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The Antidotal Action of Thiosulfate Following Acute Nitroprusside Infusion in Dogs

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The authors previously demonstrated in dogs that a bolus dose of sodium thiosulfate maintained enhanced cyanide metabolism throughout a 1-h infusion of sodium nitroprusside (SNP). To further test this antidotal action, a bolus dose of thiosulfate (150 $mg \cdot kg^{-1}$) was given to eight dogs at *the end* of a 60-min near-lethal infusion of nitroprusside (3 $mg \cdot kg^{-1}$). Within 2 min of the antidote, mean plasma thiocyanate levels (70.3 $\mu mol \cdot l^{-1}$) were significantly higher than those of seven control dogs given nitroprusside only (45.9 $\mu mol \cdot l^{-1}$, $P = 0.002$) and plateaued at 153.8 $\mu mol \cdot l^{-1}$ within 60 min, while the control values only reached 79.1 $\mu mol \cdot l^{-1}$ ($P < 0.001$). Although differences between plasma cyanide levels in the two groups only attained significance 1 h after administering the antidote (0.8 *vs.* 2.74 $\mu mol \cdot l^{-1}$, $P = 0.03$), red blood cell cyanide concentrations were significantly lower in the antidote group within 5 min (166 *vs.* 225 $\mu mol \cdot l^{-1}$, $P = 0.004$) and remained so throughout the 2-h observation period. Compared with the controls, there was an impressive reduction in mean half-lives of plasma cyanide (25.1 *vs.* 74.1 min) and red blood cell cyanide (22.4 *vs.* 203.6 min). Similarly, peak cyanide levels occurred much sooner following the antidote (mean times: plasma cyanide 2.9 *vs.* 5.9 min; red blood cell cyanide 0.25 *vs.* 11 min). Whereas mean blood lactate levels remained elevated for at least 1 h after infusion in the controls, they showed a decrease within 5 min in the antidote dogs, becoming significantly lower 25 min later ($P < 0.01$). These results suggest that thiosulfate alone is a sufficient antidote for cyanide toxicity arising from excessive SNP administration. The data also suggest that red blood cells may be involved in the detoxication process. (Key words: Anesthetic techniques: hypotension, induced; nitroprusside. Enzymes: 3-mercaptopyruvate sulfurtransferase; rhodanese. Pharmacology: nitroprusside; thiosulfate. Toxicity: cyanide; nitroprusside.

THE POSSIBILITY OF CYANIDE (HCN) intoxication during sodium nitroprusside (SNP) infusions is now well appreciated, and, accordingly, maximum doses and dose rates for acute[1–3] and chronic administration[4,5] have been recommended. In addition, a number of studies have investigated the effectiveness of HCN antagonists in preventing toxicity when high-dose rates of SNP are unavoidable.[1,4,6–10]

It is generally agreed that sodium thiosulfate is the least toxic and most effective of the antidotes for prevention and treatment of HCN toxicity from SNP overdose. Studies in dogs have shown that thiosulfate, given either as a prophylactic bolus dose prior to SNP infusion[8] or infused while SNP is administered,[4,9] limits the increase in blood HCN levels. Similarly, studies in patients have demonstrated that its continuous infusion, either in parallel[1,7] or mixed with the SNP,[10] enhances HCN metabolism. Recommendations therefore have been made that whenever SNP is infused, thiosulfate always should be administered.[10] However, low doses of SNP now are employed generally for hypotensive surgery, and toxicity has become a rare event. Consequently, anesthetists may well be loath to infuse another agent routinely when, in the great majority of cases, it will prove unnecessary. In addition, during chronic SNP administration, a simultaneous infusion of thiosulfate may present problems because of enhanced plasma thiocyanate (SCN) accumulation and the danger of hypovolemia.[4] It therefore would seem preferable to give a bolus dose of sodium thiosulfate only if the SNP dose/dose rate becomes excessive.

