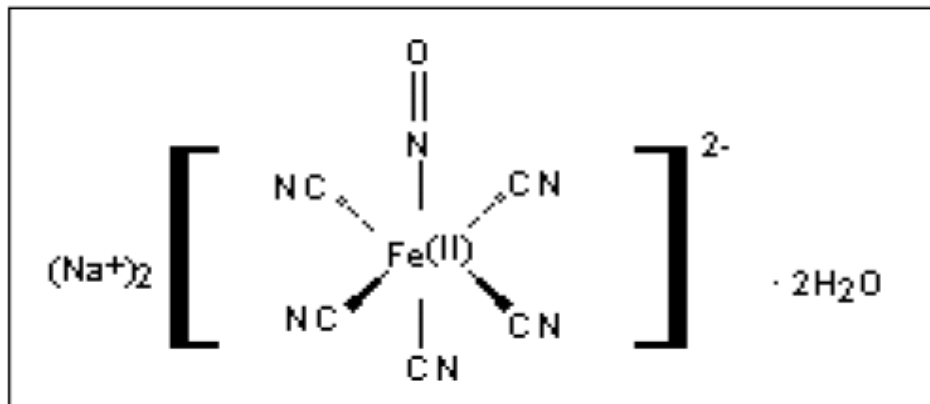


Bon Secours Richmond
Pharmacy & Therapeutics Committees
Sodium Thiosulfate and Sodium Nitroprusside Admixture
5/05

Recommendations

- Sodium thiosulfate will be added to all sodium nitroprusside (SNP) infusions to prevent cyanide toxicity.
 - 1 gm (10 ml of 10%) of sodium thiosulfate will be added to each 100 mg bag of nitroprusside (10:1 ratio).
 - Thiosulfate prevents the development of toxic cyanide levels.
- Cyanide and thiocyanate levels are recommended to monitor for cyanide toxicity in patients who are not receiving concurrent thiosulfate. Note: Cyanide and thiocyanate toxicity are two different entities.
- Thiocyanate levels are recommended for patients receiving nitroprusside with thiosulfate. Note: Thiosulfate prevents toxic cyanide levels even at high nitroprusside infusion rates.
 - Nitroprusside infusion of 2-5 mcg/kg/min may give toxic thiocyanate levels in:
 - 7-14 days in patients with normal renal function
 - 3-6 days in renal failure, unless they are receiving concurrent dialysis. Thiocyanate clearance rates during dialysis approach the blood flow rate of the dialyzer.



Findings

Indications SNP:

- Immediate reduction of blood pressure of patients in hypertensive crises, controls hypotension in order to reduce bleeding during and after surgery, reduces preload and afterload in heart disease (short-term).

Action of SNP:

- Potent, rapid-acting vasodilator.

Mechanism of Action of SNP:

- Causes peripheral vasodilation by direct action on venous and arteriolar smooth muscle, reduces peripheral resistance and decreases preload; increases cardiac output by decreasing afterload; reduces aortal and left ventricular impedance. Nitroprusside reacts with sulfhydryl groups in the cell walls of vascular smooth muscle. Sulfhydryl groups in the cell wall donate electrons to the ferrous group in nitroprusside, resulting in an unstable compound that release cyanide and nitric oxide.

Pharmacokinetics of Nitroprusside:

- T_{1/2} - 2-3 minutes.
- Onset of action – 0.5-5 minutes
- Duration of action - 1-10 minutes.
- Distribution: mainly extracellular and intravascular.
- Nitroprusside is an designated as an essential drug by the World Health Organization

Dose of SNP:

- Current labeling - 0.3 to 10 mcg/kg/minute for parenteral nitroprusside. Infusion at the maximum dose rate should never last more than 10 minutes (without thiosulfate).
- Patients that do not respond to sodium nitroprusside at rates ≥ 10 mcg/kg/minute without thiosulfate for 10 minutes should have the drug discontinued and an alternative agent instituted.

Toxicology of SNP:

- SNP is 44% cyanide by weight.
- Metabolism – Nitroprusside is rapidly converted to cyanide ions in the bloodstream.
- One molecule of sodium nitroprusside release 5 cyanide ions, one ion combines with methemoglobin to form cyanmethemoglobin, and 4 cyanide ions, which are detoxified by combining with a sulfhydryl group of endogenous thiosulfate. Conversion to thiocyanate is an irreversible reaction that occurs in the liver and kidneys. Methemoglobin sequesters cyanide as cyanmethemoglobin. Normal blood methemoglobin concentrations have a binding capacity for cyanide released from 18 mg of nitroprusside.
- The spontaneous detoxification rate of nitroprusside to thiocyanate is approximately 2 mcg/kg/minute. At higher infusion rates cyanide is generated at a rate that exceeds detoxification and accumulates. Patients with decreased thiosulfate stores may be at risk for cyanide toxicity at lower infusion rates. Risk for cyanide accumulation occurs if more than 1.5 mg/kg is given over 3-4 hours (6.25 mcg/kg/min). Life threatening intoxication may occur with 5-10 mcg/kg/min given for 5-10 hours.
- A healthy adult has adequate thiosulfate stores to detoxify 50 mg of nitroprusside (0.5 mcg/kg/min for 24 hours). Body stores of thiosulfate can be lowered by malnutrition, surgery, and diuretic administration. Neonates and newborns may have inadequate thiosulfate stores. Once stores of thiosulfate are depleted and available methemoglobin is saturated, cyanide levels in tissue and blood rise.
- Detoxification of cyanide is described pharmacokinetically as a zero-order process, as the enzyme that detoxifies cyanide (rhodanese) is present in the body in large excess relative to its substrates. The rate-limiting step is the availability of thiosulfate. The margin of safety for sodium nitroprusside infusion may be increased by simultaneous intravenous infusion of sodium thiosulfate.
- Cyanide inactivates cytochrome oxidase in the mitochondria, which disrupts cellular respiration. The inactivation of cytochrome oxidase results in tissue anoxia and an anaerobic metabolism resulting in lactic acid formation and metabolic acidosis.
- Cyanide toxicity is manifest as CNS dysfunction, cardiac instability (particularly tachyphylaxis), and oxygenation/pH changes, see table below. The three most frequently reported signs or symptoms of cyanide intoxication are unconsciousness, dyspnea, and cyanosis (dark bluish or purplish coloration of the skin, nail beds, lips, or mucous membranes).
- Clinical indicators of cyanide toxicity may be behavioral and may be erroneously attributed to ICU psychosis.
- Plasma cyanide concentrations have been shown to correlate with the infusion rate of nitroprusside in 24 patients (51 samples), micromole/liter = $0.267 \times$ infusion rate in mcg/kg/min - 0.0733 $R=0.64$ $p < 0.001$. Toxic cyanide level: 9 micromole/liter for assay used.
- Cardiac surgery patients have experienced cyanide toxicity at average infusion rates of 2.5 mcg/kg/min or less. Seven patients in one study had toxic concentrations and three died from presumed cyanide poisoning.
- The FDA spontaneous reporting system as of 1992, had 142 cases involving nitroprusside, including 25 fatalities.
- The package insert for Nitroprusside states that thiosulfate coadministration should be considered for patients receiving infusion rates above 2 mcg/kg/min.
- Cyanide levels
 - Normal: < 20 mcg/dl (ARUP Manual)
 - Potentially Toxic : > 50 mcg/dl (ARUP Manual)
 - Metabolic Disturbances (from ABC's of Interpretive Laboratory Data): > 100 mcg/dl
 - Lethal (from ABC's of Interpretive Laboratory Data): > 300 mcg/dl. (To convert units of mcg/dl to international units in micromol/L, multiply by 0.385).

