Case report
DOI: 10.3345/kjp.2010.53.8.805
Korean J Pediatr 2010;53(8):805-808

Successful treatment by exchange transfusion of a young infant with sodium nitroprusside poisoning

Jong Geun Baek, M.D., Hoar Lim Jeong, M.D., Ji Sook Park, M.D., Ji Hyun Seo, M.D., Eun Sil Park, M.D., Jae Young Lim, M.D., Chan Hoo Park, M.D., Hyang Ok Woo, M.D., Hee Shang Youn, M.D., and Jung Sook Yeom, M.D.

Department of Pediatrics, Gyeongsang National University School of Medicine, Jinju, Korea

Received: 23 March 2010, Revised: 19 April 2010
Accepted: 25 May 2010
Corresponding author: Jung Sook Yeom, M.D.
Department of Pediatrics, Gyeongsang National University School of Medicine, 92 Chilam-dong, Jinju 660-751, Korea
Tel: +82.55-750-8161, Fax: +82.55-752-9339
E-mail: polo96@daum.net

Although sodium nitroprusside (SNP) is often used in pediatric intensive care units, cyanide toxicity can occur after SNP treatment. To treat SNP-induced cyanide poisoning, antidotes such as amyl nitrite, sodium nitrite, sodium thiosulfate, and hydroxycobalamin should be administered immediately after diagnosis. Here, we report the first case of a very young infant whose SNP-induced cyanide poisoning was successfully treated by exchange transfusion. The success of this alternative method may be related to the fact that exchange transfusion not only removes the cyanide from the blood but also activates detoxification systems by supplying sulfur-rich plasma. Moreover, exchange transfusion replaces cyanide-contaminated erythrocytes with fresh erythrocytes, thereby improving the blood's oxygen carrying capacity more rapidly than antidote therapy. Therefore, we believe that exchange transfusion might be an effective therapeutic modality for critical cases of cyanide poisoning.

Key words: Nitroprusside, Exchange transfusion, Cyanides, Poisoning, Detoxification, Infant

Introduction

The sodium nitroprusside (SNP) is often used in pediatric intensive care units because of its strongly antihypertensive properties[1] and various pharmacokinetic advantages[2]. However, cyanide toxicity, the most lethal complication, can occur after SNP treatment. Antidotal therapy is the treatment of choice in cases of cyanide poisoning. In general, exchange transfusion can be useful in poisoning cases because it activates the detoxification systems and removes some of the toxic agents from the blood more rapidly than does antidote therapy. Here, we report the first case of a 2-month-old infant whose SNP-induced cyanide poisoning was successfully treated by exchange transfusion rather than by the use of antidotes.

Case report

A 2-month-old male infant was brought to the emergency room due to cough, fever, and dyspnea. At the time of presentation to the emergency room, the following vital signs were recorded: blood pressure, 95/40 mmHg; pulse rate, 187/min; respiration rate, 66/min; and body temperature, 37.8℃. Oxygen saturation was 80% in room air. A chest X-ray revealed consolidation in the right lung. Venous blood gas analysis showed the following results: pH, 7.23; carbon dioxide partial pressure (pCO_2), 65 mmHg; and oxygen partial pressure (pO_2), 18 mmHg. The white blood cell (WBC) count and hemoglobin level were 8,300/mm^3 and 10.7 g/dL, respectively. The C-reactive protein (CRP) level was markedly increased (111 mg/L). The infant developed serious dyspnea and failed to maintain oxygen saturation; he subsequently underwent

mechanical ventilation after being hospitalized in the intensive care unit. He was diagnosed to have aspiration pneumonia and was treated with antibiotics and an anti-inflammatory dose of steroids.

