Vasoactive agents used in the neonatal intensive care unit

Agent	Mechanism of action	Clinical considerations
Predominant vasopressors		
Dopamine	It has mixed β-1 and α-adrenergic effects, in addition to its dopaminergic effects. Up to 25% of dopamine is converted to norepinephrine. It can have an unpredictable effect in premature infants. Due to the relative abundance of α-1 receptors in preterm infants, vasoconstrictive effects can occur at low levels, leading to increased SVR and PVR and potentially reducing CO and end-organ perfusion.45	Dopamine exhibits many extracardiac effects including impaired cerebral autoregulation46 and pituitary suppression resulting in reduced levels of thyroid stimulation hormone and thyroxine in addition to prolactin.47 Higher doses of dopamine may be associated with arrhythmias.48 The use of dopamine should be reconsidered. Recent data suggest that dopamine is associated with increased mortality, neurological injury and morbidity including NEC.49 50 This finding of increased mortality and morbidity is also observed in older children.51
Norepinephrine	A potent vasopressor as it has predominant α-1 effects and weaker β-1 effects. Norepinephrine will raise BP without and effective increase in CO. Norepinephrine may decrease PVR through α-2 stimulation and nitric oxide release. In term infants with acute pulmonary hypertension, norepinephrine can increase PVR but to a lesser ratio than SVR, with an associated improvement in pulmonary blood flow.52	It may be a useful agent to use in severe cases of vasodilatory shock associated with NEC and/or sepsis. Norepinephrine demonstrates favourable survival and postuse morbidity compared with dopamine in preterm infants with sepsis, and therefore, it may be the preferred first-line agent clinical scenarios of septic shock.49
Vasopressin	It exerts its effects through V1 receptors, resulting in an increase in SVR through phospholipid-mediated calcium release and a theoretical fall in PVR secondary to nitric oxide release.53 Its antidiuretic properties are mediated through V2 receptors, found in the collecting ducts of the kidneys.	It has a potential role in the treatment of severe diastolic hypotension in infants with septic shock who do not respond to more traditional vasopressors and/or corticosteroids. Given its potential PVR-lowering properties, it may have a role in the treatment of pulmonary hypertension. The lack of chronotropic effects makes it an ideal choice in situations where maintaining vascular tone without an increase in heart rate is required. Clinical examples include severe septal hypertrophy secondary to gestational diabetes and hypertrophic obstructive cardiomyopathy.27 It must be used with caution, as evidence of safety is currently lacking and there are reports that it may lead to oliguric renal failure or liver necrosis secondary to compromised splanchnic perfusion in some patients.54

Agent	Mechanism of action	Clinical considerations
Predominant inotropes		
Epinephrine	An endogenous catecholamine with β-1 effects at lower doses and α-adrenergic effects at higher doses, resulting in a combined inotropic and vasopressor effect Low-dose epinephrine may increase CO in neonates more effectively than dopamine. This is achieved through β-1 stimulation, which results in an increase in SV and heart rate.	Prolonged use may be associated with myocardial ischaemia and dysfunction as it increases myocardial oxygen demand. At higher doses, it is an effective vasopressor, raising both SVR and PVR through α-adrenergic stimulation. Epinephrine use in preterm infants is associated with a rise in lactate and blood glucose levels; this effect may be independent of dosing and duration and can be reversed with discontinuation of therapy.55
Dobutamine	A synthetic inotrope with predominant β-1-mediated increase in myocardial SV, heart rate and β-2 vascular vasodilatory action; it increases CO and reduces SVR. This could result in a marginal increase in BP.56 57	Due to the relative lack of expression of β-2 receptors in preterm vasculature, its vasodilatory effect is not generally seen in this population, although caution is still advised with higher doses. Dobutamine is considered in clinical situations of increased afterload and impaired myocardial contractility such as cold shock, asphyxia and pulmonary hypertension.
Inodilator		
Milrinone	Acts via phosphodiesterase III inhibition, thereby increasing the bioavailability of cyclic AMP; this leads to vasodilation in systemic and pulmonary vasculature in addition to inotropic and lusitropic myocardial effects.	In the literature, evidence of its use in neonates is limited to case series demonstrating an improvement in oxygenation when used in combination with inhaled nitric oxide in the setting of acute pulmonary hypertension.58 59 Its lusitropic and potential inotropic properties make it an effective agent in the presence of right ventricular and left ventricular dysfunction in the setting of pulmonary hypertension. In addition, it has been used in preterm infants following patent ductus arteriosus ligation to prevent low CO states and subsequent respiratory deterioration.60

- BP, blood pressure; CO, cardiac output; NEC, necrotising enterocolitis; PVR, pulmonary vascular resistance; SV, stroke volume; SVR, systemic vascular resistance.

Mullaly R, El-Khuffash AF. Haemodynamic assessment and management of hypotension in the preterm. Archives of Disease in Childhood - Fetal and Neonatal Edition 2024;109:120-127.