- It takes 1-2 days to obtain results of cyanide blood levels.
- Thiocyanate levels
 - Nonsmoker: 1-4 mcg/ml (ARUP Manual)
 - Smoker: 3-12 mcg/ml (ARUP Manual)
 - Toxic: > 50 mcg/ml (833 micromole/liter) (ARUP Manual)
 - Life Threatening 200 mcg/ml (3333 micromole/liter)
 - Values seen while on nitroprusside therapy: 6-29 mcg/ml
 - Thiocyanate levels are of no value in determining the presence of cyanide toxicity.
 - Assay is performed Monday through Friday by ARUP

Conversion factors

Cyanide

Milligrams/liter or microgram/ml *38.5=micromole/liter
 200 micromoles/liter=5 mg/liter (SNP Package Insert)

Thiocyanate

Milligrams/liter or microgram/ml *17.2= micromole/liter
 50 micromole/liter= 3 mg/liter (SNP Package Insert)
 1 millimole/liter= 60 mg/liter (SNP Package Insert)
 3450 micromole/liter= 200 mg/liter (Vesey CJ, Br J Anaeth 1985,57,148-55)

Thiosulfate

0.1 micromole/liter=11 mg/liter (SNP Package Insert)

Risk Factors for Nitroprusside-Induced Cyanide Toxicity:

- Infusions > 2 mcg/kg/minute after only 2-3 hours may result in toxic levels.
- Infusions > 5-10 mcg/kg/minute given over a 5-10 hour period can lead to life-threatening intoxication.
- Elevated cyanide levels, metabolic acidosis and marked clinical deterioration have been reported in patients who received nitroprusside infusion at recommended rates for only a few hours. Therefore, any patient receiving nitroprusside is at risk for developing cyanide poisoning.
- Malnutrition, surgery and diuretic administration can lower body's stores of thiosulfate.
- Neonates and newborns may have low stores of thiosulfate.

Clinical Manifestations of Cyanide Toxicity:

CNS dysfunction: -Headache -Anxiety -Disorientation -Lethargy -Seizures -Coma -Cerebral death
Cardiovascular instability: -Hypertension (tachyphylaxis) → hypotension -ECG changes <ul style="list-style-type: none"> • Tachycardia → bradycardia • ST-T wave changes • Dysrhythmias • AV block • Cardiovascular collapse
Changes in oxygenation/pH -Tachypnea → apnea -Venous hyperoxemia: red venous blood, increased mixed venous O ₂ contents,

decrease O₂ consumption, narrow arteriovenous oxygen difference, brick-red skin (occasional cyanosis)

-Hyperglycemia

-Metabolic acidosis

- Elevated blood lactate and/or elevated lactate: pyruvate ratio

Other:

-Nausea, vomiting, abdominal pain

-Increased salivation

*Symptoms of cyanide poisoning vary based on individual differences and comorbidity factors.

Prevention of Nitroprusside-Induced Cyanide Intoxication:

- Poisoning with nitroprusside is preventable.
- Providing the sulfur donor thiosulfate as a mixed infusion with nitroprusside accelerates the detoxification of cyanide, making toxicity virtually impossible. Cyanide levels do not increase even at high nitroprusside infusion rates (10 mcg/kg/min) for prolonged durations (days) when thiosulfate is given concomitantly.
- Sodium thiosulfate is indicated for the treatment of cyanide poisoning.
- A 10:1 ratio of thiosulfate to nitroprusside (i.e., 500 mg thiosulfate to 50 mg nitroprusside) as a mixed infusion is used as prophylaxis.
- Thiosulfate does not interact to decrease the effectiveness of nitroprusside and it does not have any significant toxicities.

Nitroprusside-Thiosulfate admixtures

- Admixtures of thiosulfate and nitroprusside are stable for 24 hours.
- The efficacy of nitroprusside is maintained with mixed with thiosulfate.
- Sodium thiosulfate is available as a 10% 10 ml (\$5.73) and 25% 50 ml (\$17.48) injection.
- 2729 vials 50 mg vials of nitroprusside were used by BSR in the last 12 months. Thiosulfate will cost \$7,818 for the admixture.

Treatment of Cyanide Toxicity:

- Treatment of cyanide poisoning
 - Discontinue nitroprusside
 - 100% oxygen
 - Intubation if needed
 - Sodium bicarbonate if pH less than 7.16
 - Cyanide Antidote kit
 - Sodium Nitrate: The recommended adult dose is 4-6 mg/kg (300-600 mg) (10-20 ml of a 3% solution) over no less than 5 minutes. One half of the dose may be repeated if needed. Methemoglobin levels should be kept below 35-40%.
 - Sodium thiosulfate: The standard dose is 150-200 mg/kg, 12.5 gm (50 ml of 250 mg/ml (25%) solution) IV for cyanide toxicity over 20 minutes.
- Hemodialysis does not remove cyanide, but does remove thiocyanate.
- Sodium nitrate induces the formation of methemoglobin, which combines with cyanide to form cyanmethemoglobin. Cyanide has a higher affinity for methemoglobin than hemoglobin. Clinical improvement and clearing of cyanosis occurs within 1-2 hours. Sodium nitrate also causes relaxation of smooth blood vessels. Ten times the therapeutic dose of sodium nitrate is toxic. Thiosulfate combines with cyanide and is converted irreversibly to thiocyanate in the liver and kidneys.
- Thiosulfate is essentially a nontoxic drug, although nausea and vomiting may occur with rapid IV administration of antidotal doses. Thiosulfate is poorly absorbed orally. Thiosulfate's half-life is 15 minutes after bolus injection. The volume of distribution is the extracellular space. One gram of sodium thiosulfate contains 290 mg of sodium.

Thiocyanate Toxicity:

- Thiocyanate is renally eliminated, 90 % of that filtered by the glomeruli is reabsorbed, with a half-life of 2.7 days in normal renal function and 9 days in renal failure, volume of distribution 0.25 l/kg. (SNP Package Insert 3 days, 6-9 days in RF)
- Thiocyanate toxicity occurs after approximately 9 days in those with normal renal function and approximately 3 days in renal failure.
- Cyanide is much more toxic than methemoglobin or thiocyanate.
- Thiocyanate is approximately 100 times less toxic than cyanide.
- Thiocyanate levels have been shown to correlate with the cumulative dose nitroprusside in 27 patients (n=51) (micromole/liter = 24.6 (mg/kg) + 74.9, R=0.95). Toxic level is 1725 micromole/liter, which corresponds to an infused dose of 70 mg/kg of nitroprusside (3.5 mcg/kg/min for 14 days).
- Thiocyanate is mildly neurotoxic (tinnitus, miosis, hyperreflexia) at serum levels of 1 mmol/L (60 mg/L). Thiocyanate toxicity may be life-threatening when levels are 3 or 4 times higher (200 mg/L, 3450 micromole/liter).
- To keep the level of thiocyanate below 1mmol/L(1000 micromole/L), a prolonged infusion of sodium nitroprusside should not be more rapid than 2 to 5 mcg/kg/minute and should be infused for less than 7 to 14 days (in patients with normal renal function) or 1 mcg/kg/minute in anuria. In patients with renal failure toxicity may occur in 3-6 days.
- If toxicity is suspected, hemodialysis over a few hours will eliminate most thiocyanate from the body. Thiocyanate clearance rates during dialysis approach the blood flow rate of the dialyzer.
- Rare patients receiving more than 10mg/kg of sodium nitroprusside will develop methemoglobinemia. (A patient receiving sodium nitroprusside at the maximum recommended rate (10mcg/kg/minute) would take over 16 hours to reach this accumulation).

