Guideline for Use of Vasopressors on the Medical High Dependency Unit

Reference no.: CG-REN/4182/23

1. Introduction

Summary:

This guideline has been developed to allow for the treatment of septic shock induced hypotension using the vasopressors noradrenaline and metaraminol in medical HDU.

Introduction:

In addition to fluid resuscitation, vasopressor therapy is a fundamental treatment of septic shock-induced hypotension as it aims to correct the vascular tone depression and at improving organ perfusion pressure. The Surviving Sepsis campaign guidelines recommend an initial target mean arterial pressure (MAP) of 65 mmHg to maintain critical organ perfusion. This goal is a reasonable endpoint to maintain hemodynamic stability, but the effects of further adjustment might be variable depending on individual characteristics.

Vasopressors used on MHDU are all vasoconstrictors that will increase blood pressure by increasing systemic vascular resistance (SVR). They will only be effective if there is sufficient fluid in the vasculature to constrict against. It is therefore imperative that volume depletion is corrected prior to starting vasopressors. Vasopressors used on MHDU will have no direct effect on cardiac output. They may worsen existing coronary ischemia.

If low blood pressure persists despite adequate fluid resuscitation consider starting noradrenaline via IV central infusion or IV metaraminol peripherally. Any initiation of vasopressors should be discussed with the Renal Consultant. Administration of vasopressors including any changes in rates must involve two registered members of staff.

2. Aim and Purpose

To provide guidance on the administration of vasopressor therapy, Noradrenaline and Meteraminol on medical HDU.

3. Main body of Guidelines

Noradrenaline:

Noradrenaline is recommended as the first choice vasopressor in treating septic shock. It works by stimulating the ‘alpha’ receptors in the blood vessel walls. Noradrenaline causes the blood vessels to narrow and this redirects the blood to vital organs. It also causes increased resistance to the heart beating and this results in an increased blood pressure.

Noradrenaline infusions are prescribed in order to increase SVR in hypotensive patients. It should only be administered by appropriately trained staff capable of monitoring the patient's condition. It should only be administered by Central Venous Access Device (CVAD) trained nurses able to monitor the patient's condition.

Noradrenaline should be administered centrally (except in special circumstances), as its potency is such that extravasation may cause necrosis of the skin. Although, whether or not noradrenaline can be safely administered via a peripheral cannula is the subject of current research.

Proposed Noradrenaline infusion starting rates:

The following are **suggested** rates, the starting rate should be individualised to each patients clinical presentation and ideal body weight.

SBP < 60	SBP 60-75	SBP 75-90	SBP >90
10-12 ml/hr	8 ml/hr	5 ml/hr	2 ml/hr

Increase the infusion rate by **2 ml/hr every 15 minutes** until the desired BP is achieved. Another important clinical sign of organ perfusion is maintenance of a urine output of 0.5ml/kg/hr (unless AKI with anuria). If at any stage during titration of the infusion BP begins to rise beyond **the** targeted range **decrease the infusion rate immediately.** Some patients will be hypersensitive to the noradrenaline and may require adjustments of **1** ml/hr instead**. Note that patients with lower ideal body weight may require lower starting rates than those with a greater ideal body weight.**

The starting rate in this protocol is set at 2 ml/hr and the maximum infusion rate is 12ml/hr.

IMPORTANT: On the medical high dependency unit patients with escalating Noradrenaline requirements greater than 12ml/hr should be discussed with the Intensive Care Unit with a view to transfer to a higher level of care if appropriate. MHDU should not routinely be administering Noradrenaline doses that are in excess of 12ml/hr.