The drawbacks of this method of administration have been claimed to be the slow onset of action and the rapid metabolism and excretion of thiosulfate.[11–13] However, our previous work[8] suggested that these problems may have been exaggerated. It was decided accordingly to study more closely the speed and efficacy of bolus doses of thiosulfate. We therefore have given it as a postinfusion injection to dogs acutely infused with SNP ($3\ mg \cdot kg^{-1}$) for 1 h and have monitored changes in plasma and red blood cell HCN, and plasma SCN, using blood lactate and base deficit as indices of cellular respiration.

Methods

Anesthesia was induced with intravenous pentobarbitone ($60\ mg \cdot kg^{-1}$) in each of 15 mongrel dogs. Endotracheal intubation was performed, and the animals then were ventilated with 60% nitrous oxide in oxygen so as to maintain arterial P_{CO_2} between 4.6 and 5.6 kPa

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(35–42 mmHg). Incremental doses of pentobarbitone were given as required. Cannulation of the femoral artery and vein were carried out to permit blood pressure monitoring, sampling of arterial blood, and infusion of drugs. A Swan Ganz® catheter was "floated" into the pulmonary artery via a cut-down on to the external jugular vein and used for monitoring pulmonary artery pressure and for the injection of sodium thiosulfate. Each preparation was allowed to stabilize before the first (baseline) samplings and measurements were made. Arterial blood was analyzed for lactate concentrations by rapid decantation into perchloric acid and subsequent enzymatic analysis (Boehringer). Samples of plasma and red blood cells were separated from arterial blood at 4° C for immediate isolation of free HCN by the method of Boxer and Rickards,[2,14] while a portion of the plasma was stored at −20° C for subsequent SCN analysis. Both HCN and SCN were measured by a modified autoanalytical technique.[15] Arterial blood gas and acid–base status were determined using an IL 413 Blood Gas Analyser.®

The animals were treated randomly either as control or antidote dogs. Mean weight (±SD) of the control animals was 21.5 ± 4.4 kg and that of the antidote group was 21.3 ± 1.8 kg. Both groups received SNP (3 $mg \cdot kg^{-1}$), by intravenous infusion over exactly 60 min, from a Braun infusion pump. The SNP solution was freshly prepared from the Analar® solid (Hopkin and Williams), and the total required dose was infused in a volume of 60 ml physiologic saline from a foil-wrapped syringe. The antidote group received a bolus injection of Analar® (BDH) sodium thiosulfate (150 mg $Na_2S_2O_3 \cdot 5\ H_2O \cdot kg^{-1}$), dissolved in 5 ml deionized water, immediately upon termination of the SNP infusion.

All blood samples and recordings were taken at 20 min and 10 min before the SNP infusion, at 30 and 60 min during infusion, and at 10, 30, 60, and 120 min after the end of the SNP administration. Additional samples of blood also were taken at 2 and 5 min following SNP infusion, for lactate, blood gases, HCN, and SCN measurements. Normal saline was infused via the pulmonary artery catheter throughout the study to replace blood loss, and the animals were killed at the termination of each experiment.

Statistical Methods

The data from the two groups of dogs were expressed as mean ± standard error of the mean (±SEM) and compared using Student's *t* test for unpaired data in the Minitab statistical package from Pennsylvania State University. A probability of 5% or less was considered significant. Half-lives ($t_{1/2}$) of plasma and red blood cell cyanide were calculated from their log values *versus* time.