Clinical Manifestations of Thiocyanate Toxicity:

Neurogenic -Confusion -Miosis -Hallucinations -Toxic psychosis -Convulsions -Coma -Death
Other -Muscle fatigue -Hyperreflexia -Nausea and Vomiting -Tinnitus -Decreased T4

Contraindications:

- Treatment of compensatory hypertension (aortic coarctation, arteriovenous shunting); high output failure; congenital optic atrophy or tobacco amblyopia; treatment of acute congestive heart failure associated with reduced peripheral vascular resistance.

Warnings:

- Metabolized to highly toxic cyanide.
- Use with extreme caution in patients with elevated intracranial pressure, hepatic and renal dysfunction and excessive hypotension.
- Watch for cyanide toxicity.

Drug Interactions:

- The hypotensive effect of sodium nitroprusside is increased by that of most other hypotensive drugs including ganglionic blocking agents, negative inotropic agents, and inhaled anesthetics.

References :

1. Schulz ,V. Hypotensive efficacy of a mixed solution of 0.1% sodium nitroprusside and 1% sodium thiosulphate. *Journal of Hypertension* 1985;3:485-89
2. Hall, VA. Sodium nitroprusside induced cyanide intoxication and prevention with sodium thiosulfate prophylaxis. *AJCC* 1992;2:19-27
3. Schulz ,V. Clinical pharmacokinetics of nitroprusside, cyanide, thiosulphate and thiocyanate. *Clin Pharmacokinet.* 1984 May-Jun;9(3):239-51
4. Vesey, CJ. Blood cyanide and thiocyanate concentrations produced by long term therapy with sodium nitroprusside. *Br J Anesthesia.* 1985;57:148-51
5. Baskin, SI. The antidotal action of sodium nitrite and sodium thiosulfate against cyanide poisoning. *J Clin Pharmacol* 1992;32:368-75
6. Johanning, RJ. A retrospective study of sodium nitroprusside use and assessment of the potential risk for cyanide poisoning. *Pharmacotherapy* 1995;15(6):773-77
7. Cole PV. Sodium thiosulphate decreases blood cyanide concentrations after the infusion of sodium nitroprusside. *Br J Anaesth* 1997;59:531-35

Review of the Literature:

The lack of transplacental movement of the cyanide antidote thiosulfate in gravid ewes.

Graeme KA, Curry SC, Bikin DS, Lo Vecchio FA, Brandon TA.

Department of Medical Toxicology, Good Samaritan Regional Medical Center, Phoenix, Arizona, USA.

A previous study reported that the co-infusion of IV sodium thiosulfate (STS) with sodium nitroprusside (SNP) to near-term gravid ewes prevented both maternal and fetal cyanide toxicity. We questioned whether maternally administered STS crossed the ovine placenta to enhance fetal transsulfuration of cyanide, or whether the fetus was dependent on maternal detoxification of cyanide after diffusion of cyanide into the maternal circulation.

Ten anesthetized, near-term gravid ewes underwent hysterotomies with delivery of fetal heads for venous catheterization. Five control ewes received IV isotonic sodium chloride solution, whereas five experimental ewes received IV STS (50 mg/kg over 15 min). Serial plasma thiosulfate concentrations in ewes and fetuses were measured over 135 min. Areas under the time-plasma thiosulfate concentration curves were calculated for experimental and control ewes at 2758 ± 197 and 508 ± 74 min \times mg⁽⁻¹⁾ \times L⁽⁻¹⁾, respectively ($P < 0.008$).

Mean areas under the curve for experimental and control fetuses were 236 ± 34 and 265 ± 23 min \times mg⁽⁻¹⁾ \times L⁽⁻¹⁾, respectively ($P > 0.5$). Maternally administered STS may prevent fetal cyanide poisoning from SNP administration without relying on STS crossing the placenta into the fetal circulation. Fetal cyanide may cross down a concentration gradient from fetal to maternal circulation, to be transsulfurated to thiocyanate in maternal tissues. IMPLICATIONS: We evaluated the mechanism of action of sodium thiosulfide (STS) in sodium nitroprusside-induced cyanide toxicity in the ewe. Fetal cyanide poisoning is alleviated by maternal administration of STS, although this cyanide antidote apparently does not cross the placenta.

Prevention of fetal and maternal cyanide toxicity from nitroprusside with coinfusion of sodium thiosulfate in gravid ewes.

Curry SC, Carlton MW, Raschke RA.

Department of Medical Toxicology, Good Samaritan Regional Medical Center, Phoenix, Arizona 85006, USA.

Coadministration of sodium thiosulfate with sodium nitroprusside (SNP) to children and adults prevents increases in cyanide concentrations during anesthesia or long-term SNP infusions. We wondered whether maternally administered sodium thiosulfate would prevent increases in fetal red cell cyanide concentrations in gravid ewes receiving SNP infusions. Under anesthesia, the fetal head was delivered through a lateral hysterotomy for catheterization of the jugular vein; the fetus was left in utero. Six control ewes near term received SNP at 25 micrograms.kg⁻¹.min⁻¹ for 4 h. Norepinephrine was used to maintain maternal mean arterial pressure at 80% baseline values. Six experimental ewes received the same treatment except that sodium thiosulfate was infused with SNP (1 g sodium thiosulfate per 100 mg SNP). Serial red cell cyanide concentrations in ewes and fetuses were followed. One control fetal death resulted from abruptio placenta, and this ewe and fetus were excluded from analysis. An additional control ewe and fetus died from apparent cyanide poisoning late during the course of the experiment. While control ewes and fetuses suffered progressive increases in red cell cyanide concentrations into the toxic range, experimental ewes and fetuses never developed toxic red cell cyanide levels (ewes $P < .003$, fetuses $P < .004$). These data, if applicable to humans, suggest that coadministration of sodium thiosulfate with SNP to pregnant women at doses currently in use for nonpregnant patients will prevent fetal, as well as maternal, cyanide toxicity.

Pharmacotherapy. 1995 Nov-Dec;15(6):773-7. Related Articles, Links

A retrospective study of sodium nitroprusside use and assessment of the potential risk of cyanide poisoning.

Johanning RJ, Zaske DE, Tschida SJ, Johnson SV, Hoey LL, Vance-Bryan K.

College of Pharmacy, University of Minnesota, Minneapolis, USA.

Sodium nitroprusside (SNP) is an effective vasodilator but is potentially dangerous due to its cyanide content. Infusion rates above 2 micrograms/kg/minute may cause cyanide to accumulate to toxic concentrations in critically ill patients. Coadministration of thiosulfate with SNP effectively and safely prevents cyanide toxicity. This study determined if patients at our institution were treated with SNP infusion rates that could cause cyanide toxicity and whether those patients were administered thiosulfate. We reviewed the charts of 36 critically ill patients treated with SNP during the previous 12 months. In 72% of patients the SNP infusion rates were above 2 micrograms/kg/minute. In 47% the rates were greater than 2 micrograms/kg/minute for 6 hours or more, and in 20% they were greater than 5 micrograms/kg/minute for up to 11 hours. None of the patients was administered thiosulfate. In a significant number of patients the infusion rates of SNP potentially exposed them to significant risk of cyanide toxicity including death.

