Nitroprusside sodium

Newborn use only

2021

Alert	High risk medication. Protect from light to avoid degradation. Acts within minutes. Monitor blood pressure (BP) closely to avoid life-threatening hypotension.(1) It should only be used as a short duration therapy in the operating room, ICU, cardiac care unit where continuous close monitoring by experienced providers is available.(1) Can cause a rare but potentially life threatening cyanide intoxication.(1, 2) Concomitant administration with sildenafil is contraindicated.
Indication	Acute severe hypertension.(3-5) Post cardiac surgery – To reduce afterload in conditions with left ventricular dysfunction.(6, 7) Post aortic surgery (e.g. coarctation of aorta repair) with acute hypertension.(1) Hypertensive acute heart failure.(8)
Action	Direct arteriolar and venous vasodilator.(9) Nitroprusside spontaneously releases nitric oxide, which activates the soluble form of guanylate cyclase producing increased levels of cyclic guanosine monophosphate (cGMP). Nitroprusside causes dose-dependent dilation of systemic and pulmonary arterial resistance and venous capacitance vessels.(6) In heart failure, decreases systemic vascular resistance (afterload) and left ventricular filling pressure (preload) and increases cardiac output.
Drug type	Antihypertensive, vasodilator.
Trade name	DBL Sodium nitroprusside 50 mg/2 mL Nitroprussiat Fides 50 mg powdered vial + 5 mL solvent (SAS during stock outage only)
Presentation	50 mg/2 mL vial (DBL brand), 50 mg powdered vial (Nitroprussiat brand)
Dose	**0.5-2 microgram/kg/min (range 0.2 – 6 microgram/kg/min).**(1, 10, 11) Generally commence treatment at 0.5 microgram/kg/min and increase by 0.5 microgram/kg/min every 15-20 minutes titrating to clinical response and toxicity. Infusion rates should remain below 2 microgram/kg/min, and it is recommended to reserve higher doses up to 6 microgram/kg/min for short periods to establish urgent blood pressure control.(3, 12)
Dose adjustment	Therapeutic hypothermia – No information. ECMO – No information. Renal impairment - Other vasoactive agents should be considered if prolonged or high doses are required. Hepatic impairment - Other vasoactive agents should be considered if prolonged or high doses are required.
Maximum dose	6 microgram/kg/min.(3)
Total cumulative dose	
Route	Intravenous
Preparation	Draw up 0.12 mL/kg (3 mg/kg) of sodium nitroprusside and add glucose 5% to make a final volume of 50 mL. Infusing at a rate of **1 mL/hr = 1 microgram/kg/min**
Administration	Continuous IV infusion using light safe infusion set, cover syringe with aluminium foil or light protective material.
Monitoring	Monitor BP closely. Measure thiocyanate levels if used for longer than three days or patient receiving high doses (≥ 3 microgram/kg/min).
Contraindications	Hypersensitivity to nitroprusside or other components.(13) Acute heart failure associated with reduced peripheral vascular resistance.(13) Compensatory hypertension (aortic coarctation or arteriovenous shunting).(13) Concomitant sildenafil.(13) Congenital (Leber) optic atrophy.(13) Inadequate cerebral circulation.(13) Systemic hypertension associated with raised intracranial pressure, and in patients with cerebrovascular disease where lowering blood pressure may cause ischaemia/stroke.
Precautions	Severe hepatic or renal impairment, impaired cerebral circulation, hypothyroidism, hyponatraemia; hypothermia. Can cause sudden and profound decrease in blood pressure.