Several hours after admission, his blood pressure increased to 110/70 mmHg. To control his blood pressure, treatment with nitroglycerin was started. However, 2 days after admission, the infant's blood pressure further increased to 120/80 mmHg after methylprednisolone pulse therapy, which was administered to control pneumonia that had worsened and progressed to acute respiratory distress syndrome. Despite nitroglycerin infused to its maximal level, the infant's blood pressure failed to normalize. Thus, SNP was started and maintained with 2.4 μg/(kg · min) until SNP-induced cyanide poisoning was diagnosed (on the ninth day of hospitalization). In an evaluation study for hypertension, there was no evidence of kidney or heart disease. On the seventh day after admission, extubation was performed, and arterial blood gas analysis finding was within the normal range. By the eighth day of hospitalization, SNP continued to be infused at a rate of 2 μg/(kg · min), and arterial blood gas analysis revealed high anion gap metabolic acidosis with compensatory respiratory alkalosis (pH, 7.44; pCO_2, 19 mmHg; pO_2, 120 mmHg; and bicarbonate level, 11 mmol/L); however, respiratory distress symptoms were not observed.

However, 1 day later, on the ninth day of admission, the respiratory rate increased gradually, and the patient showed symptoms of air hunger, moaning sound, nasal flaring, and irritability. The heart rate increased to 190/min. And the patient had myoclonic seizures. The infant's skin was cherry-red in color, and arterial blood gas analysis revealed a worsening of the high anion gap metabolic acidosis (pH, 7.27; pCO_2, 12 mmHg; pO_2, 281 mmHg; and bicarbonate level, 5 mmol/L). Although the plasma lactic acid level exhibited a marked increase to 122 mmol/L, lung sounds were normal, and a chest X-ray revealed improvement in the pneumonic infiltration. No evidence of sepsis or severe sepsis was found; there was no fever, normal WBC count (7,280/mm^3) and hypertension rather than hypotension. The infection or inflammation was controlled (CRP was markedly decreased to 3.5 mg/dL). Thus, SNP toxicity was diagnosed, and SNP infusion was stopped. Since a suitable antidote drug was not available, we performed an exchange transfusion immediately after SNP toxicity was diagnosed. After one volume of exchange transfusion, the acidosis improved to a pH of 7.44, a pCO_2 of 25 mmHg, a pO_2 of 118 mmHg, and a bicarbonate level of 17 mmol/L. However, tachypnea was still observed and the pCO_2 level was low. Plasma lactate was markedly decreased but not yet normalized (40 mmol/L). Consequently, a second volume of exchange transfusion was administered. Thereafter, the blood gas and plasma bicarbonate levels normalized (pH, 7.43; pCO_2, 35 mmHg; and bicarbonate level, 23 mmol/L), plasma lactate was further decreased (31 mmol/L), the respiratory rate stabilized, and the patient improved clinically (Fig. 1). The infant was discharged from the hospital on the 20th day after hospitalization without any neurological deficits.

Discussion

Although SNP has been used safely to treat many neonates[3], infants[4] and children[5], cyanide intoxication should be considered if unexplained tachypnea, tachycardia, lactic acidosis, irritability, and seizures occur after SNP administration[6]. Reported risk factors associated with cyanide toxicity from SNP administration include prolonged infusion duration and/or high doses of SNP[7], as indicated by several cases of cyanide toxicity in patients who had received more than 2 μg/(kg · min) SNP or had been infused for more than 24 hours[5, 8]. Moreover, children and neonates may be more susceptible to cyanide toxicity because of lower thiosulfate storage levels[9]. In the present case, the infant had several risk factors

