Adrenaline (epinephrine) IV infusion

Newborn use only

2020

Alert	1:10,000 (1 mg/10 mL) ampoule is the preferred preparation for adrenaline infusion.
Indication	Treatment of hypotensive shock with or without myocardial dysfunction.
Action	Catecholamine with alpha and beta adrenergic actions. Haemodynamic effects are dose dependent: • At low doses of 0.01–0.1 microgram/kg/minute primarily stimulates cardiac and vascular beta 1- and beta 2-adrenoreceptors leading to increased inotropy, chronotropy, conduction velocity and peripheral vasodilation. • At doses greater than 0.1 microgram/kg/minute adrenaline also stimulates vascular and cardiac alpha 1-receptors causing vasoconstriction and increased inotropy. The net effects are increases in blood pressure and systemic blood flow caused by the drug-induced increases in systemic vascular resistance (SVR) and cardiac output.[1]
Drug type	Inotropic vasopressor.
Trade name	Aspen Adrenaline 1: 10,000 Adrenaline Acid Tartrate injection; Adrenaline 1:1,000 Adrenalin Acid Tartrate injection.
Presentation	1 mg/10 mL or 1:10,000 ampoule [100 microgram/mL] 1 mg/mL or 1:1,000 ampoule [1000 microgram/mL]
Dose	Low dose: 0.05–0.1 microgram/kg/minute High dose: 0.1–1 microgram/kg/minute
Dose adjustment	
Maximum dose	
Total cumulative dose	
Route	Continuous IV infusion.
Preparation	**Preparation using 1:10,000 (1 mg/10 mL) ampoule** **LOW CONCENTRATION IV infusion** **Infusion Strength** | **Prescribed amount** 1 mL/hour = 0.05 microgram/kg/minute | 150 microgram/kg adrenaline and make up to 50 mL Draw up 150 microgram/kg (1.5 mL/kg) of 1:10,000 adrenaline and add glucose 5%, glucose 10% or sodium chloride 0.9% to make a final volume of 50 mL with a concentration of 3 microgram/kg/mL. Infusing at a rate of **1 mL/hour = 0.05 microgram/kg/minute.** **HIGH CONCENTRATION IV infusion** **Infusion Strength** | **Prescribed amount** 1 mL/hour = 0.2 microgram/kg/minute | 600 microgram/kg adrenaline and make up to 50 mL Draw up 600 microgram/kg (6 mL/kg) of 1:10,000 adrenaline and add glucose 5%, glucose 10% or sodium chloride 0.9% to make a final volume of 50 mL with a concentration of 12 microgram/kg/mL. Infusing at a rate of **1 mL/hour = 0.2 microgram/kg/minute.** **For infants requiring fluid restriction consider:** **VERY HIGH CONCENTRATION IV infusion*** **Infusion Strenght** | **Prescribed amount** 1 mL/hour = 0.4 microgram/kg/minute | 1200 microgram/kg adrenaline and make up to 50 mL Draw up 1200 microgram/kg (12 mL/kg) of 1:10,000 adrenaline and add glucose 5% ONLY to make a final volume of 50 mL with a concentration of 24 microgram/kg/mL. Infusing at a rate of **1 mL/hour = 0.4 microgram/kg/minute.** ***Stability data only available for 5% glucose for very high concentration.** **Preparation using 1:1,000 (1 mg/mL) ampoule – Occasionally used for infants>4 kg: 1:1000 (1 mg/mL) ampoule is not commonly kept in the NICUs** **LOW CONCENTRATION IV infusion**

<table>
<tr><td></td><td>
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Draw up 150 microgram/kg (0.15 mL/kg) of 1:1000 adrenaline and add glucose 5%, glucose 10% or sodium chloride 0.9% to make a final volume of 50 mL with a concentration of 3 microgram/kg/mL. Infusing at a rate of 1 mL/hour = 0.05 microgram/kg/minute.