AmJCritCare. 1992Sep;1(2):19-25. Related Articles, Links

Sodium nitroprusside-induced cyanide intoxication and prevention with sodium thiosulfate prophylaxis.

Hall VA, Guest JM.

Department of Veterans Affairs Medical Center, Denver, Colo. 80220.

Sodium nitroprusside is an antihypertensive agent used frequently in the critical care setting. Recently, the Food and Drug Administration (FDA) published a report that led to a labeling change emphasizing the pharmacokinetics of nitroprusside with metabolism to highly toxic cyanide. Infusion rates greater than 2 mcg/kg/minute cause the serum concentration of cyanide to increase proportionately. Although evidence validates that cyanogenesis occurs with nitroprusside administration, prevention and treatment of cyanide poisoning is rarely instituted in clinical practice. Although evidence validates that cyanogenesis occurs with nitroprusside administration, prevention and treatment of cyanide poisoning is rarely instituted in clinical practice. Simultaneous infusion of thiosulfate with nitroprusside provides the sulfur donor necessary to prevent cyanide accumulation. Cyanide combines with thiosulfate to form the less toxic sodium thiocyanate, which is then excreted. A 10:1 ratio of nitroprusside to thiosulfate in the infusion eliminates the possibility of cyanide intoxication without altering the efficacy of nitroprusside.

JClinPharmacol. 1992 Apr;32(4):368-75. Related Articles, Links

The antidotal action of sodium nitrite and sodium thiosulfate against cyanide poisoning.

Baskin SI, Horowitz AM, Nealley EW.

The combination of sodium thiosulfate and sodium nitrite has been used in the United States since the 1930s as the primary antidote for cyanide intoxication. Although this combination was shown to exhibit much greater efficacy than either ingredient alone, the two compounds could not be used prophylactically because each exhibits a number of side effects. Sodium thiosulfate was the first compound reported to be an effective antidote for cyanide poisoning. It serves as a good source of sulfur to overcome the rate-limiting availability of endogenous sulfur for the conversion of cyanide to the less toxic and excretable thiocyanate. In moderate cyanide poisoning, sodium thiosulfate has been successfully used as monotherapy. It undergoes rapid elimination, and therefore high plasma levels are needed for treatment of cyanide toxicity. In order to be effective a threefold higher concentration of thiosulfate is required as compared with cyanide. The standard dose is 50 ml of a 250mg/ml (25%) solution IV. Sodium thiosulfate is not well absorbed orally and so therefore must be given by IV. Nausea and vomiting have been documented with rapid IV administration and osmotic disturbances and cathartic activity represent some other potential adverse effects. Fortunately, at high plasma concentrations, sodium thiosulfate does not show significant toxic effects. This review discusses the pharmacodynamics, pharmacokinetics, and toxicology of the individual agents, and their combination.

Br J Anaesth. 1987 May;59(5):531-5.

Sodium thiosulphate decreases blood cyanide concentrations after the infusion of sodium nitroprusside.

Cole PV, Vesey CJ.

Plasma and red cell cyanide, and plasma thiocyanate, concentrations were measured in 30 patients undergoing elective nitroprusside-induced hypotension. One randomly selected group (n = 15), who received 0.21-0.70 mg kg⁻¹ over periods of 50-160 min, were given a bolus of sodium thiosulphate 10.6-38.5 mg kg⁻¹ immediately on cessation of the nitroprusside administration. The other group, who received infusions of 0.11-0.85 mg kg⁻¹ for periods of 59-197 min, received no antidote. Cyanide concentrations, expressed as a percentage of the immediate post-infusion values, were significantly lower in the treated group in all subsequent blood samples (at 10, 30 and 60 min; plasma cyanide P less than 0.05; red cell cyanide P less than 0.001). Improved cyanide metabolism was further demonstrated by a sharp increase in mean plasma thiocyanate concentration (P less than 0.05) in the group receiving the antidote.

JHypertens.1985 Oct;3(5):485-489. Related Articles, Links

Hypotensive efficacy of a mixed solution of 0.1% sodium nitroprusside and 1% sodium thiosulphate.

Schulz V, Loeschcke G.

A mixed solution of 0.1% sodium nitroprusside and 1% sodium thiosulphate (50 mg sodium nitroprusside and 500 mg of sodium thiosulphate -'SNP-thiosulphate') was given as i.v. infusion to 80 patients, 30 of whom were hypertensive emergencies and 50 were surgical cases requiring induction of hypotension. This treatment lowered the blood pressure (BP) by an average of 30% of the initial levels in the hypertensive patients and 30-40% of the initial levels in the surgical patients. The mean effective dose in the hypertensive patients was 2.4 micrograms/kg/min compared with about 3 micrograms/kg/min in 40 cases treated with sodium nitroprusside as mono-infusion. For deliberate hypotension in surgical patients the mean doses of SNP, used here in the mixed infusion with thiosulphate, were 1.0 and 2.3 micrograms/kg/min, compared with 1.3-7.5 micrograms/kg/min in 181 patients treated with SNP as monotherapy. In contrast to conventional therapy with SNP, the infusion of SNP-thiosulphate even at extremely high dose rates did not produce toxic concentrations of prussic acid in the blood. In no case was a rise observed in the cellular enzymes as an indirect indication of hypoxic cell damage. SNP-thiosulphate is thus at least as effective at lowering BP as SNP infused alone, and has a substantially lower toxicity risk.

Treatment of 30 hypertensive emergencies with SNP-thiosulphate.

Age, Mean (range)	Sex	Mean blood pressure before (mmHg)	Mean blood pressure during (mmHg)	Mean duration of treatment, hours (range)	Mean Total Sodium Nitroprusside Dose, mg (range)	Mean rate Sodium Nitroprusside Infusion Rate (mcg/kg/min) (range of means for individual patients)	Mean maximum rate SNP (mcg/kg/min) (range of maximum for individual patients)	Mean Serum Thiocyanate (nmol/ml) (range)
47 (1-71) years	20 males, 10 females	212 ± 28 114 ± 20	145 ± 14 83 ± 9	100 (6-432)	1110 (14-5160)	2.4 (0.2-7.1)	5.8 (0.5-21.4)	549 (50-1659)

Table 1. Treatment of 30 hypertensive emergencies with SNP-thiosulphate. Mean percentage reduction of blood pressure approximately 30%, duration of treatment up to 17 days, mean total dose >1g SNP. There was no appreciable cyanide (CN) accumulation and no rise in enzyme levels.

