ND[c]	80	120	0	3	Survival

KCN, potassium cyanide; $Hg(CN)_2$, mercury cyanide; ND, not determined; CN, cyanide; $Au(CN)_2$, gold cyanide; UK, unknown; BrCN, bromide cyanide. [a]Delay between poisoning and first blood sampling; [b]cyanide poisoning resulted from the inhalation of cyanogen bromide; [c]this patient did not undergo blood sampling before antidotal treatment; cyanide poisoning was subsequently confirmed.

Table 2. Arterial blood gases in 11 cases of acute cyanide poisoning at admission

Patients	Arterial pH	Arterial $Paco_2$, Torr	Arterial Pao_2, Torr	Anion Gap, mmol/L
1	7.16	24.2	446.6	39.0
2	7.22	53.6	84.0	37.5
3	7.33	37.2	131.3	32.4
4	7.24	19.4	513.8	49.8
5	7.36	37.4	102.8	26.4
6	7.27	18.7	169.7	19.3
7	7.38	27.0	491.3	29.3
8	ND	ND	ND	ND
9	7.38	48.0	65.3	21.7
10	7.57	22.8	94.2	21.4
11	ND	ND	ND	ND

ND, not determined.

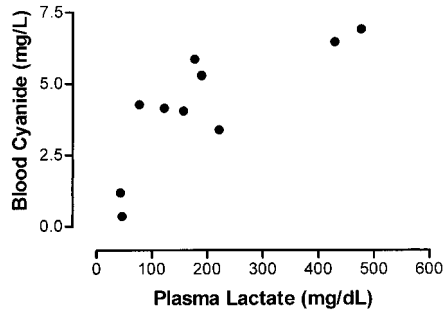


Figure 1. Correlations between blood cyanide and plasma lactate concentrations before antidotal treatment.

Table 3. Supportive and specific treatments in 11 cases of acute cyanide poisoning

Patients	Duration of MV, Days	Catecholamines: Type	Catecholamines: Duration of Infusion, Hrs	Cumulative Dose of HOCo, g	Other Antidotes
1	11	E, I	2.5	10	—
2	2.5	Db, Dp, E	62	10	—
3	ND	—	—	5	BAL, 200 mg DMSA, 400 mg
4	3	Db, E, NE	58	15	Thiosulfate, 16 g
5	ND	—	—	5	—
6	0.7	—	—	10	Thiosulfate, 16 g
7	4	—	—	20	—
8	1	Db	1	10	—
9	ND	—	—	5	—
10	ND	—	—	5	—
11	2	Db, Dp	22	10	—

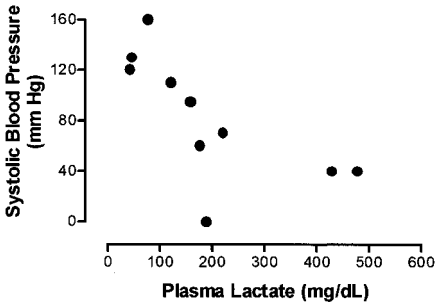
MV, mechanical ventilation; HOCo, hydroxocobalamin; E, epinephrine; I, isoproterenol; Db, dobutamine; Dp, dopamine; ND, not done; BAL, British anti-Lewisite; DMSA, succimer; NE, norepinephrine.

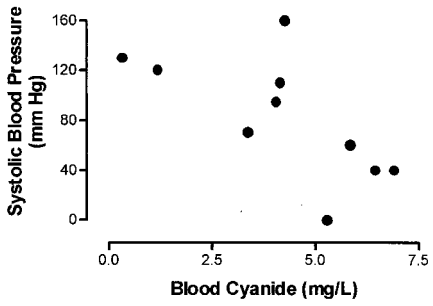
cyanide in blood were best described using a mono-exponential model in two patients (patients 4 and 7), with half-lives of 1.5 and 4.8 hrs, respectively (Table 4). The kinetics of cyanide were best described by a two-exponential model in three other patients (patients 1, 3, and 6) (Table 4), with early half-lives of 0.8, 0.2, 1.2 hrs, respectively. In these patients, a late elimination rate of cyanide was observed with late half-lives of 20.5, 11.5, and 7.9 hrs, respectively. The beginning of this late phase of elimination corresponded to blood cyanide concentrations of 1.25, 0.65, and 0.76 mg/L, respectively. The median early half-life of plasma lactate was 3.2 hrs (n = 5, 0.8–6.5) (Table 4).