Side Effects:

- Headaches
- Bradycardia
- Hypertension
- Peripheral Ischaemia
- Necrosis at injection site

Noradrenaline

Dose	See table above on initial rates See flowchart in Appendix 1 on adjusting rate according to response
Preparation	Pharmacy will dispense: 15mg noradrenaline in 297ml sodium chloride 0.9% = 50micrograms/ml.
Administration	Continuous infusion via a Central Line only. Use the Noradrenaline program on the Baxter Evo IQ Infusion Pump The noradrenaline solution should be colourless and protected from light. If you notice that the solution looks cloudy **DO NOT** use and return to pharmacy. Ensure the noradrenaline is ordered from pharmacy in plenty of time. **DO NOT** allow the noradrenaline infusion to run out.
Shelf-life	Protect from light 24hours at room temperature
Monitoring	Ensure the patient has the appropriate form of monitoring for their blood pressure, i.e. arterial line or effective Non-Invasive BP (NIBP) which can be set at 2 minute intervals for 10 minutes at any rate change Once the patient's blood pressure begins responding to the noradrenaline be sure to wean the noradrenaline infusion to the minimum rate required to meet the patient's target blood pressure. Monitor your patient closely and **DO NOT** leave them unattended until you have the noradrenaline infusion at the optimum rate for the patients' blood pressure to maintain a urine output of 0.5ml/kg/hr (unless AKI with anuria)
Additional information	Ensure the doctor has provided clear guidelines on the patients' systolic or mean arterial pressure (MAP) that you need to aim for. Rising noradrenaline requirements especially after being stable for >4 hours should prompt reassessment of the patient and consideration of other potential causes. A further fluid challenge should be considered. Fluid challenge should be given at least once every 12 hours and the response assessed by a clinician.
Flushing	To avoid adverse effects resulting from an unintentional 'bolus' dose, flush at the same rate the medicine was administered. When the infusion is discontinued disconnect the administration set and aspirate the contents of the central venous access device, then flush it with sodium chloride 0.9%.

Sample Label	**DRUGS ADDED TO THIS INFUSION**			
	PATIENT'S NAME			WARD 407
	DRUG IV Noradrenalinein 297ml 5% Glucose *To be infused via CENTRAL line only*	AMOUNT 15mg	ADDED BY	CHECK BY
	DATE ADDED TIME ADDED	EXP. DATE EXP. TIME		BATCH No.
	DISCONTINUE IF CLOUDINESS OR PRECIPITATE DEVELOPS			

Metaraminol:

Indications for Use

Metaraminol can be used for the short-term management of hypotension if the patient has no central line access. It is administered via a peripheral cannula and can be given as an IV bolus or infusion. The Surviving Sepsis campaign guidelines suggest consideration of peripheral inotropes to optimise organ perfusion in absence of a central line. The vasopressor effect of metaraminol begins 1-2 minutes following intravenous injection. It also has a longer duration of action compared with noradrenaline, with a single dose of metaraminol potentially lasting between 20 minutes to one hour.

The actions of metaraminol are similar to those of noradrenaline but it is much less potent. It can be used to support blood pressure in the following circumstances;

- Where patient is admitted to medical HDU with a MAP of below 65mmHg and it is not immediately possible for a central line to be inserted.
- Where a patient is admitted with septic shock and MAP is below 65mmHg but there are signs of improvement and the duration of inotropic support is expected to be short

In all cases where peripheral inotropes are used the threshold for switching to noradrenaline via a central line should be low. The following situations should be considered an indication for switching to noradrenaline;

- If the need for vasopressors is going to exceed 24-48 hours
- If dose requirement is high and increasing, needing frequent bag changes and high volumes
- If a central line is inserted for other reasons, metaraminol should be switched to noradrenaline

Where possible metaraminol should be monitored by arterial line as noradrenaline would be.

Peripheral inotropes should be administered via the largest possible gauge cannula, ideally green and sited in the antecubital fossa, as they may cause venous irritation and tissue damage in the event of extravasation.

In event of extravasation, the infusion should be discontinued and medical staff alerted.