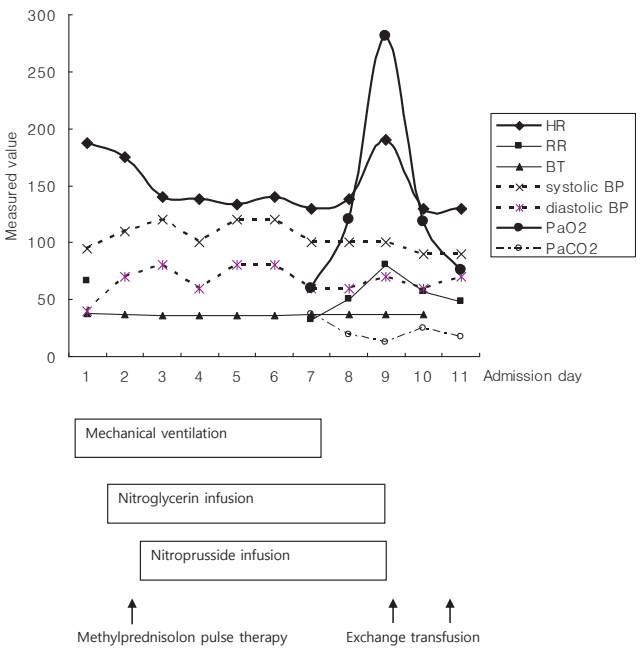

Fig. 1. Changes in vital signs and blood gas analysis findings during hospitalization. Sodium nitroprusside poisoning was diagnosed after 9 days of hospitalization. At that time, the patient showed unexplained tachypnea, tachycardia, irritability, and seizures. PaO_2 was extremely high and $PaCO_2$ was lower than the normal range. The plasma lactic acid level exhibited a marked increase to 122 mmol/L. These were recognized as the classical symptoms and signs of cyanide toxicity. The patient was stabilized after exchange transfusion. Abbreviations: HR, heart rate; RR, respiratory rate; BT, body temperature; BP, blood pressure; PaO_2, partial arterial oxygen pressure; $PaCO_2$, partial arterial carbon dioxide pressure.

for SNP infusion-associated cyanide toxicity; specifically, he was very young (2 months old) and had received a high dose [>2 μg/(kg · min)] of SNP for several days.

In this case, the infant showed the classical symptoms and signs of cyanide toxicity, i.e., tachycardia, tachypnea without respiratory problems, unexplained metabolic acidosis, irritability, and seizures. It was not possible to measure the blood cyanide concentrations in our hospital, but the plasma lactate concentrations were 122 mmol/L. Plasma lactate concentrations that exceed 10 mmol/L correlate with blood cyanide concentrations that exceed 40 μmol/L[10], and it has been shown that clinical toxicity appears when the blood cyanide concentration exceeds 40 μmol/L[11]. In adults, the fatal level of cyanide is generally considered to exceed 100-115 μmol/L[10]. Although nitroglycerin induced lactic acidosis might contribute to some portions of the patient's plasma lactate, his symptoms and sings were very typical to cyanide toxicity, we made a diagnosis of SNP-induced cyanide toxicity consequently. A key strategy to manage cyanide poisoning is to administer sulfur donors; sodium thiosulfate is usually used in clinical practice[12]. However, antidotes were not immediately available to us. Albumin can exhibit enzyme-like behavior and use bound elemental sulfur to detoxify cyanide[13, 14]. Thus, to supply sulfur donors and remove the cyanide and thiocyanate, we performed exchange transfusion.

Since exchange transfusion activates the detoxification systems and can clear some toxins from the blood more rapidly than antidotes, it can be useful for poisoning cases. Exchange transfusion has been used successfully to treat neonates or infants who have been poisoned with salicylate[15], theophyllin[16], phenobarbital[17], and other agents. A study in cats revealed that blood exchange transfusion is also an effective way to treat acute cyanide poisoning[18]. While the usefulness of blood exchange transfusion for pediatric cases of cyanide or nitroprusside poisoning has not yet been reported, we reasonably assumed that exchange transfusion would also be efficacious for cyanide poisoning. This is because exchange transfusion not only removes cyanide and thiocyanide from the blood but also activates the detoxification systems by supplying blood with abundant amounts of sulfur moieties. More importantly, exchange transfusion replaces cyanide-contaminated erythrocytes with fresh erythrocytes, thereby improving the blood's oxygen carrying capacity more rapidly than does antidote therapy. Therefore, we believe that exchange transfusion might be an effective therapeutic modality in a critical case of cyanide poisoning.

Cyanide poisoning causes cessation of oxidative phosphorylation and induces histotoxic anoxia, especially of the central nervous and cardiovascular systems; at high levels, it can lead to death. Exchange transfusion causes complications in 5% to 10% of infants even though the risk of death from the procedure is only 0.3/100 procedures[19]. In weighing the risks and benefits of using exchange transfusion therapy, we considered our patient to be at a serious risk from cyanide poisoning (based on classic cyanide poisoning signs and a markedly high level of plasma lactate without renal or heart problems or evidence of sepsis) and concluded that exchange transfusion provided more benefits than risks. Therefore, the infant received two rounds of exchange transfusion, after which his plasma lactic acid levels dropped markedly, the irritability and seizures disappeared, and his blood pCO_2 levels and vital signs normalized. No complications of exchange transfusion were observed.