Case	Age (sex)	Hypertensive emergencies	Blood pressure		SNP-thiosulphate				GOT (IU)			
			Before (mmHg)	During (mmHg)	Duration (h)	SNP (mg)	Rate SNP ($\mu\text{g}/\text{kg}/\text{min}$)		CN ⁻ (nmol/ml)	SCN ⁻ (nmol/ml)	Before	During
							Mean	Maximum	RBC PLASMA			
1	16 (f)	Hypertensive encephalopathy	180/90	140/70	122	3800	7.1	16.0	22	1450	22	26
2	37 (m)	Intracranial haemorrhage	200/110	150/90	140	1120	1.9	2.1	10	460	9	7
3	80 (f)	Acute left ventricular failure	250/160	160/80	55	180	0.8	2.2	9	410	11	13
4	70 (m)	Acute aortic dissection	200/120	120/80	139	1780	3.0	4.9	14	1194	53	66
5	40 (m)	Malignant hypertension	240/130	150/90	92	810	2.1	2.8	11	371	12	8
6	66 (m)	Head injury	200/100	150/80	114	2210	2.3	8.1	19	739	14	21
7	65 (m)	Acute left ventricular failure	220/90	140/80	12	48	1.0	1.2	5	151	22	31
8	1 (m)	Hypertensive encephalopathy	190/120	120/80	38	17	0.2	4.0	3	364	3	4
9	73 (m)	Acute left ventricular failure	220/120	140/90	12	14	0.3	0.5	1	112	15	12
10	31 (f)	Eclampsia	240/120	150/80	147	4230	6.9	8.3	22	1505	22	8
11	67 (f)	Acute left ventricular failure	260/100	150/80	80	960	2.9	6.1	14	746	6	6
12	21 (f)	Hypertensive encephalopathy	190/110	150/90	89	1780	4.8	8.3	19	1008	12	7
13	65 (m)	Acute aortic dissection	180/80	130/70	126	1260	2.4	3.8	5	455	14	16
14	43 (m)	Acute aortic dissection	200/100	140/80	258	5160	4.8	5.8	14	1659	8	11
15	24 (f)	Malignant hypertension	200/130	160/90	152	1640	2.9	7.4	7	830	22	28
16	12 (f)	Hypertensive encephalopathy	180/110	140/80	31	328	4.2	11.2	9	343	7	13
17	29 (m)	Post-operative bleeding	220/120	150/90	9	64	1.2	6.0	1	336	46	37
18	61 (m)	Acute aortic dissection	170/80	120/60	432	900	0.5	1.9	15	637	19	17
19	28 (f)	Malignant hypertension	220/140	150/90	18	50	0.7	2.0	1	98	21	7
20	53 (m)	Malignant hypertension	190/120	150/90	112	835	1.8	3.4	3	726	8	8
21	52 (m)	Acute myocardial infarction	170/80	130/70	102	92	0.2	0.9	1	60	72	10
22	64 (m)	Acute myocardial infarction	180/90	130/70	22	60	0.6	2.2	1	60	76	36
23	71 (m)	Acute left ventricular failure	180/90	130/70	9	72	1.4	3.6	1	264	14	19
24	26 (m)	Malignant hypertension	190/110	160/95	13	205	3.4	6.8	2	290	7	12
25	48 (m)	Acute aortic dissection	230/130	160/90	13	205	3.4	6.8	2	290	7	12
26	74 (f)	Malignant hypertension	220/110	150/90	92	1200	5.0	21.4	9	357	64	50
27	43 (f)	Malignant hypertension	260/140	180/100	7	40	1.4	6.6	4	168	24	21
28	66 (m)	Malignant hypertension	240/120	140/80	6	60	2.6	3.1	1	106	8	13
29	19 (m)	Hypertensive encephalopathy	240/120	140/80	47	880	3.8	8.6	10	535	9	14
30	67 (m)	Intracranial haemorrhage	250/150	160/90	47	880	3.8	8.6	10	535	9	14
			240/120	140/80	408	3100	2.0	4.2	7	648	7	11
			240/110	140/70	107	410	0.9	9.5	12	389	14	42
Mean \pm s.e.m. (47 \pm 22 years, 20 males, 10 females)			212 \pm 26/ 114 \pm 20	145 \pm 14/ 83 \pm 9	100 \pm 106	1110 \pm 1365	2.4 \pm 1.9	5.6 \pm 4.5	8.4 \pm 7.0	549 \pm 438	21 \pm 20	19 \pm 15

GOT, glutamic-oxaloacetic transaminase.

Table 2. Induction of hypotension with infusion of SNP-thiosulphate in 50 patients during surgery.

	Neurosurgery mean \pm s.e.m. (range)	Cardiac surgery mean \pm s.e.m. (range)
Number of cases (male/female)	30 (17/13)	20 (14/6)
Blood pressure		
Systolic before	142 \pm 31 (100-230)	148 \pm 11 (130-170)
Systolic during	87 \pm 21 (60-150)	99 \pm 11 (80-120)
Diastolic before	81 \pm 12 (60-110)	85 \pm 12 (70-110)
Diastolic during	47 \pm 12 (40-80)	57 \pm 10 (40-80)
SNP-thiosulphate infusion		
Duration (min)	91 \pm 61 (20-260)	88 \pm 62 (20-230)
Total dose (mg SNP)	14 \pm 16 (2-72)	6 \pm 5 (1-22)
Maximum rate SNP ($\mu\text{g}/\text{kg}/\text{min}$)	3.3 \pm 2.7 (0.7-10)	1.8 \pm 2.2 (0.5-10)
Mean rate SNP ($\mu\text{g}/\text{kg}/\text{min}$)	2.3 \pm 1.9 (0.4-7.1)	1.0 \pm 0.5 (0.1-2)

BrJAnaesth. 1985 Feb;57(2):148-55. Related Articles, Links

Blood cyanide and thiocyanate concentrations produced by long-term therapy with sodium nitroprusside. Vesey CJ, Cole PV.

Blood cyanide (HCN) or plasma thiocyanate (SCN) concentrations, or both, were measured in 30 patients (ages 11 months-72 yr) receiving sodium nitroprusside (SNP) for 12-314 h. Sequential measurements in three of these patients (infused 5, 12 and 13 days) showed that HCN concentrations varied with dose rate, while SCN concentrations increased linearly with increasing SNP dose. The average duration of infusion for sodium nitroprusside was 100 h (ranging from 6 hours to 432 hours) and the average cyanide level was 8.4 nmol/ml (ranging from 1 nmol/ml to 22 nmol/ml; potentially toxic is >19.25 nmol/ml). The accumulated data confirmed that the rate of administration (0.3-6.5 micrograms kg⁻¹ min⁻¹) determined the plasma HCN concentrations (0-3.8 mumol litre⁻¹; y = 0.267 X -0.0733; r = 0.64; n = 51; P less than 0.001). Thus, if prolonged exposure to plasma HCN concentrations greater than 1 mumol litre⁻¹ is to be avoided, the maximum safe sustained dose

rate of SNP will lie near to 4 micrograms kg⁻¹ min⁻¹. In addition the maximum total dose of sodium nitroprusside, in patients with normal renal function, should be around 70 mg/kg for less than 14 days. Likewise, the SCN results (30--880 mumol litre⁻¹) confirmed the close relationship between plasma concentrations and the total SNP dose (0.44-32.9 mg kg⁻¹; $y = 24.6x + 74.9$; $r = 0.95$, $n = 51$, P less than 0.001). The thiosulphate, infused with the sodium nitroprusside at a dose ration of 10:1, involved no additional risk to the patient. However, when sodium nitroprusside is infused for several days at medium dosage rates (2-5 mcg/kg/minute), toxic levels of thiocyanate can occur after 7 to 14 days of infusion in patients with normal renal function. In patients with severely restricted renal function toxicity can be expected after about 3-6 days. Therefore, we suggest that, to avoid SCN toxicity (plasma SCN greater than 1.75 mumol litre⁻¹), in the absence of SCN monitoring, the total SNP dose should be less than 70 mg kg⁻¹ in patients with normal renal function.