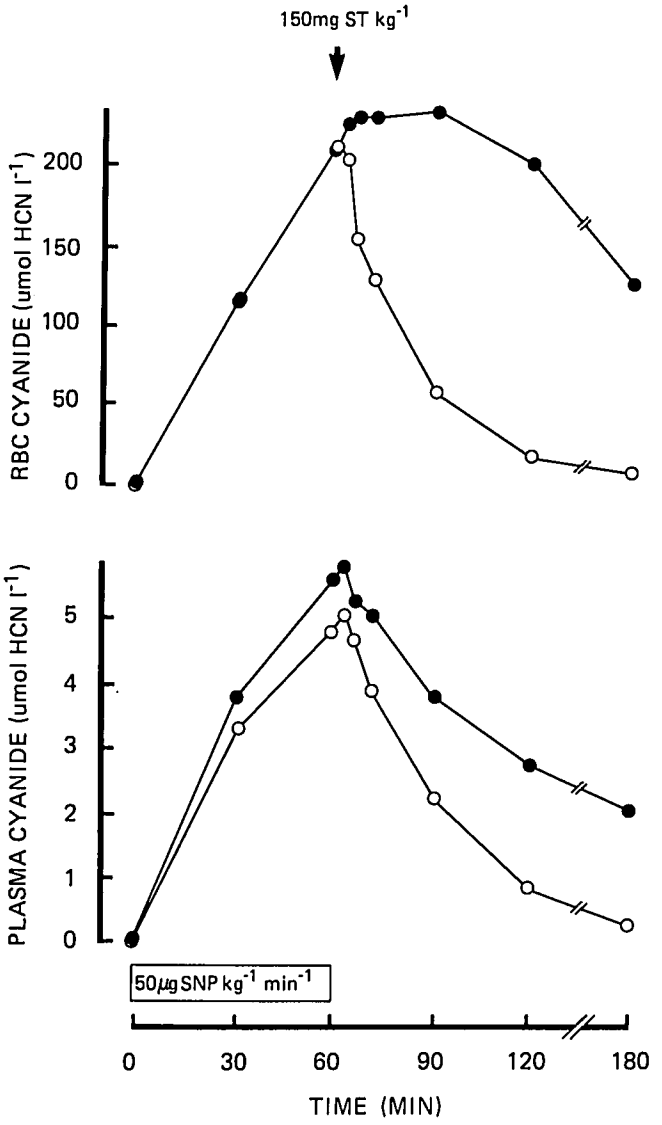

FIG. 1. Mean red blood cell and plasma cyanide concentrations in two groups of dogs during and for 2 h following a 1-h infusion of sodium nitroprusside (SNP). One group, the controls (n = 7) (—— ● ——), received no cyanide antidote, whereas the second group (n = 8) (—— O ——) was given a bolus injection of sodium thiosulfate (ST) at the end of the SNP infusion.

Results

The changes in mean blood HCN and SCN concentrations are displayed in figs. 1 and 2, and the numeric values, SEM, and statistical significance of the differences between the two groups of dogs are given in table 1. The plasma HCN levels showed no significant differences except at 60 and 120 min postantidote ($P = 0.03$ and $P = 0.02$). However, mean red blood cell HCN levels were significantly different 5 min after the antidote was given and remained so until the end of the experiment ($P < 0.01$ at 65 and 180 min, $P < 0.001$ at 70–120