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For infants requiring fluid restriction consider:
VERY HIGH CONCENTRATION IV infusion*
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Draw up 1200 microgram/kg (1.2 mL/kg) of 1:1000 adrenaline and add glucose 5% ONLY to make a final volume of 50 mL with a concentration of 24 microgram/kg/mL. Infusing at a rate of 1 mL/hour = 0.4 microgram/kg/minute.
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</td></tr>
<tr><td>Administration</td><td>Continuous IV infusion preferably via dedicated central line.
Use with caution via a peripheral line.</td></tr>
<tr><td>Monitoring</td><td>Continuous heart rate, ECG and blood pressure monitoring preferable.
Assess urine output and peripheral perfusion frequently.
Observe IV site closely for blanching and extravasation.</td></tr>
<tr><td>Contraindications</td><td>Arrhythmia and tachyarrhythmia.
Cardiovascular disease resulting in arterial narrowing including cerebrovascular disease, coronary artery disease and digital ischaemia.
Phaeochromocytoma.
Thyrotoxicosis.
Glaucoma.
Known hypersensitivity to sympathomimetic amines.</td></tr>
<tr><td>Precautions</td><td>Ensure adequate circulating blood volume prior to commencement.
Potent chronotrope and vasopressor – may cause excessive tachycardia, severe hypertension and ventricular arrhythmias.
May cause lactic acidosis and hyperglycaemia.</td></tr>
<tr><td>Drug interactions</td><td>Hypotension may be observed with concurrent use of vasodilators such as glyceryl trinitrate, nitroprusside and calcium channel blockers.
Concurrent use of digitalis glycosides may increase the risk of cardiac arrhythmias.
Concurrent use of IV phenytoin with adrenaline may result in dose dependent, sudden hypotension and bradycardia.</td></tr>
<tr><td>Adverse reactions</td><td>Tachycardia and arrhythmia.
Systemic hypertension especially at higher doses.
May cause hypokalaemia.
Tissue necrosis at infusion site with extravasation.
Digital ischaemia.</td></tr>
<tr><td>Compatibility</td><td>Fluids: Glucose 5%, glucose 10%, Hartmann’s, sodium chloride 0.9%. Stability data only available for 5% glucose for very high concentration.
Y-site: Amino acid solutions. Amiodarone, anidulafungin, atracurium, bivalirudin, caspofungin, cisatracurium, dexmedetomidine, dobutamine, dopamine, ethanol, fentanyl, glyceryl trinitrate, heparin sodium, milrinone, morphine sulfate, pancuronium, potassium chloride, ranitidine, remifentanil, sodium nitroprusside, tigecycline, tirofiban, vecuronium.</td></tr>
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	No information: Adrenaline HCL is compatible with noradrenaline bitartrate but no stability data is available for Adrenaline acid tartrate and noradrenaline bitartrate
Incompatibility	**Fluids**: Sodium bicarbonate. **Y-site**: Aciclovir, aminophylline, ampicillin, atropine, azathioprine, calcium chloride, calcium gluconate, cefalotin, chloramphenicol, digoxin, ergometrine, ganciclovir, hyaluronidase, hydrocortisone sodium succinate, indomethacin, phenobarbitone sodium, sodium bicarbonate, thiopentone, vancomycin.
Stability	Diluted solution: Stable for 24 hours below 25°C.
Storage	Store below 25°C. Protect from light. Discard remainder after use.
Excipients	
Special comments	Preferably administered via "dedicated" line to avoid accidental bolus. Do not use as a side line with maintenance fluids. Discard if exhibiting colour change.