Side Effects

- Headache
- Hypertension
- Nausea
- Reflex bradycardia
- Peripheral ischaemia
- May cause vasospasm

Contra-indications

Metaraminol should not be used in:

◦ **Asthmatic patients (due to potential hypersensitivity risk to one of the preservatives)**

◦ **Patients taking or who have taken monoamine oxidase inhibitors (MAOI) including Linezolid in the previous 14days.**

Dosing Metaraminol

See monograph below. To make an infusion of IV metaraminol, 50mg of metaraminol is diluted in 250ml of 0.9% saline or 5% dextrose to give a concentration of 0.2mg/ml. The starting rate in this protocol is set at 2.5ml/hr (0.5mg/hr) and the maximum infusion rate is 50ml/hr (10mg/hr).

Metaraminol is much less potent than noradrenaline and there is no relationship between the doses of each requiredhttps://www.medicines.org.uk/emc/product/7111/smpc to sustain MAP.

It is possible that in profoundly hypotensive patients a higher dose may be needed as a starting rate, in this instance 6ml/hr (1.2mg/hr) is suggested.

Patients requiring greater than 15ml/hr (3mg/hr) should be considered for conversion to noradrenaline. When switching to noradrenaline, consult the table on page 2 for the starting rate.

Bolusing Metaraminol

Unlike noradrenaline, metaraminol can be bolused if the physician feels it is clinically indicated.

PLEASE NOTE: the concentration of metaraminol for administering an IV bolus is different from the concentration used for the infusion (see monograph for instructions).

For an IV bolus, a solution of Metaraminol 10mg in 20mL saline needs to be made (please see monograph on the next page) and this produces a concentration of 0.5mg/1ml.

1ml (i.e. 0.5 mg) of this solution can then be bolused and the infusion rate increased to maintain effect.

Discontinuation

When target blood pressure is consistently reached with a rate of 1-2ml/hr (i.e. 0.2mg – 0.4mg/hr) then the infusion can be safely discontinued.

Metaraminol

Dose	**IV infusion** Initial rate to be used is 2.5ml/hr (i.e. 0.5mg/hr). Usual rate to be used is 0 - 50ml per hour (i.e. 0 – 10mg per hour). See metaraminol flow chart on starting and adjusting rate according to response. **Slow IV bolus over 3 - 5 minutes** (Emergency **ONLY**). 0.5mg/1ml via a large peripheral vein.
Preparation	Each 1mL ampoule contains 10mg metaraminol (10mg/ml). Metaraminol can be given as an IV bolus or infusion. Infusion should be considered first line unless bolus doses have been requested by the Consultant/ Registrar. **IV infusion (concentration 0.2mg per ml):** 1. Withdraw 5mL from a 250mL bag of sodium chloride 0.9% or glucose 5%. Discard. 2. Draw up 5mL (50mg) of metaraminol (from the ampoules) using a filter needle. 3. Add the 5mL (50mg) of metaraminol to the 250ml infusion bag. **IV bolus (10mg in 20mL solution, concentration 0.5mg per ml):** 1. Draw up 1mL (10mg) of metaraminol from the ampoule with a 30mL syringe. 2. Dilute with sodium chloride 0.9% to make up to a volume of 20mL. **CARE: this produces a different concentration to metaraminol infusion.** In dire emergency metaraminol can be given undiluted.
Administration	

	For IV infusion, administer with an infusion pump via central line or a large peripheral vein (e.g. antecubital fossa). For the standard infusion dilution (50mg in 250mL) use the metaraminol 50mg in 250ml program in the Medical HDU section of the Baxter Evo IQ Infusion Pump. For continuous infusions, avoid administration in lines where other drugs or fluids may be bolused or flushed. Glucose 5% can be used as a diluent if patient is hypernatraemic. Do not allow the infusion to run out. A new infusion should be prepared promptly when the previous one is due to finish. When stopping the infusion, reduce the rate of infusion gradually. Abrupt withdrawal can cause acute hypotension. After discontinuation, flush the peripheral cannula with sodium chloride 0.9% at the same rate the medicine was infused to avoid adverse hemodynamic effects.

