DOPamine
Newborn use only

2023

Alert	Ensure dopamine has a dedicated line. DO NOT BOLUS.
Indication	Hypotension. (1-3) May also be used to improve renal perfusion. (4-6)
Action	Catecholamine with alpha and beta adrenergic, dopaminergic and serotoninergic actions Haemodynamic effects are dose dependent. (7) • Low dose: 1 to 5 microgram/kg/min – increases renal blood flow and glomerular filtration rate. (4) • Intermediate dose: 5 to 10 microgram/kg/min – increases cardiac output and blood pressure in addition to renal blood flow. • High dose: 10 to 20 microgram/kg/min – systemic vasoconstrictor effect outweighs all other effects. (8) Reduces renal blood flow. (7)
Drug type	Sympathomimetic, Inotropic vasopressor.
Trade name	Dopamine (DBL) concentrate
Presentation	200mg/5mL ampoule
Dose	**Hypotension*** 5-20 microgram/kg/minute Initiate at 5-10 microgram/kg/minute. Titrate dose as per response. Doses higher than 10 microgram/kg/minute require caution. Discuss with neonatologist. Clinical response is expected within a few minutes after entry of the drug into circulation. * If response is suboptimal, dose can be increased every 10-30 minutes until desired response is obtained or maximum dose is reached. (9-12) **Renal perfusion** 1-5 microgram/kg/min. ***NOTE:** The time from the initiation of infusion to the entry of the drug into circulation may influence the time it takes to see the clinical effect. This lag time can be reduced by (a) starting temporarily at a higher dose by increasing the infusion rate, and/or (b) priming the line as close to the entry point as possible to reduce the dead space – however, care should be taken not to deliver excess volume that may result in tachycardia and hypertension."
Dose adjustment	Therapeutic hypothermia: Limited data in neonates to guide dose adjustments. ECMO: Limited data in neonates to guide dose adjustments. Renal impairment: Limited data in neonates to guide dose adjustments. Hepatic impairment: Limited data in neonates to guide dose adjustments.
Maximum dose	20 microgram/kg/minute
Total cumulative dose	
Route	Continuous IV infusion.
Preparation	**SINGLE STRENGTH continuous IV infusion** **Infusion strength** | **Prescribed amount** 1 mL/hour = 10 microgram/kg/minute | 30 mg/kg dopamine and make up to 50 mL Draw up 0.75 mL/kg (30 mg/kg) of dopamine and add glucose 5%# to make a final volume of 50 mL. Infusing at a rate of **1 mL/hour = 10 microgram/kg/minute.** **DOUBLE STRENGTH continuous IV infusion** **Infusion strength** | **Prescribed amount** 1 mL/hour = 20 microgram/kg/minute | 60 mg/kg dopamine and make up to 50 mL Draw up 1.5 mL/kg (60 mg/kg) of dopamine and add glucose 5%# to make a final volume of 50 mL. Infusing at a rate of **1 mL/hour = 20 microgram/kg/minute.** **QUARDRUPLE STRENGTH continuous IV infusion – Can be used for infants up to 2500 g.*** **Infusion strength** | **Prescribed amount** 1 mL/hour = 40 microgram/kg/minute | 120 mg/kg dopamine and make up to 50 mL Draw up 3 mL/kg (120 mg/kg) of dopamine and add glucose 5%# to make a final volume of 50 mL. Infusing at a rate of **1 mL/hour = 40 microgram/kg/minute.** *Maximum diluted concentration is 6 mg/mL.