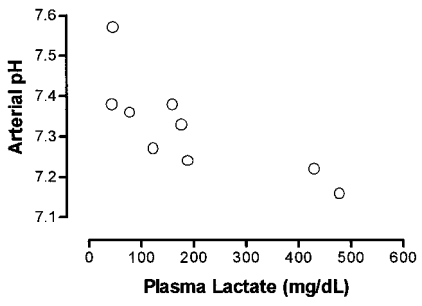
TK-TD Relationships of Plasma lactate and Blood Cyanide Concentrations. The visual inspection of the plot of plasma lactate concentrations against blood cyanide concentrations showed a plateau phase in patients 1 and 6 (Fig. 4). During the plateau phase, an important decrease in blood cyanide concentrations was not associated with any significant decrease in plasma lactate concentrations. Table 5 summarizes the E_0, Emax, Hill coefficient, and C_{50} in these two patients. The C_{50} values of blood cyanide were 1.7 mg/L and 1.2 mg/L, respectively,

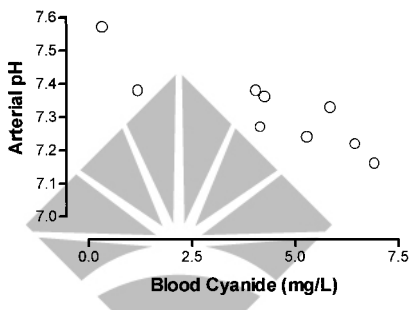
which corresponds with a dramatic decrease in plasma lactate concentrations.

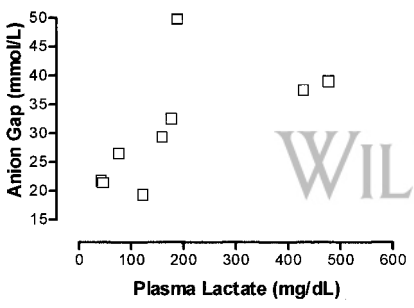
Sensitivity and Specificity of Plasma Lactate Levels for Cyanide Intoxication. For the nine patients with repeated blood specimen collections, the value of plasma lactate concentration with the best compromise between sensitivity and specificity for prediction of cyanide toxicity (blood cyanide concentration of ≥1.0 mg/L) was 72 mg/dL (8 mmol/L), with a sensitivity of 94% and a specificity of 70%; the positive and negative predictive values were 64% and 98%, respectively. In the six patients who did not receive a sustained catecholamine infusion (Table 3), the sensitivity of a plasma lactate concentration of 72 mg/dL was 92%, the specificity was 85%, and the positive and negative predictive values were 86 and 97%, respectively (Fig. 5).











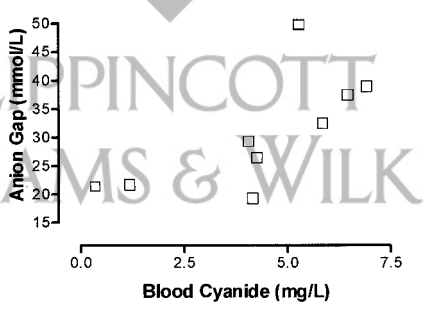


Figure 2. Correlations between plasma lactate concentrations and systolic blood pressure, arterial pH, and anion gap before antidotal treatment.

Figure 3. Correlations between blood cyanide concentrations and systolic blood pressure, arterial pH, and anion gap before antidotal treatment.

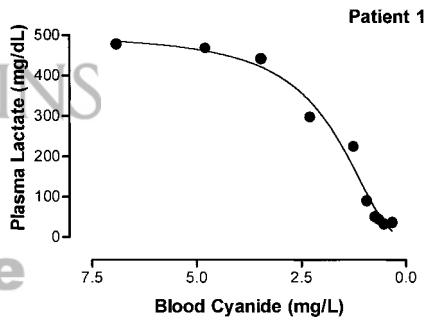
DISCUSSION

Lactic acidosis is found in a great number of critical illnesses and is thus nonspecific (37, 38). Furthermore, poisonings by carbon monoxide (39), azide (40), and hydrogen sulfide (41), among others, can induce lactic acidosis. Our results should be regarded in light of this major limitation. It is of utmost importance to reiterate that the design of our study limits any predictive value of plasma lactate to those situations in which cyanide poisoning is highly suspected. Indeed, the confirmatory value of lactic acidosis was only assessed in patients with a history consistent with cyanide poisoning. Cyanide poisoning was confirmed by measurement of blood cyanide concentrations. There are several further limitations to our study. Acute

Table 4. Half-life of plasma lactate and blood cyanide in seven cases of acute cyanide poisonings

	Plasma Lactate Half-Lives, Hrs	Blood Cyanide Half-Lives, Hrs	
Patients	Early	Early	Late
1	3.2	0.8	20.5
2	3.2	ND	ND
3	4.0	0.2	11.5
4[a]	ND	1.5	
6	0.8	1.2	7.9
7[a]	6.5	4.8	
11	1.4	ND	

ND, not determined.
[a]Toxicokinetics of cyanide in patients 4 and 7 best fit a monoexponential model.