Shelf-life	Stable between 2-8°C for 24 hours after dilution
Additional information	Contact the ward or on call Pharmacist if unsure of the calculations Glucose 5% can be used as a diluent if patient is hypernatraemic
Monitoring	Continuous blood pressure and cardiac monitoring for the duration of the infusion Monitor fluid balance Monitor peripheral vein infusion site for signs of extravasation, which can cause local tissue necrosis Rising metaraminol requirements, especially after being stable for 4hours, should prompt reassessment of the patient and consideration of other potential causes. Further fluid challenges should be considered. Fluid challenge should be considered at least once every 12 hours and the response assessed by a clinician
Cautions	**Metaraminol should not be used in:** ◦ **Asthmatic patients (due to potential hypersensitivity risk to one of the preservatives)**

<table>
<tr><td></td><td>◦ Patients taking or who have taken monoamine oxidase inhibitors (MAOI) including Linezolid in the previous 14days.

If either of these applies consult supervising consultant before starting therapy.

Hypersensitivity to Metaraminol or sulfites (contains sodium metabisulfite)</td></tr>
<tr><td>Sample Label</td><td>
<table>
<tr><td colspan="4">DRUGS ADDED TO THIS INFUSION</td></tr>
<tr><td colspan="3">PATIENT’S NAME</td><td>WARD

407</td></tr>
<tr><td>DRUG

IV Metaraminol

In 250ml Sodium Chloride 0.9% / Glucose 5% infusion</td><td>AMOUNT

50mg

Concentration:

0.2mg/ml</td><td>ADDED BY</td><td>CHECK BY</td></tr>
<tr><td>DATE ADDED

TIME ADDED</td><td colspan="2">EXP. DATE

EXP. TIME</td><td>BATCH No.</td></tr>
<tr><td colspan="4">DISCONTINUE IF CLOUDINESS OR PRECIPITATE DEVELOPS</td></tr>
</table>
</td></tr>
</table>

4. References (including any links to NICE Guidance etc.)

Surviving Sepsis Campaign 2021Guidelines www.survivingsesisi.org

Medicines.org.uk. 2022. *Metaraminol 10mg/mL Solution for Injection or Infusion - Summary of Product Characteristics (SmPC) - (emc)*. [online] Available at: <https://www.medicines.org.uk/emc/product/7111/smpc> [Accessed 18 February 2022].

Medusa.wales.nhs.uk. 2022. Noradrenaline [online] Available at: <https://medusa.wales.nhs.uk/IVGuideDisplayNewFormat.asp> [Accessed 18 February 2022].

Medusa.wales.nhs.uk. 2022. *Metaraminol*. [online] Available at: <https://medusa.wales.nhs.uk/IVGuideDisplayNewFormat.asp> [Accessed 18 February 2022].

Smh-gas.org.uk. 2022. [online] Available at: <http://smh-gas.org.uk/wp-content/uploads/2016/12/mataraminol-guideline.pdf> [Accessed 18 February 2022].