	#Sodium chloride 0.9% can be used as a diluent, but only to make a maximum concentration of 3.2 mg/mL dopamine solution.
Administration	Continuous intravenous infusion via a central line. Use with caution via a peripheral line (preferably low dose and for short duration).
Monitoring	Continuous heart rate, ECG and blood pressure Assess urine output and peripheral perfusion frequently. Observe intravenous site closely for blanching and extravasation.
Contraindications	Arrhythmia, tachyarrhythmia and phaeochromocytoma.
Precautions	Hypovolaemia- Ensure adequate circulating blood volume prior to commencement. May increase pulmonary hypertension.
Drug interactions	Glyceryl trinitrate, nitroprusside and calcium channel blockers: May cause hypotension Digitalis glycosides: May increase the risk of cardiac arrhythmias. Phenytoin: May result in dose dependent, sudden hypotension and bradycardia.
Adverse reactions	Ectopic beats, tachycardia and arrhythmia. Systemic and pulmonary hypertension, especially at higher doses. Reversible suppression of prolactin and thyrotropin secretion. Tissue necrosis at infusion site with extravasation, uraemia, mydriasis
Compatibility	Fluids: Glucose 5%, glucose 10%, glucose in sodium chloride 0.9%, glucose 5% in Hartmann's, Hartmann's, mannitol 20%, sodium chloride 0.9% Y-site: Amino acid solutions,* amifostine, amiodarone, anidulafungin, atracurium, aztreonam, bivalirudin, caffeine citrate, caspofungin, ceftaroline fosamil, ciprofloxacin, cisatracurium, dexmedetomidine, dobutamine, esmolol, ethanol, fluconazole, foscarnet, glyceryl trinitrate, granisetron, haloperidol lactate, heparin sodium, hydrocortisone sodium succinate, labetalol, lignocaine, linezolid, methylprednisolone sodium succinate, metronidazole, midazolam, milrinone, morphine sulfate, mycophenolate mofetil, noradrenaline, pancuronium, pethidine, piperacillin-tazobactam (EDTA-free), potassium chloride, ranitidine, remifentanil, sodium nitroprusside, streptokinase, tigecycline, tirofiban, vecuronium, verapamil, zidovudine. *ANMF medical group consensus: TPN compatibility is complex. There is limited information on pharmaceutical compatibility of dopamine with neonatal PN formulations. Please refer to Micromedex IV compatibility section for further information.
Incompatibility	Fluids: Sodium bicarbonate and other alkaline solutions. Y-site: Aciclovir, alteplase, ampicillin, azathioprine, cephazolin, chloramphenicol, diazoxide, esomeprazole, ganciclovir, ibuprofen, indomethacin, insulin (short-acting), phenytoin, sodium bicarbonate, thiopentone.
Stability	Ampoule: Store below 30°C. Protect from light. Diluted solution: Stable for 24 hours below 25°C.
Storage	Store below 25°C Protect from light. Discard remainder after use.
Excipients	sodium metabisulfite
Special comments	Discard admixtures exhibiting colour change.
Evidence	**Efficacy** **Hypotension** In a random effects meta-analysis of 7 trials (n=286) in preterm infants Dopamine was found to significantly increase mean and systolic arterial blood pressure. For the increase in blood pressure, Dopamine was associated with a significantly greater overall efficacy than Dobutamine, colloid or hydrocortisone alone. Dopamine was also associated with increased cerebral blood flow with a greater increase in hypotensive than in normotensive preterm infants. (1-2) However, in these meta-analyses, no differences were found among regimens regarding survival and other secondary clinical outcomes. A considerable inter-individual variability in blood pressure response has been reported in the included studies. (3) (LOE I, GOR B) In systematic review of 28 RCTs and 12 different comparisons of 6 commonly used vasopressors in adult patients, Gamper et at found insufficient evidence to recommend any one of the vasopressors over others in the assessed doses. The choice of a specific vasopressor may therefore be individualized and left to the discretion of the treating physicians. (13) (LOE I, GOR B)

Dose escalation: Comparative data to guide the dose escalation strategy is very limited. Randomised control trials comparing efficacy of inotropes in neonatal patients increased dopamine dose after allowing a variable period of 10 -30 minutes for optimal effect. (9-12)

Septic shock

In a RCT Baske et al compared Dopamine (10–20 µg/kg/min) or Adrenaline (0.2–0.4 µg/kg/min) as a first-line vasoactive medication in 40 neonates for successful reversal of fluid-refractory septic shock. The mean gestational age of participants at birth was 30 weeks and their mean postnatal age at treatment was 6 days. Reversal of shock was defined as achievement of systolic and diastolic blood pressure > fifth centile, capillary refill time < 3 seconds and a left ventricular output ≥ 150 mL/kg/min. The proportion of neonates achieving reversal of shock by 45 min, haemodynamic stability anytime during therapy and all-cause mortality by 28 days were comparable in the two groups. Moreover, the two groups had comparable lactate clearance, duration of vasoactive therapy and incidence of intraventricular haemorrhage, bronchopulmonary dysplasia, necrotising enterocolitis and retinopathy of prematurity. In the subgroup of extremely low birthweight infants (n=18), Adrenaline was more efficient in achieving hemodynamic stability but there were no differences in the other outcomes. (10) A systematic review of two pediatric and one neonatal RCT comprising of 220 participants with septic shock also reported comparable efficacy of Dopamine and Adrenaline for the treatment of septic shock. (14)