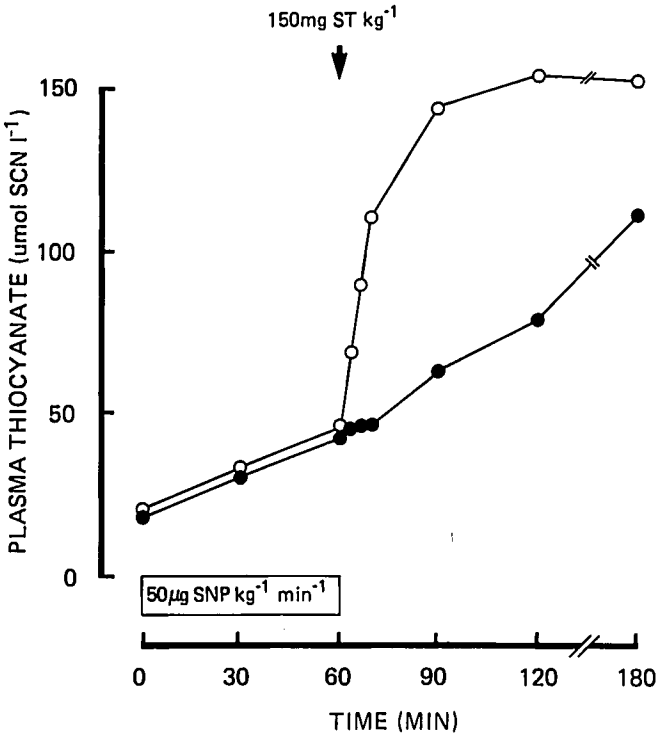

FIG. 2. The effect of a bolus injection of sodium thiosulfate (ST) (——O——) on mean plasma thiocyanate concentrations in dogs (n = 8) when given at the end of a 1-h infusion of sodium nitroprusside (SNP). A similar group of dogs (n = 7) receiving no antidote acted as controls (——●——).

min). Two minutes after injection, the red blood cell HCN values in seven of the antidote dogs had decreased, but in the eighth dog there was an increase. If the latter result is omitted, then the mean red blood cell HCN levels of the two groups, 2 min after the antidote (table 1), are also significantly different ($P = 0.05$).

The most dramatic differences between the two groups were displayed by the post-SNP plasma SCN concentrations. In the antidote animals these showed a rapid increase, while only a slow increase was seen in the controls (fig. 2). Plasma SCN levels in the two groups were very significantly different throughout the postantidote period ($P < 0.01$ at 62 min, $P < 0.001$ at 65–120 min, and $P < 0.05$ at 180 min).

Blood lactate and base deficit results are presented in table 2. Both mean blood lactate and mean base deficit remained elevated in the control dogs for at least 60 min following infusion, while in the dogs receiving antidote, levels began to decrease within 5 and 30 min, respectively. However, because of the large SDs, differences in blood lactate concentrations between the two groups only became significant 30 min after infusion ($P < 0.01$ at 90 min, $P < 0.001$ at 120 min and $P = 0.003$ at 180 min) and base deficit only after 60 min ($P < 0.01$ at 120 min and $P < 0.03$ at 180 min).

The differences between the two groups following SNP infusion are illustrated further by the numbers of dogs in which a decrease in the measured variables had occurred at each sampling time (tables 1 and 2) and by comparison of the times of peak HCN levels and their half-lives ($t_{1/2}$) (fig. 3).

Correlations between the various measurements are given in table 3. Base deficit showed a good correlation with blood lactate, and both were better correlated with red blood cell HCN than with plasma HCN. However, the correlations between base deficit and HCN levels in the antidote dogs were lower than in the controls, probably because of the rapid changes in HCN induced by thiosulfate. The decreases in RBC HCN levels showed a better correlation with increases in plasma SCN concentrations than did the decreases in plasma HCN. Additionally, both log plasma and log RBC HCN levels, following SNP infusion, showed a statistically significant negative linear correlation with time in both groups of dogs.

No side effects, other than transient hypotension (for 30–60 s; mean decrease in systolic pressure 8.5% ± 4.8% SEM) were seen on injection of the thiosulfate.

Discussion

Our previous study[8] demonstrated that a bolus dose of thiosulfate (75 $mg \cdot kg^{-1}$), given 5 min prior to the start of an infusion of 1.5 $mg \cdot SNP \cdot kg^{-1}$ (a constant rate of 25 $\mu g \cdot kg^{-1} \cdot min^{-1}$ for 1 h), maintained plasma and red blood cell HCN at very low levels throughout the period of infusion, while plasma SCN concentrations climbed rapidly to reach a maximum at its termination. This contrasted with the controls where high HCN levels were reached during the infusion and plasma SCN continued to increase for 2 h after the SNP administration. These observations demonstrated that the antidotal action of a bolus dose of thiosulfate was maintained for at least 1 h and was rapid enough to facilitate the removal of HCN as it was released from the infused SNP.