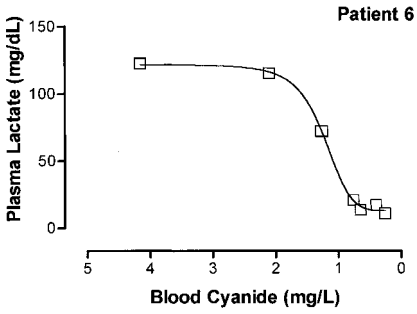


Figure 4. Toxicodynamic-toxicokinetic relationships between blood cyanide and plasma lactate concentrations in two cases of acute cyanide poisoning.

The immediate and serial measurement of plasma lactate concentrations is useful in assessing the severity of cyanide poisoning.

pure cyanide poisoning is fortunately rare, thus this study deals with only a very small number of patients. Furthermore, blood specimens were collected on the spot in four patients and stored at ambient temperature before the analyses were completed. Such a delay could have resulted in an increase in plasma lactate concentration and a decrease in blood cyanide concentration (42).

Several factors can contribute to the development of lactic acidosis in cyanide poisoning. Beside its mitochondrial effects, cyanide induces a number of systemic effects that can eventually lead to lactic acidosis, including an increase in blood glucose concentration (20, 21, 43, 44), a release of catecholamines (45), a decrease in heart rate and systolic blood pressure (21, 44), cardiac failure (46, 47), central apnea (30, 48, 49), and seizures (21, 50). Transient seizures were witnessed in only two patients and thus seem to be only an occasional factor. However, unwitnessed seizures occurring in the prehospital phase cannot be excluded. Low respiratory rate or apnea was noted in six patients in the prehospital phase. Furthermore, there was a significant inverse correlation between plasma lactate concentrations and respiratory rate, leading us to conclude that cyanide-induced respiratory effects may contribute to the increase in plasma lactate concentration. Lactic acidosis occurred in four patients with systolic blood pressure and pulse rate within the normal range, suggesting that lactic acidosis can occur without obvious cardiovascular failure. However, the significant inverse correlation of the systolic blood pressure with both the blood cyanide and the plasma lactate concentrations suggests that cyanide-induced cardiovascular failure should be considered as an important factor in the development of lactic acidosis in cyanide poisoning.

Table 5. Sigmoidal toxicodynamic-toxicokinetic relationships in patients 1 and 6

Patients	E_0, mg/dL	Emax, mg/dL	C_{50}, mg/L	n	r^2
1	2.7 (38.0)	502 (71)	1.7 (0.2)	2.2 (0.6)	0.98
6	12.6 (1.8)	109 (4)	1.2 (0.03)	5.4 (0.9)	0.99

E_0, the baseline value of plasma lactate concentration; Emax, the difference between the maximal value of plasma lactate concentration reached during the plateau phase and E_0; C_{50}, the blood cyanide concentration corresponding to half the Emax; n, the Hill factor.

$$E = Emax \times C^n/(C_{50}{}^n + C^n) + E_0$$

E, the plasma lactate concentration; C, the corresponding blood cyanide concentration. Results are expressed as value (SE).

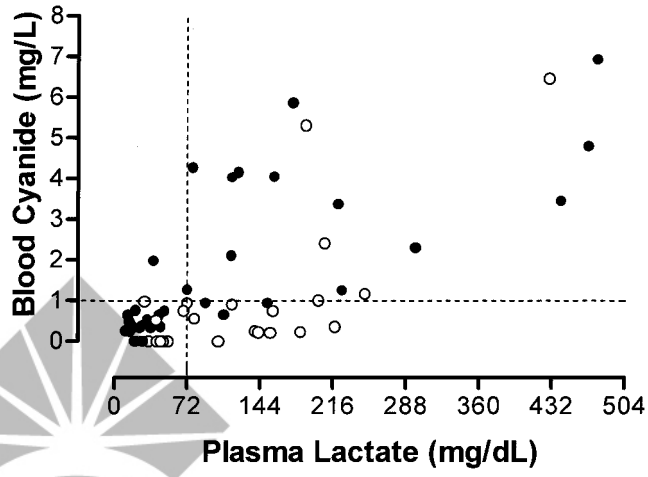


Figure 5. Relationship between blood cyanide and plasma lactate concentrations in the nine patients with repeated blood specimen collections over the course of their poisonings. The *black circles* indicate the results obtained in patients who did not receive sustained infusion of catecholamines; the *open circles* denote the results obtained in patients who received sustained infusion of catecholamines (see Table 3 for an explanation). A blood cyanide concentration of 1 mg/L is considered toxic (*horizontal broken line*). A plasma lactate of 72 mg/dL (*vertical broken line*) represents the best compromise between sensitivity and specificity for a blood cyanide concentration of ≥1 mg/L.