Good quality data from randomised control trials or prospective studies for comparing Dopamine and Noradrenaline for management of septic shock in neonates are lacking. In a retrospective cohort study, Nissimov et al investigated the clinical outcomes of extremely preterm neonates who received either Dopamine (n=113) or Noradrenaline (n=43) as a first line agent for management of septic shock in two different epochs. Dopamine was administered at a dose of 5 -20 mcg/kg/min and noradrenaline at 0.05-0.4 mcg/kg/min. Infants who received Noradrenaline had a lower episode related mortality (OR 0.55; 95% CI 0.33-0.92), new neurological injury (OR 0.32; 95% CI 0.13-0.82) and subsequent NEC/sepsis (OR 0.34, 95% CI 0.18 - 0.65). (15) A meta-analysis of 11 RCTs in adult patients which compared Dopamine and Noradrenaline for septic shock showed no statistically significant difference in the mean arterial pressure but favourable effect of Noradrenaline on heart rate, cardiac index and urine output. The Noradrenaline group had 11% reduction in absolute risk of all-cause mortality at 28 days. (11) Baseline severity of illness and development of arrhythmias during treatment were significant predictors of mortality. (16, 17)

Effect on pulmonary arterial pressure

In a small cohort of 18 preterm infants with a mean gestational age of 28 weeks and postnatal age 4 days Dopamine was used for treatment of hypotension. Transthoracic cardiac ultrasound was used to assess pressure gradient through the patent ductus arteriosus (PDA) and estimate mean pulmonary arterial pressure. Authors noted increase in both systemic and pulmonary arterial pressures after a mean Dopamine dose of 13 mcg/kg/min was reached. The mean systemic blood pressure increased by 41% and the mean pulmonary arterial pressure increased by 43%. The pulmonary to systemic mean arterial pressure (PAP/SAP) ratio increased in 50% infants and in 18% infants unidirectional left to right shunt across the PDA became bidirectional due to increased PAP/SAP ratio. (9)

Dopamine to prevent renal dysfunction in indomethacin-treated preterm newborn infants

Dopamine improved urine output (2.5 vs 1.8 ml/kg/hour) but there was no evidence of effect on serum creatinine, incidence of oliguria (urine output < 1ml/kg/hour) or frequency of failure to close the ductus arteriosus. (5) (LOE I, GOR B) Moreover, evidence from well-performed clinical studies to support the routine use of low dose Dopamine for improving renal function in critically ill neonates is insufficient. (6)

Safety

Dopamine increases heart rate and has a higher propensity to develop cardiac arrythmias. (9, 16,17) Limited data suggest higher dose dopamine may reduce cardiac output. (8,18) (LOE II, GOR C) There is insufficient safety data in neonates for use at doses > 20 micrograms/kg/min. In a systematic review, Sassano-Higgins did not find statistically significant difference in adverse neurological outcome between dopamine, dobutamine, adrenaline, colloid or Hydrocortisone administration when used for hypotension. (2) In a secondary analysis of a prospectively enrolled cohort of 61 neonates, Solanki et al reported the effect of Dopamine (n=33) on cerebral autoregulation. The mean birth weight of the subjects was 849 g and the mean gestation was 26 weeks. In this study, significantly less epochs without Dopamine exposure were associated with impaired cerebral autoregulation compared with Dopamine exposure epochs (14.5% vs. 30.7%; p< 0.001). (19) However, presence of hypotension, gestational age at birth and postnatal age independently affect cerebral autoregulation and are important confounders. (20)

Pharmacokinetics

The cardiovascular and renal effects of dopamine result from its direct action on dopaminergic, serotonergic and alpha/ beta adrenoceptors. Its effects are dose dependent with some overlap in receptor