Evidence	Efficacy: Treatment of hypotension in preterm infants: A single study of adrenaline 0.125−0.5 microgram/kg/minute versus dopamine 2.5−10 microgram/kg/minute reported they are equally effective at treating hypotension and increasing cerebral blood flow in very preterm infants. Adrenaline is associated with worse acid base status and increased hyperglycaemia. No difference in clinical outcomes was reported. [1−3] A single study of adrenaline 0.125, 0.250, 0.375, 0.5 microgram/kg/minute versus dopamine 5, 10, 15, 20 microgram/kg/minute reported dopamine reduced left ventricular output (LVO) 10% compared to a 14% increase in LVO with adrenaline. Dopamine and adrenaline caused significant increases in mean BP and pulmonary artery pressure. (LOE II, GOR C) Infants and children with septic shock: Early administration of adrenaline 0.1–0.3 microgram/kg/minute was associated with increased survival compared to dopamine. [4] (LOE II, GOR B) Vasopressors for hypotensive shock (newborns excluded): In treatment of hypotensive shock beyond the newborn period, there was no difference in mortality comparing adrenaline and other vasopressors (noradrenaline, noradrenaline and dobutamine, or noradrenaline and dopexamine). [5] (LOE I, GOR B) Summary: Adrenaline may be used in hypotensive neonates with vasodilatory shock with or without myocardial dysfunction, particularly those with septic shock or unresponsive to other inotropes. (LOE II, GOR B) Safety: Adrenaline may be associated with worse acid base status and increased hyperglycaemia.[3] Adrenaline is a potent vasoconstrictor. [6] Pharmacokinetics: The onset of action is rapid and after intravenous infusion the half-life is approximately 5−10 minutes. [7] However, the half-life of intravenous adrenaline has not been reported in sick newborn infants. The plasma half-life of intratracheal adrenaline for newborn resuscitation is likely to average approximately50 minutes.[8]
Practice points	
References	1. Pellicer A, Bravo MDC, Madero R, Salas S, Quero J, Cabañas F. Early systemic hypotension and vasopressor support in low birth weight infants: Impact on neurodevelopment. Pediatrics. 2009;123:1369-76. 2. Pellicer A, Valverde E, Elorza MD, Madero R, Gayá F, Quero J, Cabañas F. Cardiovascular support for low birth weight infants and cerebral hemodynamics: A randomized, blinded, clinical trial. Pediatrics. 2005;115:1501-12. 3. Valverde E, Pellicer A, Madero R, Elorza D, Quero J, Cabanas F. Dopamine versus epinephrine for cardiovascular support in low birth weight infants: analysis of systemic effects and neonatal clinical outcomes. Pediatrics. 2006;117:e1213-22. 4. Ventura AMC, Shieh HH, Bousso A, Góes PF, Fernandes IDCFO, De Souza DC, Paulo RLP, Chagas F, Gilio AE. Double-blind prospective randomized controlled trial of dopamine versus epinephrine as first-line vasoactive drugs in pediatric septic shock. Critical Care Medicine. 2015;43:2292-302. 5. Havel C, Arrich J, Losert H, Gamper G, Mullner M, Herkner H. Vasopressors for hypotensive shock. The Cochrane database of systematic reviews. 2011:CD003709.

	6. Noori S, Seri I. Neonatal blood pressure support: the use of inotropes, lusitropes, and other vasopressor agents. Clinics in perinatology. 2012;39:221-38. 7. Fitzgerald GA, Barnes P, Hamilton CA, Dollery CT. Circulating adrenaline and blood pressure: the metabolic effects and kinetics of infused adrenaline in man. European journal of clinical investigation. 1980;10:401-6. 8. Schwab KO, von Stockhausen HB. Plasma catecholamines after endotracheal administration of adrenaline during postnatal resuscitation. Archives of disease in childhood Fetal and neonatal edition. 1994;70:F213-7. 9. Young TE, Mangum B [2008]. Neofax: A manual of drugs used in neonatal care. Acorn Publishing, Inc. Raleigh, NC 27619 10. Australian Injectable Drugs Handbook, 6th Edition, Society of Hospital Pharmacists of Australia 2014.

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