In this second study, in order to further examine the speed of action of thiosulfate, dogs were infused with twice the previous dose of SNP (3 $mg \cdot kg^{-1}$; 50 $\mu g \cdot kg^{-1} \cdot min^{-1}$ for 1 h) and double the dose of antidote was injected at the end of the infusion (150 mg $Na_2S_2O_3 \cdot 5\ H_2O \cdot kg^{-1}$ = 12× the stoichiometric amount theoretically required to "neutralize" the HCN from the SNP dose). The SNP infusion rate employed must be close to the lethal one for dogs as indicated by the rapid increase in blood lactate and base deficit, the death of one of the control animals some 90 min after the infusion, and the fact that an equivalent dose rate of sodium cyanide has been demonstrated to be lethal within 30 min.[16]

TABLE 1. Comparison of Mean Plasma and Red Blood Cell Cyanide and Plasma Thiocyanate in Dogs Receiving No Cyanide Antidote with Those in Dogs Given Thiosulfate at the End of SNP Infusion

	Plasma Cyanide (μmol/l)							Red Cell Cyanide (μmol/l)							Plasma Thiocyanate (μmol/l)				
	Control (n = 7)			Antidote (n = 8)				Control (n = 7)			Antidote (n = 8)				Control (n = 7)		Antidote (n = 8)		
Sample Time	$\bar{x}$	SEM	D*	$\bar{x}$	SEM	D*	*P*	$\bar{x}$	SEM	D*	$\bar{x}$	SEM	D*	*P*	$\bar{x}$	SEM	$\bar{x}$	SEM	*P*
−10	0.19	0.06	—	0.10	0.04	—	0.24	0.3	0.5	—	0.2	0.03	—	0.25	19.6	1.97	20.6†	2.95	0.78
30‡	3.75	0.65	—	3.42	0.21	—	0.62	116.3	12.59	—	115.9	12.13	—	0.98	31.3†	3.47	34.3	3.47	0.57
60‡§	5.58	0.77	—	4.65	0.31	—	0.26	208.1	12.93	—	209.8	10.04	—	0.92	43.6	4.31	45.0	4.03	0.81
62	5.80	0.85	3	5.00	0.59	6	0.44	219.8	13.30	2	202.7¶	20.47	7	0.51	45.9	5.10	70.3	3.61	0.002
65	5.26	0.88	4	4.60	0.77	7	0.58	225.1	16.48	2	166.0	7.18	8	0.004	46.7	4.95	89.0	4.31	<0.001
70	5.11	0.74	4	3.96	1.94	6	0.40	223.5	16.82	3	130.1	5.48	8	<0.001	48.1	5.52	111.1	5.20	<0.001
90	3.84	0.94	6	2.32†	0.78	7	0.25	229.1	25.85	4	53.1	2.16	8	<0.001	65.1	9.03	145.3†	7.96	<0.001
120	2.74	0.81	7	0.80	0.20	8	0.03	198.4	28.12	6	16.5	2.47	8	<0.001	79.1	10.51	153.8	7.42	<0.001
180	2.08	0.69	6	0.28†	0.09	7	0.02	123.6	38.55	7	5.1	0.23	8	0.006	112.4	12.21	152.4	7.07	0.012

* D = no of dogs showing a decrease in HCN level compared with the preceding value.
† One value missing.
‡ Sampling times during an infusion of 3 mg SNP kg^{-1} for 1 h.
§ Bolus sodium thiosulfate (150 $mg \cdot kg^{-1}$) given at this point.
¶ If one anomalous RBC HCN value is omitted $\bar{x}$ = 183.8, SEM = 9.03, n = 7 and *P* = 0.05.