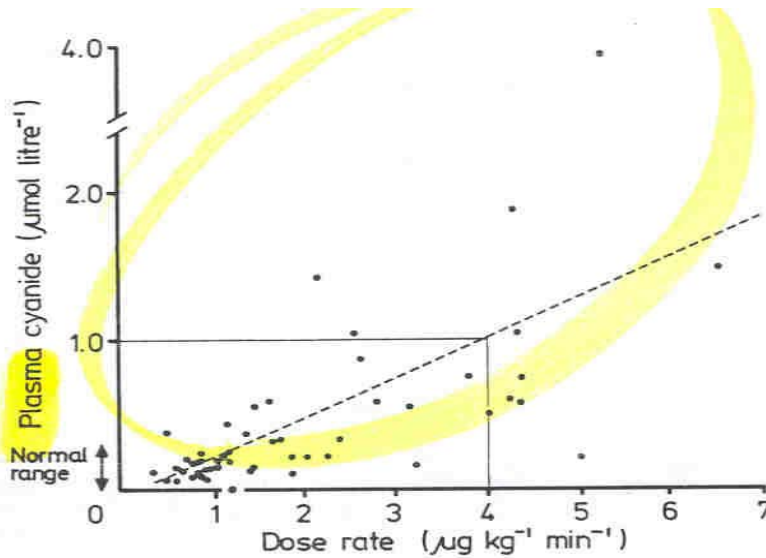


FIG. 4. Plasma cyanide (HCN) concentrations obtained from 24 of the patients, plotted against the nitroprusside (SNP) infusion rates. Correlation: $r = 0.64$, $n = 51$, $P < 0.001$; $y = 0.267x - 0.0733$. The diagram also indicates that a critical value of HCN 1 $\mu\text{mol litre}^{-1}$ in plasma corresponds to an infusion rate of SNP 4 $\mu\text{g kg}^{-1} \text{min}^{-1}$.

Lethal 9 micromole/liter

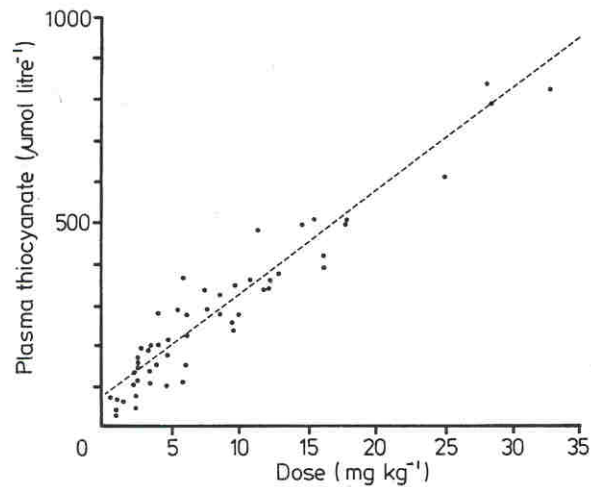


FIG. 6. Plasma thiocyanate (SCN) concentrations, recorded in 27 patients, plotted against sodium nitroprusside (SNP) dose. Correlation: $r = 0.95$, $n = 51$, $P < 0.001$, $y = 24.6x + 74.9$. Assuming the linear relationship between plasma thiocyanate and nitroprusside dose holds at higher values, extrapolation suggests that a critical value of SCN $1725 \mu\text{mol litre}^{-1}$ in plasma corresponds to an infused dose of SNP 70 mg kg^{-1} .

Clin Pharmacokinet. 1984 May-Jun;9(3):239-51.

Clinical pharmacokinetics of nitroprusside, cyanide, thiosulphate and thiocyanate.

Schulz V.

Sodium nitroprusside decomposes within a few minutes after intravenous infusion to form metabolites which are pharmacologically inactive but toxicologically important. Free cyanide, which represents 44% w/w of the sodium nitroprusside molar mass, is formed and must be detoxified in the body into thiocyanate using thiosulphate as substrate. Nitroprusside penetrates cell membranes slowly. At therapeutic dose levels its distribution is probably mainly extracellular. Contact with the sulphhydryl groups in the cell walls, however, immediately initiates breakdown of the molecule. Sodium nitroprusside taken orally is not absorbed from the gastrointestinal tract to any appreciable extent. Cyanides in the body form prussic acid, which can rapidly penetrate mucous and cell membranes. In the blood, about 99% of the prussic acid binds to the methaemoglobin of erythrocytes. At normal physiological levels, however, the total body methaemoglobin of an adult human can only bind about 10mg of prussic acid; this is a small fraction of the amounts usually infused therapeutically as sodium nitroprusside. The endogenous detoxification of prussic acid exhibits zero-order kinetics. The limiting factor is a sulphur donor, principally thiosulphate, which is available in the body in only limited amounts. The rate of spontaneous detoxification of prussic acid in humans is only about 1 microgram/kg/min, corresponding to a sodium nitroprusside infusion of about 2 microgram/kg/min. This dose limit set by the prussic acid toxicity of sodium nitroprusside can, however, be increased considerably by simultaneous infusion of thiosulphate. A

lack of thiosulphate can be detected early by a rise of the prussic acid concentration in the erythrocytes. Thiosulphate taken orally is not absorbed by the body. After intravenous infusion, its serum half-life is about 15 minutes. Most of the thiosulphate is oxidised to sulphate or is incorporated into endogenous sulphur compounds; a small proportion is excreted through the kidneys. Thiocyanate taken orally is completely absorbed by the body. In healthy persons its volume of distribution is approximately 0.25 L/kg and the serum half-life about 3 days; elimination is mainly renal. Thiocyanate toxicity does not represent a serious therapeutic problem with intravenous infusion of sodium nitroprusside.

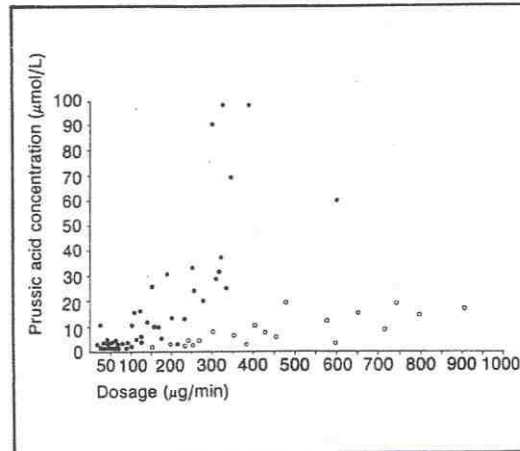


Fig. 2. Maximum prussic acid concentrations in the erythrocytes during therapy with sodium nitroprusside as a function of the mean dosage (● = sodium nitroprusside 'monoinfusion'; ○ = sodium nitroprusside + thiosulphate 'mixed infusion'). Treatment was for deliberate hypotension in 50 patients, for hypertensive crisis in 17 patients, and for dissecting aortic aneurysm in 3 patients (after Schulz et al., 1982).