	Prolonged infusions and renal impairment increases the risk of cyanide toxicity, metabolic (lactic) acidosis and death. Discontinue and give antidote.
Drug interactions	Ganglion blocking agents and other antihypertensive agents, volatile liquid anaesthetics, inhaled anaesthetics, negative inotropes and most other circulatory depressants potentiate the hypotensive action of sodium nitroprusside. The transition from sodium nitroprusside to oral antihypertensive therapy may predispose to severe, sudden hypertension. Concomitant administration with sildenafil can enhance the hypotensive effect of nitroprusside resulting in potentially life threatening hypotension and should be avoided.
Adverse reactions	Bradycardia, severe hypotension, flushing, palpitation, substernal pain. May cause tachycardia. ECG changes, restlessness, hypothyroidism, abdominal pain, intestinal obstruction, nausea. Methemoglobinaemia Cyanide or thiocyanate toxicity: Cyanide toxicity (normal range < 0.2 microgram/mL; toxic > 2 microgram/mL): Tachycardia, sweating, hyperventilation, arrhythmias, marked metabolic/lactic acidosis. Thiocyanate toxicity - Symptoms may occur at levels > 35 microgram/mL. Seizures, muscle spasms and vomiting may appear at 50-100 microgram/mL. Treatment should be discontinued if levels are > 120 microgram/mL. Raised intracranial tension (rare).(13)
Compatibility	Fluids: Glucose 5% only Y site: Amikacin, amiodarone, azithromycin, aztreonam, bivalirudin, caffeine citrate, calcium gluconate, cefazolin, cefotaxime, cefoxitin, ceftazidime, dexamethasone, dexemedetomidine, dopamine, esmolol, fentanyl, fluconazole, furosemide, gentamicin, heparin, hydrocortisone, hydromorphone, indomethacin, isovuconazole, insulin aspart, insulin regular, ketamine, levosimendan, linezolid, lorazepam, magnesium sulfate, mannitol, methylprednisolone, metoclopramide, metronidazole, micafungin, midazolam, milrinone, morphine sulfate, naloxone, nitroglycerine, norepinephrine, octreotide, ondansetron, pancuronium, benzylpenicillin, potassium chloride, propofol, sodium bicarbonate, sugammadex, suxamethonium, tacrolimus, tigecycline, tobramycin, TPN, vancomycin, vasopressin, vecuronium.
Incompatibility	Aciclovir, caspofungin, ceftazidime, ceftriaxone, trimethoprim-sulfamethoxazole, dobutamine, levofloxacin, metoprolol, pantoprazole, phenytoin, voriconazole.
Stability	Prepare immediately before use. Discard any unused solution. Discard if the solution changes to dark brown, blue, green, red or contains visible particulates.(3,4) For continuous infusion: Diluted solution should be used within 24 hours.
Storage	Store below 25˚C. Protect from light.
Excipients	
Special comments	Ensure adequate circulating blood volume.
Evidence	**Efficacy** Sodium nitroprusside (SNP) is used for both operative and non-operative control of hypertension. SNP infusions are occasionally used during cardiopulmonary bypass (CPB) to (a) achieve uniform perfusion for cooling, (b) treat increased blood pressures, and (c) speed the rewarming process.(4, 5) Data on neonates are limited to case reports and retrospective series.(2, 3, 12, 14, 15) SNP was administered to 58 neonates, all refractory to conventional intensive therapy. Sodium nitroprusside was found to be effective and safe in this group. SNP was infused at 0.2 to 6.0 microgram/kg/min for periods of 10 minutes to 126 hours. Toxic effects were not observed.(3) Deliu reported a case of preterm infant (30^{+2} week gestation) with hypertensive crisis on day 3 of life requiring nitroprusside which was commenced at 1 microgram/kg/minute and increased up to 3 microgram/kg/minute. SNP was gradually reduced slowly at 0.2 microgram every 2 hours and stopped on day 7.(12) **Safety** Each SNP molecule contains 5 cyanide molecules that are released during enzymatic breakdown of the SNP molecule to an unstable radical state. One of these cyanide molecules binds with a methemoglobin molecule, formed during the enzymatic breakdown of the SNP molecule, to form cyanomethemoglobin. The remaining 4 cyanide molecules are transformed into thiocyanate. There is a concern of cyanide

	toxicity with nitroprusside therapy. A case of SNP induced cyanide toxicity was reported in a 3-week old newborn with major renal anomaly and renal dysfunction in which serum thiocyanate levels never reached levels normally considered to be toxic. SNP was titrated to a dose of 8 microgram/kg/min in this case. The neonate experienced severe bradycardia and hypotension 12 hours after reaching and maintaining the maximum infusion rate. These adverse effects were attributed to cyanide toxicity, even though the patient's serum thiocyanate level was only 2 mg/dL.(14) Schulz et al reported a neonate who received SNP at 2–5 microgram/kg/min in the first few days after birth. After 30 hours of treatment, cyanide accumulation was found to have reached toxic levels. Intravenous administration of 100 mg/kg of sodium thiosulphate promptly lowered the cyanide level.(15) In contrast, a case series of 58 neonates who received high doses (6 microgram/kg/min) for longer than 48 hours reported no clinical signs or symptoms of cyanide toxicity with very few developing elevated cyanide levels.(3) A literature review by Thomas et al found that sodium nitroprusside is generally safe in critically ill paediatric patients, but cyanide and thiocyanate toxicity may occur in patients with specific risk factors including renal dysfunction, prolonged infusion duration (≥ 24 hours) and/or high doses of nitroprusside (>2 microgram/kg/min).(16) Shorter courses (lasting < 48 hours) may be less likely to induce cyanide toxicity.(17, 18) Routine monitoring of cyanide levels may not be warranted.(16) There was also a case report of lactic acidosis in a neonate with congenital heart disease. In this case, a dose of up to 2.5 microgram/kg/minute for up to 6 days was used.(19) **Pharmacokinetics** Nitroprusside has a short half-life of 2 minutes.(6) Onset of action is immediate and the effect lasts during the infusion only and ceases immediately after cessation of infusion.(9)
Practice points	Toxicity can be minimised by avoiding prolonged administration and high doses and by limiting its use in renal impairment.
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