Alternatives to NORADRENALINE

NORADRENALINE SPARING GUIDANCE

All agents to be administered via CVC

	Non-septic Syndromes		Septic shock	
	Low CO	***Normal CO***	***Low CO or IHD***	***Normal CO***
First choice	**Noradrenaline or Metaraminol at a very low dose**	**Metaraminol**	**Noradrenaline +/- Dobutamine**	**Noradrenaline**>0.3 mcg/kg/min add **Vasopressin**[#]
Second choice	**Dobutamine +Metaraminol**	**Phenylephrine**	**Noradrenaline+ dobutamine +/- Vasopressin**	**Adrenaline** >0.2 mcg/Kg/Min +/- **Vasopressin**
	Dobutamine + Phenylephrine			**Adrenaline** >0.2 mcg/kg/min +/- **Terlipressin***
Third choice	**Dopamine**	**Dopamine**	**Adrenaline +/- Vasopressin**	**Dopamine**
				Terlipressin *

All administered as an infusion. [#]See BSUH administration guideline *Terlipressin in Septic Shock has a higher complication rate, use if vasopressin is not available.

VASOPRESSIN (AKA Argipressin) *(Dilute 20 units to 50mL with glucose 5% (to give 0.4units/mL). Surviving Sepsis Guidelines recommend infusion of 4.5mL/hour (0.03units/min). Infusion may titrated between 1.5mL/hour (0.01units/min) and 6mL/hour (0.04units/min). Vasopressin should be slowly weaned down and off before the noradrenaline is stopped. Reduce the vasopressin infusion rate by half every 30 minutes down to 0.01units/hour (1.5mL/hour) then stop.*

Vasopressin is Anti Diuretic Hormone (ADH) and improves blood pressure by constriction of vascular smooth muscle. The use of vasopressin in septic shock is suggested by the Surviving Sepsis Guidelines in cases where the use of noradrenaline is not achieving the target MAP, or as a N**oradrenaline sparing agent** when noradrenaline doses are medium/high. Vasopressin may be **added** to noradrenaline in **resistant septic shock** where the noradrenaline dose has reached **0.3mcg/kg/min** or more and steroids have been considered. Vasopressin is added with the aim of either raising the MAP or decreasing the noradrenaline dose. **Vasopressin is at Consultant Intensivist request only and must not to be used as the sole vasopressor.**

METARAMINOL *(Dilute 20mg to 40mL with Sodium Chloride 0.9% to give 0.5mg/ml.Titrate dose to response.*

Metaraminol bitartrate (metaraminol) is a potent synthetic sympathomimetic amine with a predominantly direct alpha agonist effect. Also, it has indirect sympathomimetic actions caused by the release of noradrenaline and adrenaline. It causes mainly peripheral vasoconstriction, resulting in increased systemic blood pressure (both systolic & diastolic). It has no chronotropic action and may induce reflex bradycardia, when used in the treatment of acute hypotension.

PHENYLEPHRINE *(Dilute 5mg to 50mL with glucose 5% or sodium chloride 0.9% to give 100mcg/ml. Initially up to 180micrograms/min (108mL/hour) then reduced to 30-60micrograms/min (18-36mL/hour) according to response. When stopping the infusion, wean off gradually, do not stop abruptly. Please, make two syringes from one bottle to avoid wastage.*

Phenylephrine acts directly almost totally on alpha-1 receptors causing vasoconstriction and increasing blood pressure, coronary and cerebral perfusion pressure. Heart rate usually slows due to reflex bradycardia. Cerebral and coronary blood flow is minimally affected. Used to treat hypotension associated with spinal and epidural anaesthesia and topically to provide vasoconstriction in the eye or nose before surgery. Large topical doses have been reported to cause significant CVS side effects including cardiac arrest.

DOBUTAMINE *(Ready to administer 250mg in 50mL vials.)*

Start at 2.5 micrograms/kg/minute and titrate to response. Maximum dose is 40 micrograms/kg/minute, but dose titration may be limited by tachycardia. Dobutamine has a short half life. When stopping the infusion, wean off gradually, do not stop abruptly). Dobutamine is predominantly a β-agonist, resulting in increased myocardial contractility with a variable effect on heart rate. β mediated vasodilatation occurs in the skeletal muscle beds – which may result in hypotension. Useful in low cardiac output states. Warning: the administration of dobutamine may worsen myocardial ischaemia and/or infarction due to the increase in myocardial work or due to tachycardia or hypotension.