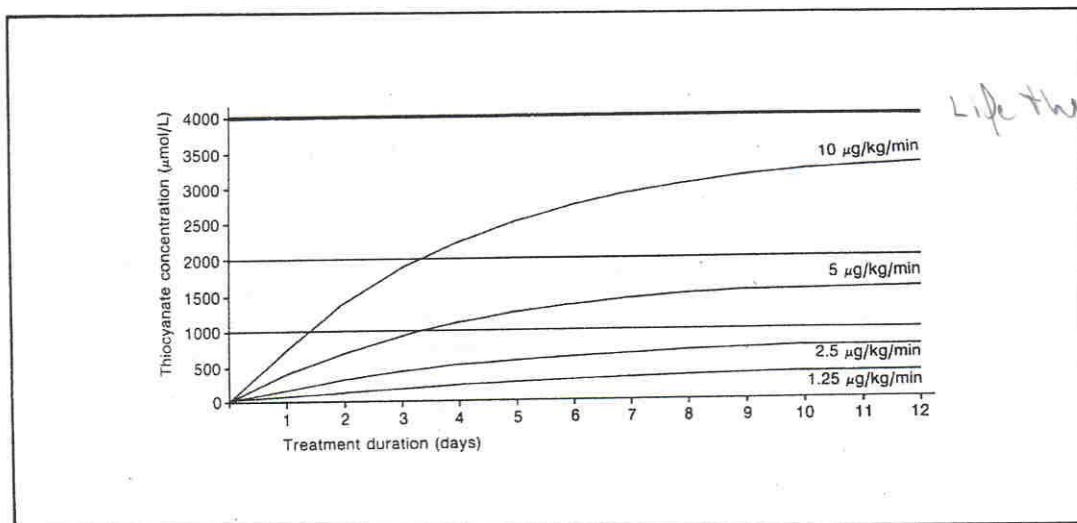


Fig. 3. Prospective accumulation of thiocyanate with monoinfusion or mixed infusion of sodium nitroprusside 1.25 to 10 µg/kg/min in patients with normal renal function. Normal physiological thiocyanate level, 50-250 µmol/L; at 1000 µmol/L, slight symptoms possible; at 2000 µmol/L, more serious symptoms; at 4000 µmol/L, life-threatening intoxication (after Schulz et al., 1979b).

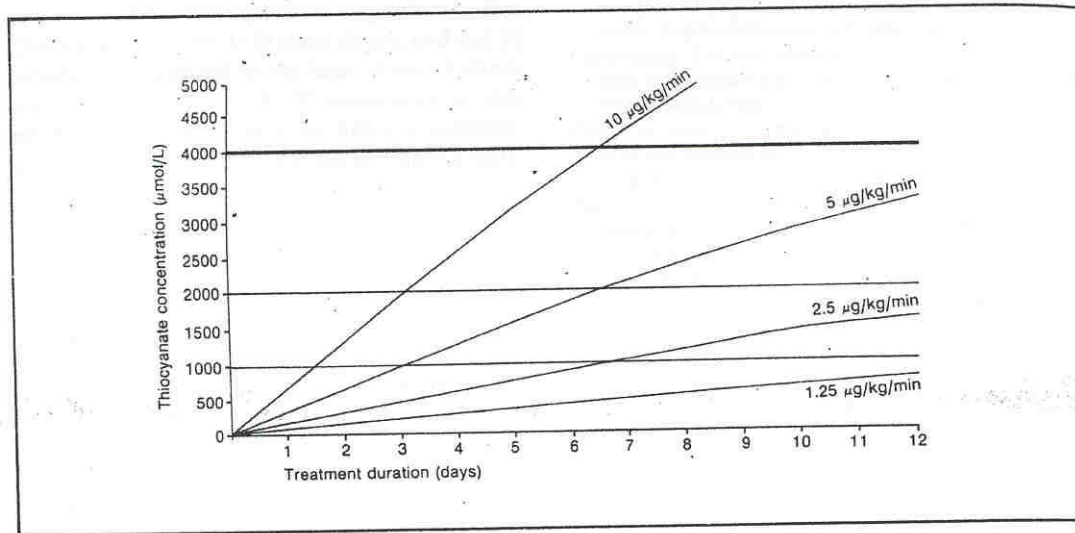


Fig. 4. Prospective accumulation of thiocyanate in anuric patients. Details as for figure 3.

Nephrol Dial Transplant. 2004 Jun;19(6):1474-9. Epub 2004 Feb 19.

Accumulation of cyanide and thiocyanate in haemodialysis patients.

Hasuike Y, Nakanishi T, Moriguchi R, Otaki Y, Nanami M, Hama Y, Naka M, Miyagawa K, Izumi M, Takamitsu Y.

Department of Internal Medicine, Division of Kidney and Dialysis, Hyogo College of Medicine, Japan.

BACKGROUND: Cyanide is a toxic agent, and its detoxification product, thiocyanate, may be a major pathogenetic substance in uraemia. Recent studies examining the myeloperoxidase(MPO)/thiocyanate system have suggested a link between thiocyanate and atherosclerosis. However, inaccuracies in conventional assays for cyanide and thiocyanate have limited the understanding of their metabolism in haemodialysis (HD) patients.

METHODS: We used high-performance liquid chromatography to measure cyanide in erythrocytes and thiocyanate in plasma in 43 HD patients and in a group of 46 healthy controls that included 15 current smokers.

To clarify the metabolic conversion of cyanide to thiocyanate in uraemic patients, we also measured cysteine and sulfate. We then used stepwise regression analysis to analyse factors that determine erythrocyte cyanide and plasma thiocyanate. **RESULTS:** Mean cyanide and thiocyanate were significantly greater in HD patients than in non-smoking controls. However, cyanide was far below lethal concentrations in dialysis patients. Thiocyanate was six to seven times greater in HD patients than in non-smoking controls, and decreases in thiocyanate following dialysis were only 19.3+/-3.5%. Multiple regression analysis showed a positive correlation between cyanide and thiocyanate in controls, but a negative correlation in HD patients. In patients, an inverse relationship between thiocyanate and BUN was also observed. **CONCLUSIONS:** The elevation of thiocyanate in patients undergoing dialysis probably is secondary to both limited efficiency of HD and deranged metabolism of cyanide and thiocyanate. Because thiocyanate is a preferred substrate for MPO, it may play a role in uraemic complications including cardiovascular events.

Intern Med. 2001 Sep;40(9):936-9.

Massive rhabdomyolysis and acute renal failure after acetonitrile exposure.

Muraki K, Inoue Y, Ohta I, Kondo K, Matayoshi Y, Kamei T.

Department of Internal Medicine, Yamaguchi Prefecture General Hospital, Hofu.

A case of systemic rhabdomyolysis after acetonitrile exposure is reported. A 35-year-old previously healthy man suffered from vomiting, convulsion and consciousness loss 15 hours after exposure to acetonitrile. Since acetonitrile is known to be metabolized into cyanide, antidote therapy against cyanide poisoning was given. On admission, pain and all-over muscle swelling were marked. Although the initial therapy was effective, rhabdomyolysis and then acute renal failure developed. Renal function improved very slowly after six weeks of hemodialysis, but atrophy of the muscles remained. The rhabdomyolysis may have been caused by toxicity of the cyanide itself in combination with hypoxia and convulsion.

Am J Emerg Med. 1991 May;9(3):264-7.

Severe cyanide poisoning from the ingestion of an acetonitrile-containing cosmetic.

Turchen SG, Manoguerra AS, Whitney C.

San Diego Regional Poison Center, University of California San Diego Medical Center 92103.

A 39-year-old woman ingested 59 mL of Super Nail Nail Off (American International Industries, Hollywood, CA) (containing 99% acetonitrile) in a suicide attempt. Following a latent period of approximately 12 hours, the patient developed cyanide poisoning with severe metabolic acidosis, seizures, and shallow respirations. She responded to the administration of sodium nitrite and sodium thiosulfate, although the administration of nitrite produced bradycardia and hypotension. She developed several relapses over the course of her hospitalization and each time responded to sodium thiosulfate administration. The patient developed hypernatremia from the sodium load given to her; hemodialysis and charcoal hemoperfusion were initiated to correct the hypernatremia and to attempt to remove cyanide, thiocyanate, and acetonitrile. On the fifth hospital day, the patient was fully recovered and was discharged.