TABLE 2. Comparison of Mean Blood Lactate and Base Deficit in Dogs Receiving No Antidote with Those in Dogs Given an Injection of Sodium Thiosulfate at the End of an Infusion of SNP

	Blood Lactate (mmol/l)							Base Deficit (mmol/l)						
	Control (n = 7)			Antidote (n = 8)				Control (n = 7)			Antidote (n = 8)			
Sample Time	$\bar{x}$	SEM	D*	$\bar{x}$	SEM	D*	*P*	$\bar{x}$	SEM	D*	$\bar{x}$	SEM	D*	*P*
−20	1.22	0.40	—	0.86	0.10	—	0.37	3.7	0.47	—	3.75	0.91	—	0.96
−10	1.16	0.37	—	0.92	0.09	—	0.52	3.7	0.56	—	4.09	1.03	—	0.76
30†	2.55	0.38	—	2.55	0.17	—	1.00	5.94	0.70	—	6.39	0.90	—	0.71
60†‡	3.73	0.48	—	3.76	0.22	—	0.95	8.69	0.85	—	8.56	0.64	—	0.91
62	3.99	0.43	1	3.77	0.23	4	0.64	—	—	—	—	—	—	—
65	4.09	0.43	3	3.57	0.21	8	0.28	—	—	—	—	—	—	—
70	4.34	0.45	1	3.43	0.23	7	0.09	9.60	0.91	1	8.84	0.66	1	0.49
90	4.32	0.56	4	2.63	0.17	8	<0.01	9.60	1.05	3	7.58	0.65	8	<0.12
120	4.33	0.50	6	1.80	0.15	7	<0.001	9.63	1.10	5	5.71	0.70	8	<0.01
180	3.29§	0.61	5	1.14	0.13	8	0.003	7.8§	1.36	5	4.59	0.84	6	0.03

* D = no of dogs showing a decrease in level compared with the preceding measurement.
† Sampling times during infusion of 3 mg SNP kg^{-1} for 1 h.
‡ Bolus thiosulfate (150 $mg \cdot kg^{-1}$).
§ One value missing.

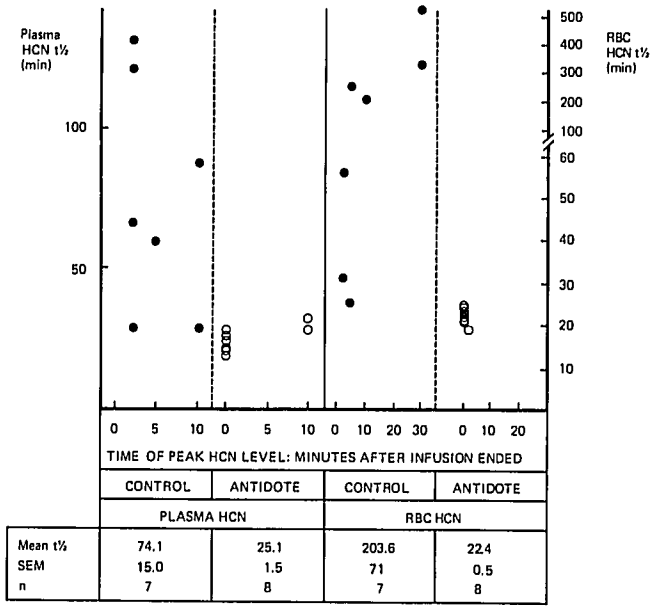

FIG. 3. Individual mean half-lives ($t_{1/2}$) of plasma and RBC HCN after the attainment of peak levels following SNP infusion (3 mg·kg^{-1} over 1 h). The diagram also indicates the times after infusion at which peak HCN levels were reached. Control dogs received no antidote, whereas the antidote group received a bolus thiosulfate injection (150 mg·kg^{-1}) at the end of infusion. Mean RBC and plasma HCN $t_{1/2}$ (±SEM) for each group are shown at the base of the figure.