	activation as well as inter-patient variability in binding affinities at different doses. In general, at low doses Dopamine receptors are preferentially activated accounting for its renal effects and at doses > 2 micrograms/kg per minute, the beta and alpha adrenoceptors are stimulated mediating its cardiovascular effects. Steady-state plasma Dopamine concentrations and plasma clearance rates were observed within 20 minutes (dose range 1−8 microgram/kg/min). There is a linear correlation between infusion rate and plasma Dopamine concentration. In one study the threshold for increases in mean arterial pressure was 50% below that for increases in heart rate. (21) The median plasma clearance of Dopamine in neonates is reported to be 385 mL/kg/minute with a large inter-individual variation. (22) Dopamine is metabolised by the monoamine oxidase and catechol-O-methyltransferase enzymes and primarily excreted by the liver. Its half-life is reported to be between 2- 9 min in different studies. (22,23)
Practice points	
References	1. Sarafidis K, Verykouki E, Nikopoulos S, et al. Systematic Review and Meta-Analysis of Cardiovascular Medications in Neonatal Hypotension. Biomed Hub. 2022 Jun 14; 7(2):70-79. 2. Sassano-Higgins S, Friedlich P, Seri I. A meta-analysis of dopamine use in hypotensive preterm infants: blood pressure and cerebral hemodynamics. J Perinatol. 2011 Oct; 31(10):647-55 3. Subhedar, N.V. and N.J. Shaw, Dopamine versus dobutamine for hypotensive preterm infants. Cochrane Database Syst Rev, 2003(3): p. CD001242 4. Crouchley JL, Smith PB, Cotten CM, et al. Effects of low-dose dopamine on urine output in normotensive very low birth weight neonates. J Perinatol. 2013 Aug;33(8):619-21 5. Barrington, K, L.P. Brion. Dopamine versus no treatment to prevent renal dysfunction in indomethacin-treated preterm newborn infants. Cochrane Database Syst Rev, 2002(3): p. CD003213 6. Plötz F, Prins I. Small-Dose Dopamine in Critically Ill Infants and Children. Anesthesia & Analgesia 99(4): p 1262-1263, October 2004. 7. Seri, I., Cardiovascular, renal, and endocrine actions of dopamine in neonates and children. J Pediatr, 1995. 126(3): p. 333–44. 8. Osborn, D., N. Evans, and M. Kluckow, Randomized trial of dobutamine versus dopamine in preterm infants with low systemic blood flow. J Pediatr, 2002. 140(2): p. 183–91. 9. Liet JM, Boscher C, Gras-Leguen C, et al. Dopamine effects on pulmonary artery pressure in hypotensive preterm infants with patent ductus arteriosus. J Pediatr 2002; 140:373-5. 10. Baske K, Saini SS, Dutta S. Epinephrine versus dopamine in neonatal septic shock: a double-blind randomized controlled trial. Eur J Pediatr. 2018 Sep; 177(9):1335-1342. 11. Pellicer A, Valverde E, Elorza MD, et al. Cardiovascular support for low-birth-weight infants and cerebral hemodynamic: a randomized, blinded, clinical trial. Paediatrics. 2005;115(6):1501-12. 12. Dempsey EM, Barrington KJ, Marlow N, et al. Hypotension in Preterm Infants (HIP) randomised trial. Arch Dis Child Fetal Neonatal Ed. 2021 Jul;106(4):398-403. 13. Gamper G, Havel C, Arrich J, et al. Vasopressors for hypotensive shock. Cochrane Database Syst Rev. 2016 Feb 15; 2(2):CD003709. 14. Wen L, Xu L. The efficacy of dopamine versus epinephrine for pediatric or neonatal septic shock: a meta-analysis of randomized controlled studies. Ital J Pediatr. 2020 Jan 14; 46(1):6. 15. Nissimov S, Joye S, Jain A, et al. Dopamine or norepinephrine for sepsis-related hypotension in preterm infants: a retrospective cohort study. Eur J Pediatr. 2023 Mar; 182(3):1029-1038. 16. Avni T, Lador A, Lev S, Leibovici L, et al. Vasopressors for the Treatment of Septic Shock: Systematic Review and Meta-Analysis. PLoS One. 2015 Aug 3; 10(8):e0129305 17. Patel GP, Grahe JS, Sperry M et al. Efficacy and safety of dopamine versus norepinephrine in the management of septic shock. Shock. 2010 Apr; 33(4):375-80. 18. Roze, J.C., et al., Response to dobutamine and dopamine in the hypotensive very preterm infant. Arch Dis Child, 1993. 69(1 Spec No): p. 59–63 19. Solanki NS, Hoffman SB. Association between dopamine and cerebral autoregulation in preterm neonates. Pediatr Res. 2020 Oct; 88(4):618-622 20. Eriksen VR, Hahn GH, Greisen G. Dopamine therapy is associated with impaired cerebral autoregulation in preterm infants. Acta Paediatr. 2014 Dec; 103(12):1221-6 21. Padbury, J.F., et al., Dopamine pharmacokinetics in critically ill newborn infants. J Pediatr, 1987. 110(2): p. 293–8 22. Rasmussen MB, Gramsbergen JB, Eriksen VR, et al. Dopamine plasma clearance is increased in piglets compared to neonates during continuous dopamine infusion. Acta Paediatr. 2018 Feb; 107(2):249-254. 23. B. K, M. S. Therapeutic Hypothermia: Implications on Drug Therapy [Internet]. Therapeutic Hypothermia in Brain Injury. InTech; 2013. Available from: http://dx.doi.org/10.5772/52667.

	24. MerativeTM Micromedex® Complete IV Compatibility (electronic version). Merative, Ann Arbor, Michigan, USA. Available at: https://www.micromedexsolutions.com/ (cited: July/24/2023).

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