The mechanism of increased blood glucose concentration in cyanide poisoning is mobilization of hepatic glycogen stores (43). One causal factor could be cyanide-induced catecholamine release. We did not measure the blood concentrations of catecholamines. However, the significant relationship between blood glucose and cyanide concentrations suggests that this metabolic disturbance is also a contributor to cyanide-induced lactic acidosis.

The blood cyanide concentration is considered the gold standard in confirmation of acute cyanide poisoning. However, the emergency measurement of blood cyanide concentrations is rarely available. Our data show that, at the time of presentation, there is a significant correlation between blood cyanide and plasma lactate concentrations in patients in whom the diagnosis is strongly suspected on a clinical basis. These results may be useful for triage in the case of multiple casualty incidents involving cyanide. With the proliferation of bedside plasma lactate analyzers, almost immediate results may be obtained from a few drops of blood (51–54).

During the course of poisoning, a plasma lactate concentration of 72 mg/dL (8 mmol/L) was associated with a sensitivity of 94%, a specificity of 70%, a positive predictive value of 64%, and a negative predictive value of 98% for a blood cyanide concentration of ≥1.0 mg/L. The specificity was further increased when patients receiving catecholamines were removed from the analysis, demonstrating the contribution of exogenous catecholamines to the production of lactate (35, 36). Thus, during the course of the poisoning, a plasma lactate concentration of >72 mg/dL (8 mmol/L) may suggest the need for repeated antidotal therapy. We must emphasize that the determination of sensitivity and specificity was performed in a very small number of pa-

tients, whereas the stepwise statistical methods employed are typically reserved for large patient populations. Thus, our results should be regarded with some caution. We have taken the liberty to use this approach to evaluate plasma lactate concentrations in patients with a history consistent with cyanide poisoning because it is such a very rare poisoning. This study suggests that early determination of plasma lactate concentration (ideally at the patient's bedside or accident scene) may be useful in assessing the presence and severity of cyanide poisoning. However, it should be emphasized that emergency management of cyanide poisoning should not await laboratory results.

Pharmacodynamic-pharmacokinetic relationships describe, in the same individual, the quantitative relationship between a drug-induced effect and the timely corresponding drug concentrations. The value of the study of pharmacodynamic-pharmacokinetic relationships in clinical pharmacology is now well recognized (33). To describe the pharmacodynamic-pharmacokinetic relationship in two cases of cyanide poisoning, we used the Hill model. Ideally, a more sophisticated model might be used, taking into account the endogenous production and elimination of lactate and the lag time between exposure to cyanide and stimulation of lactate production (55). However, this model requires the determination of the baseline rate of production and elimination of lactate in the studied patients. This cannot be easily performed in poisoned patients. In forensic medicine, a blood cyanide of $\geq$1.0 mg/L is generally considered to represent a potentially toxic concentration (34). The TK-TD relationships showed that a decline in blood cyanide concentrations to 1.7 mg/dL and 1.2 mg/dL was associated with a dramatic decrease in plasma lactate concentrations. These data support the assumption of the value of 1.0 mg/L as a threshold for cyanide toxicity in humans. However, TK-TD relationships were performed only during the late phase of cyanide poisoning. We cannot assume that the C_{50} measured during the late phase is similar to that observed during the absorption-distribution phase.

All our patients were treated with hydroxocobalamin; two patients also received sodium thiosulfate. Both hydroxocobalamin and thiosulfate result in the formation of stable complexes, namely, cyanocobalamin and thiocyanate. A word of caution is in order, as it has been shown that the administration of methemoglobin-forming agents (such as sodium nitrite) results in an increase in blood cyanide concentration compared with pretreatment values (56–58), presumably because cyanide *in vivo* is drawn to and reversibly bound by the ferric ion of methemoglobin, then released in the strong acid milieu employed in most analytic methods. One would expect that plasma lactate concentrations would be lower in such patients relative to the measured blood cyanide. Our results should thus be interpreted in this context.

CONCLUSION

In patients with a clinical history consistent with cyanide poisoning, before antidotal treatment, plasma lactate concentration correlated positively with blood cyanide concentration and anion gap and inversely with systolic blood pressure, spontaneous respiratory rate, and arterial pH. During the course of cyanide poisonings treated with hydroxocobalamin and sodium thiosulfate, a plasma lactate concentration of $\geq$72 mg/dL (8 mmol/L) was sensitive (94%) but moderately specific (70%) for a blood cyanide concentration of $\geq$1 mg/L. The specificity was further improved in patients not receiving catecholamines. We conclude that the serial measurement of plasma lactate concentrations is useful in assessing the severity of cyanide poisoning.

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