In the control group of dogs, the HCN released from the infused SNP maintained increased lactate and base deficit levels for at least an hour after the SNP infusion had ceased. In contrast, both of these indices began to decrease less than 30 min after the dose of thiosulfate. This reflected the concomitant rapid decreases in plasma and red blood cell HCN, and the rapid increases in plasma SCN in the antidote dogs (figs. 1 and 2). Others have demonstrated that thiosulfate enhances the speed of HCN metabolism and that it also limits its peripheral distribution in dogs.[17]

Breakdown and release of HCN will continue after SNP administration ceases so that HCN toxicity may be delayed.[18] This is illustrated by the control dogs where the variations in time at which peak HCN levels were reached indicate considerable individual differences in the rate of SNP breakdown (fig. 3). Also, the variation in HCN $t_{1/2}$ in the control animals shows that there are wide differences in the ability to detoxicate HCN at these high levels. No doubt this reflects variability in endogenous supplies of thiosulfate and, possibly, in the degree of inhibition of the detoxication mechanisms by elevated blood HCN.[19] However, the bolus thiosulfate injection, given at the end of SNP infusion, dramatically decreased HCN $t_{1/2}$, virtually removing individual differences in detoxication rates and preventing late increases in HCN levels.

It generally is considered that HCN is converted to SCN by the action of the enzyme rhodanese (thiosulfate:cyanide sulfurtransferase, EC.2.8.1.1), which is widely distributed in the tissues and present in high concentration in the liver and kidneys.[19] However, rhodanese is relatively inaccessible, being confined to the matrix of the mitochondria[20] where thiosulfate only gains access slowly.[19,21,22] In addition, SCN traverses cell membranes by simple diffusion[23] and, therefore, after formation from HCN, would be expected to enter the plasma at a slow rate. These characteristics of the rhodanese system seem incompatible with the rapid elevation of plasma SCN in the antidote dogs. Several observations, both from this work and that reported by others, suggest the red blood cell as a possible site for HCN detoxication.

This experiment has demonstrated differences in the degree and speed of the reduction of red blood cell and plasma HCN as a consequence of an injection of sodium

TABLE 3. Correlations between Various Measurements Made in Dogs Infused with SNP (3 mg·kg^{-1}) for 1 h (One Group Acted as the Controls, while a Second Group Received a Bolus Injection of Thiosulfate (150 mg·kg^{-1}) at the End of SNP Administration)

Measures Correlated	Control Group (n = 7)			Antidote Group (n = 8)		
	r	df	P	r	df	P
RBC HCN *vs.* plasma HCN (0–180 min)	0.62	58	<0.001	0.73	66	<0.001
Base deficit *vs.* plasma HCN (0–180 min)	0.69	36	<0.001	0.24	52	<0.1
Base deficit *vs.* RBC HCN (0–180 min)	0.71	36	<0.001	0.38	52	<0.01
Lactate *vs.* plasma HCN (0–180 min)	0.51	60	<0.001	0.70	67	<0.001
Lactate *vs.* RBC HCN (0–180 min)	0.63	60	<0.001	0.84	67	<0.001
Lactate *vs.* base deficit (0–180 min)	0.74	36	<0.001	0.42	52	<0.01
Log plasma HCN *vs.* time (62–180 min)	−0.64	47	<0.001	−0.89	51	<0.001
Log RBC HCN *vs.* time (62–180 min)	−0.55	47	<0.001	−0.97	51	<0.001
Decrease in plasma HCN *vs.* increase in plasma SCN (62–180 min)	0.66	40	<0.001	0.58	44	<0.001
Decrease in RBC HCN *vs.* increase in plasma SCN (62–180 min)	0.86	40	<0.001	0.89	44	<0.001

thiosulfate. Thus, RBC HCN levels in the animals given the antidote were significantly lower than in the control group ($P = 0.004$) 5 min after the antidote, whereas plasma HCN levels differed significantly ($P = 0.03$) only after the lapse of 1 h. In the antidote group itself, the mean RBC HCN $t_{1/2}$ was lower than plasma HCN $t_{1/2}$ (22.4 min *vs.* 25.1 min). Not surprisingly, this difference was small and did not achieve statistical significance (paired $t = 2.2$, $P = 0.064$), since HCN passes rapidly from the plasma into the red blood cell.[24,25] A further and important observation, previously made in humans,[2] was the fact that the increases in plasma SCN, following SNP infusion in both groups of dogs, were better correlated with the decreases in RBC HCN levels than with decreases in plasma HCN concentrations (table 3).