In summary, while exchange transfusion is not considered as the primary treatment option for treating SNP infusion-associated cyanide poisoning, it may be an effective alternative modality for treating this condition if antidotes are not available.

References

1) Moffett BS and Price JF. Evaluation of sodium nitroprusside toxicity in pediatric cardiac surgical patients. Ann Pharmacother 2008;42:1600-4.
2) Gilboa N and Urizar RE. Severe hypertension in newborn after pyeloplasty of hydronephrotic kidney. Urology 1983;22:179-82.
3) Benitz WE, Malachowski N, Cohen RS, Stevenson DK, Ariagno RL, Sunshine P. Use of sodium nitroprusside in neonates: Efficacy and safety. J Pediatr 1985;106:102-10.
4) Linakis JG, Lacouture PG, Woolf A. Monitoring cyanide and thiocyanate concentrations during infusion of sodium nitroprusside in children. Pediatr Cardiol 1991;12:214-8.
5) Schulz V. Clinical pharmacokinetics of nitroprusside, cyanide, thiosulphate and thiocyanate. Clin Pharmacokinet 1984;9:239–51.
6) Friederich JA, Butterworth JF 4th. Sodium nitroprusside: twenty years and counting. Anesth Analg 1995;81:152-62.
7) Thomas C, Svehla L, Moffett BS. Sodium-nitroprusside-induced cyanide toxicity in pediatric patients. Expert Opin Drug Saf 2009;8:599-602.
8) Przybylo HJ, Stevenson GW, Schanbacher P, Backer C, Dsida RM, Hall SC. Sodium nitroprusside metabolism in children during hypothermic cardiopulmonary bypass. Anesth Analg 1995;81:952-6.
9) Schulz V, Bonn R, Kindler J. Kinetics of elimination of thiocyanate in 7 healthy subjects and in 8 subjects with renal failure. Klin Wochenschr 1979;57:243-7.
10) Kulig K. Cyanide antidotes and fire toxicology. N Engl J Med 1991;325:1801-2.
11) Baud FJ, Barriot P, Toffis V, Riou B, Vicaut E, Lecarpentier Y, et al. Elevated blood cyanide concentrations in victims of smoke inhalation. N Engl J Med 1991;325:1761-6.
12) Geller RJ, Barthold C, Saiers JA, Hall AH. Pediatric cyanide poisoning: Causes, manifestations, management, and unmet needs. Pediatrics 2006;118:2146-58.
13) Way JL. Cyanide intoxication and its mechanism of antagonism. Annu Rev Pharmacol Toxicol 1984;24:451-81.
14) Fasco MJ, Iii CR, Stack RF, O'hehir C, Barr JR, Eadon GA. Cyanide

adducts with human plasma proteins: Albumin as a potential exposure surrogate. Chem Res Toxicol 2007;20:677-84.

15) Manikian A, Stone S, Hamilton R, Foltin G, Howland MA, Hoffman RS. Exchange transfusion in severe infant salicylism. Vet Hum Toxicol 2002;44:224-7.

16) Shannon M, Wernovsky G, Morris C. Exchange transfusion in the treatment of severe theophylline poisoning. Pediatrics 1992;89:145-7.

17) Sancak R, Kucukoduk S, Tasdemir HA, Belet N. Exchange transfusion treatment in a newborn with phenobarbital intoxication. Pediatr Emerg Care 1999;15:268-70.

18) Tauberger G, Karzel K, Roezel V. The efficacy of blood exchange transfusions in the treatment of acute cyanide poisoning (author's transl). Arch Toxicol 1974;32:189-97.

19) Stoll BJ. Anemia in the newborn infant. In: Kliegman RM, Jenson HB, Behrman RE, Stanton BF, editors. Nelson textbook of pediatrics. 18th ed. Philadelphia: Saunders Co, 2007:771-2.