Int J Artif Organs. 1989 Jun;12(6):347-55

Cyanide poisoning: pathophysiology and current approaches to therapy.

Gonzales J, Sabatini S.

Texas Tech University Health Sciences Center, Dep. of Internal Medicine, Lubbock.

Considering the difficulties following the administration of nitrites (or aminophenols) or cobalt-EDTA as well as the ineffectiveness of hydroxycobalamin and pyruvate, we feel that a more sensible treatment for acute cyanide intoxication is hemodialysis combined with the intravenous administration of sodium thiosulfate. The addition of hemodialysis to such a regimen is helpful in three ways. First, it removes the small extracellular reservoir of cyanide, particularly if the poison is still being absorbed from the gastrointestinal tract. Second, it corrects the severe lactic acidosis seen in virtually all cases of cyanide toxicity. As with most poisons death from metabolic acidosis alone is likely. Third, the removal of thiocyanate, the end product of cyanide metabolism, results in a maneuver which should decrease both tissue and plasma cyanide levels. The immediate treatment of acute cyanide intoxication is supportive, as it is with most all drugs and poisons. Gastric lavage using activated charcoal should be initiated immediately to remove any remaining cyanide in the gastrointestinal tract. Simultaneously, high flow oxygen should be administered either by nasal cannula or by endotracheal intubation. Correction of the metabolic acidosis should be instituted with bicarbonate. Immediate hemodialysis should be performed with the concomitant administration of thiosulfate. Animal studies suggest that continuous infusion of thiosulfate (12 mg/kg/hr) is more effective for treating cyanide intoxication than is bolus administration (41, 51). Bolus administration is the currently recommended form of thiosulfate therapy in humans. The Lilly kit contains a 50 ml ampule of thiosulfate having 12.5 gm, which in adults may be repeated once at one-half the dose.(ABSTRACT TRUNCATED AT 250 WORDS)

J Med. 1988;19(5-6):345-51

Cyanide and thiocyanate blood levels in patients with renal failure or respiratory disease.

Cailleux A, Subra JF, Riberi P, Tuchais E, Premel-Cabic A, Allain P.

Laboratoire de Pharmacologie, C.H.U., Angers, France.

Whole blood cyanide and plasma thiocyanate were measured by a headspace gas chromatographic method and a colorimetric method, respectively, in 16 healthy subjects, in 10 patients with respiratory disease and in 12

patients on chronic dialysis for renal failure. In healthy subjects, whole blood cyanide and plasma thiocyanate concentrations were significantly higher in smokers (1.8 +/- 0.4 mumol/l; 206 +/- 74 mumol/l) than in non-smokers (0.8 +/- 0.4 mumol/l; 74 +/- 19 mumol/l). In renal failure patients on hemodialysis, no difference was noted in cyanide levels (0.6 +/- 0.4 mumol/l), but there was a significant increase in plasma thiocyanate levels during the interdialysis period (62 +/- 24 mumol/l; 91 +/- 24 mumol/l). No difference in cyanide and thiocyanate levels of patients with respiratory disease was seen, in agreement with a weak pulmonary elimination of cyanide.

Am J Nephrol. 1985;5(2):121-6.

Treatment of acute cyanide intoxication with hemodialysis.

Wesson DE, Foley R, Sabatini S, Wharton J, Kapusnik J, Kurtzman NA.

A dramatic response was noted in a patient at our hospital who received hemodialysis therapy for severe acidosis secondary to an unknown toxin, subsequently identified as cyanide. We were unable to find any information concerning the hemodialysis clearance and extraction ratio of cyanide; thus, we studied the effect of hemodialysis in dogs receiving a constant infusion of cyanide with and without a simultaneous infusion of thiosulfate. The hemodialysis clearance of cyanide in the presence of thiosulfate was 38.3 +/- 5.4 ml/min with an extraction ratio of 0.43 +/- 0.06 (n = 4). Hemodialysis was found to increase the lethal dose of cyanide without thiosulfate infusion, and a further increase was noted with the thiosulfate infusion. Thiosulfate promotes mitochondrial metabolism of cyanide to thiocyanate. The end product, thiocyanate, is quickly removed by hemodialysis. We believe that the demonstrated effectiveness of hemodialysis in the treatment of acute cyanide intoxication is related not only to the hemodialysis clearance of cyanide, but also to the removal of its metabolic end product, thiocyanate. Based on our observations, we feel that hemodialysis is an effective adjunct in the treatment of acute cyanide intoxication.

J Toxicol Clin Toxicol. 1982 Nov;19(9):965-74.

In-vivo and in-vitro hemodialysis studies of thiocyanate.

Pahl MV, Vaziri ND.

Dialysis clearance of thiocyanate was studied using in-vivo and in-vitro systems. The in-vivo studies were performed in a patient with renal failure receiving sodium nitroprusside infusion for accelerated hypertension. In-vitro studies were carried out under experimental conditions similar to those of the in-vivo experiment. Plasma thiocyanate level consistently fell with single passage through the dialyzer. In-vivo dialysance of thiocyanate averaged 82.8 ml/min as compared to urea dialysance of 129.6 ml/min. The in-vitro studies revealed an average thiocyanate dialysance of 102.3 as compared to a urea dialysance of 138.6 ml/min. Removal of thiocyanate by hemodialysis was further verified by recovery of significant amounts of thiocyanate in the outgoing dialysate. The thiocyanate clearance calculated directly from the amount recovered in the dialysate and mean plasma concentration was 82.2 ml/min, a value closely approximating that obtained using the transdialyzer concentration gradient. We conclude that hemodialysis is effective in removing thiocyanate and can be used as adjunct in the treatment of thiocyanate toxicity particularly in the presence of renal failure in which thiocyanate excretion is impaired.

J Toxicol Clin Toxicol. 1982 Jul;19(5):475-82.

Combined antidotal and hemodialysis treatments for nitroprusside-induced cyanide toxicity.

Marbury TC, Sheppard JE, Gibbons K, Lee CS.

A case report is presented for a patient with nitroprusside-induced cyanide intoxication. The patient received approximately 1 g sodium nitroprusside through an intravenous infusion of the drug over 6 d. The toxicity was treated with antidotes, sodium nitrite and sodium thiosulfate, followed by hemodialysis. Hemodialysis significantly removed thiocyanate but not cyanide from the patient's extracorporeal circulation. The removal of thiocyanate by hemodialysis enhanced the liberation of cyanide from the cytochrome oxidase. Hemodialysis is a significant addition to the therapy of cyanide toxicity, particularly for intoxicated patient with reduced renal function

Am J Dis Child. 1978 Oct;132(10):988-9.

Prolonged nitroprusside and intermittent hemodialysis as therapy for intractable hypertension.

Elberg AJ, Gorman HM, Baker R, Wenger AJ, Strauss J.

Nitroprusside was used with intermittent hemodialysis over a 26-day period in a 6-year-old boy with intractable hypertension. Hemodialysis effectively removed thiocyanate from the blood, thus preventing its accumulation and subsequent toxic manifestations. Prolonged nitroprusside infusion maintained arterial blood pressure at acceptable levels until the patient became responsive to other antihypertensive therapy.

Forensic Sci. 1974 Aug;4(1):87-9.

Acute renal failure following potassium ferrocyanide poisoning treated with peritoneal dialysis.

Nagaratnam N, Alagaratnam K, Thambapillai AJ, Wijemanne HS.