A role for the red blood cell in the detoxication of HCN is also compatible with the observation that injected thiosulfate limits the tissue distribution of HCN.[17] In fact, a number of isolated reports have claimed demonstration of the enzyme rhodanese in the red blood cell.[26-28] There is more evidence, however, for the presence of 3-mercaptopyruvate:cyanide sulfurtransferase (EC.2.8.1.2), which transfers sulfur from 3-mercaptopyruvate (a metabolite of the amino acid cysteine) to sulfite and cyanide to produce thiosulfate and thiocyanate, respectively:[19,29]

$$\underset{\text{mercaptopyruvate}}{HSCH_2COCOO^-} + ENZ \rightarrow \underset{\text{pyruvate}}{CH_3COCOO^-} + ENZS \quad (1)$$

$$ENZS + \underset{\text{sulfite}}{SO_3^{2-}} \rightarrow ENZ + \underset{\text{thiosulfate}}{S_2O_3^{2-}} \quad (2)$$

$$ENZS + \underset{\text{cyanide}}{CN^-} \rightarrow ENZ + \underset{\text{thiocyanate}}{SCN^-} \quad (3)$$

It has been suggested that at high thiosulfate concentration, equation (2) may be reversed.[29] The enzyme then could act like rhodanese, as in equation (3). Indeed, electrophoretic studies have shown that the rhodanese activity of human erythrocytes is identified with 3-mercaptopyruvate sulfurtransferase.[29]

This theoretic concept certainly accords with our findings that sodium thiosulfate provides a highly effective, rapid onset antidote to HCN poisoning induced by SNP overdose in dogs. Although previous work has indicated that HCN detoxication is more rapid in the dog,[25] there is no reason to believe that the basic mechanism is any different in humans and that our conclusions may not be extrapolated to humans. In practice, it is highly unlikely that any patient would be infused with a dose/dose rate of SNP as high as that given to our dogs and yet, in all of the animals given thiosulfate, HCN clearance and correction of metabolic disturbances were attained rapidly. It therefore is our opinion that thiosulfate does not need to be given as a simultaneous infusion each time SNP is used. Such a practice would result in many patients unnecessarily receiving an extra drug with the use of additional or special infusion routes and equipment. Bolus injection is simpler, allows selection, and, as we have demonstrated, is very effective.

As already indicated, a very brief period of hypotension was the only observed side effect of the injection of sodium thiosulfate. This is particularly notable, since the drug, at a mean concentration of 64%, was given as a rapidly injected bolus into the pulmonary artery. It is normally recommended that a 25% solution of thiosulfate should be given by slow intravenous injection at a rate of 2.5–5 $ml \cdot min^{-1}$.[30] In fact, thiosulfate is an extremely safe HCN antagonist.[31] In this it may be contrasted with cobalt EDTA and nitrites. The former is toxic in high dose,[32,33] while the nitrites have the distinct disadvantages of 1) reducing the effective haemoglobin concentration by 25–40%,[30,31] due to methaemoglobin formation; and 2) exerting a hypotensive action.[33] The rationale for the use of nitrites lies in the allegedly low capacity and slow rate of thiosulfate-sulfur transfer to HCN, the combination of HCN with methaemoglobin being a more rapid reaction producing a synergistic effect with thiosulfate.[31] Our work has demonstrated that, in fact, injected thiosulfate alone encourages the rapid formation of SCN from HCN. While it is true that this study does not fully reflect the effects of acute cyanide ingestion, the quantities of HCN involved are comparable and the dose used therefore must be very nearly a lethal one (see above). Despite this, thiosulfate was capable of dealing with the HCN released. We therefore question whether nitrites, with their inherent drawbacks, are necessary in the treatment of cyanide poisoning from any cause, particularly when additional supportive measures can play a large part in recovery from cyanide poisoning.[34] In any case, the use of nitrites certainly would seem to be superfluous when dealing with HCN intoxication from SNP infusion.

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