ADRENALINE (EPINEPHRINE) *(Dilute8mg to 50mL with glucose 5%).* Start at 0.02 micrograms/kg/minute and titrate to response. Doses up to 3 micrograms/kg/minute may be *required (rarely). Please consult ITU handbook for dosing. Adrenaline has a short half-life; when stopping the infusion, wean off gradually, do not stop abruptly)*

Adrenaline is a non-selective adrenergic agonist with potent beta1 (β1) and moderate alpha1 (α) and beta2 (β2) receptor activity. Increased myocardial force of contraction (positive inotropic effect) and heart rate (positive chronotropic effect) occur as a result of β1 receptor stimulation. Systemic vascular resistance is increased overall because the stimulation of α1 receptors results in peripheral vasoconstriction which counters the vasodilation due to β2 receptor activation. These β2 effects also relax bronchial smooth muscle and stabilise mast cells.

DOPAMINE *(Dilute 200mgto 50 mL with glucose 5% or sodium chloride 0.9%)*

Start at 2.5 micrograms/kg/minute and titrate to response. Doses used usually up to 20 micrograms/kg/minute although higher doses may be required in severe cases. The lowest possible dosage that maintains these effects should be used. *Higher doses may cause renal vasoconstriction. Dopamine has a short half life. When stopping the infusion, wean of gradually, do not stop abruptly.*

Beta 1 and dopamine-receptor agonist. Increasing alpha effects seen as dose escalates. Useful "rescue inotrope". Renal protection does not occur.

TERLIPRESSIN *(Dilute 1mg to 50mL with glucose 5% or sodium chloride 0.9% to give 0.02mg/mL. Start infusion rate at 2.5mL/hour (0.05mg/hour) and titrate up to 10mL/hour (0.2mg/hour).*

Terlipressin will take 20-30 minutes to take effect.Terlipressin should be slowly weaned down and off before the noradrenaline is stopped. Reduce the terlipressin infusion rate by half every 30 minutes down to 0.05units/hour (2.5mL/hour) then stop. **Terlipressin is at Consultant Intensivist request only and must not to be used as the sole vasopressor.**

Terlipressin is a powerful Vasopressin V1 receptor agonist which causes systemic vasoconstriction and raises blood pressure. It helps to override the splanchnic vasodilatation seen in hepato-renal syndrome and thus improve renal perfusion and lower creatinine levels. Terlipressin itself is inactive, but is converted to lysine-vasopressin by tissue enzymes. Terlipressin (TP) is a synthetic vasopressin analogue used in the management of patients with septic shock. *BMC Anesthesiol* 2020; 20 (1), 58 and *Intensive Care Med.* 2018 Nov; 44(11):1816-1825

Drug	Clinical Indication	α1	β1	β2	DA	V1/V2
Adrenaline (epinephrine)	Shock (cardiogenic, vasodilatory), cardiac arrest, bronchospasm/ anaphylaxis, symptomatic bradycardia	+++++	+++++	+++	N/A	N/A
Noradrenaline (norepinephrine)	Shock (cardiogenic, vasodilatory), low cardiac output with low systemic vascular resistance	+++++	+++	++	N/A	N/A
Dobutamine	Low cardiac output (decompensated heart failure, cardiogenic shock, sepsis induced myocardial dysfunction)	+	+++++	+++	N/A	N/A
Metaraminol	Hypotension with adequate filling	+++++	+	0	N/A	N/A
Phenylephrine	Hypotension	+++++	0	0	N/A	N/A
Vasopressin (argipressin)	Shock (cardiogenic, vasodilatory or septic), Cardiac arrest	N/A	N/A	N/A	N/A	+++++
Dopamine	Low cardiac output increases myocardial contractility	+++	+++	+++	+++++	N/A
Terlipressin	HRS and septic shock	N/A	N/A	N/A	N/A	++++

Vasopressors and alternatives to NA