5. Documentation Controls

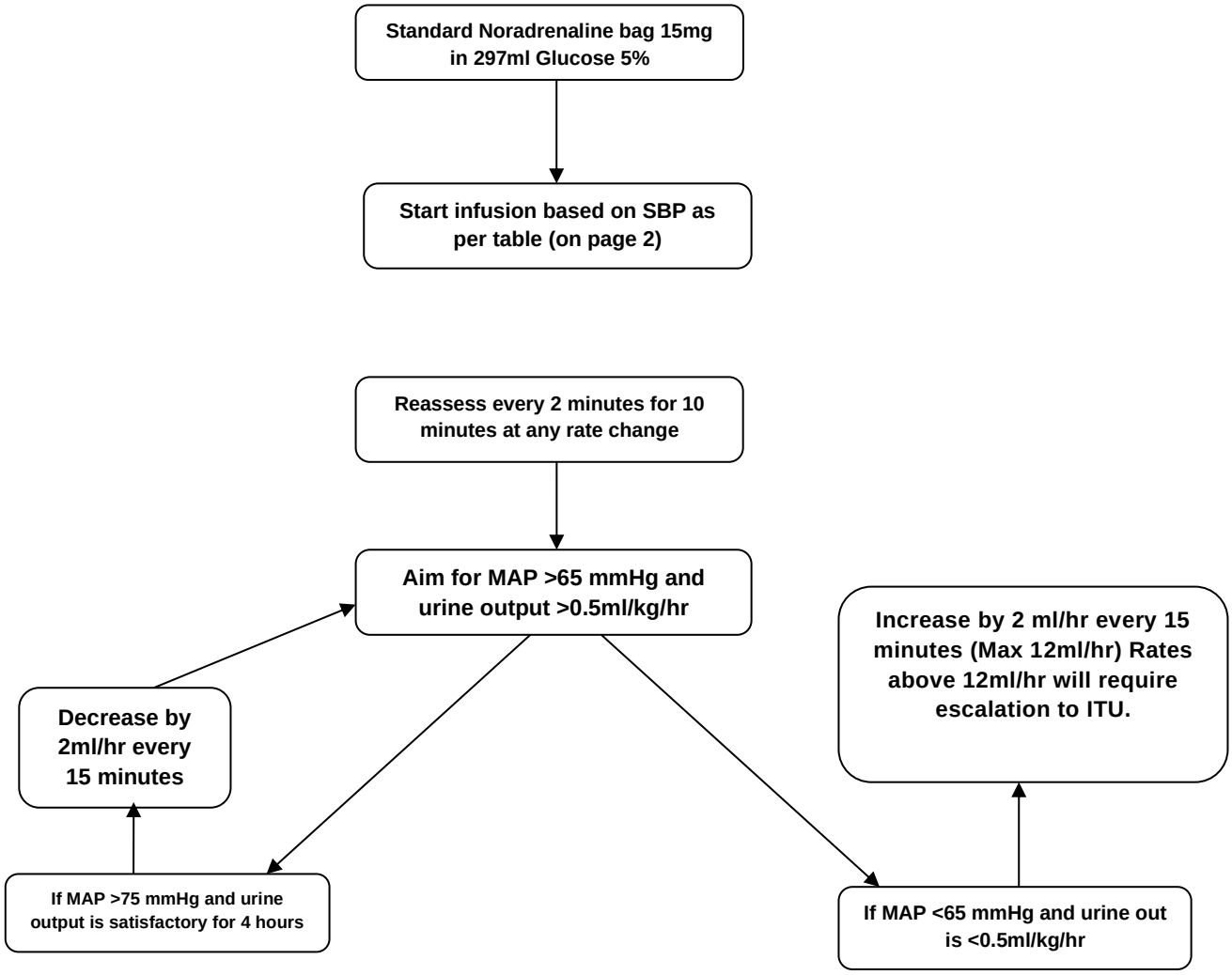
Reference Number CG-REN/4182/23	**Version:**		**Status** Final	
Version / Amendment History	Version	Date	Author	Reason
	1	May 2023	Dr Crowley	New Guideline
	1.1.0	Feb 2024	Sadaf Fatima	Amendment due to different concentration of Norad bags.Approved in Renal and by Medicines Safety Lead.
Intended Recipients: Clinical Staff on ward 407 MHDU				
Training and Dissemination: Induction				
Development of Guideline: Sadaf Fatima, Renal and Acute Medicine Pharmacist Maya Daas, Advanced Pharmacist – Renal Services Dr.Lisa Crowley Consultant Nephrologist				
Consultation with: Ward 407 Nursing Staff, Renal Consultants				
Linked Documents: None				
Keywords: Medical HDU, Vasopressors				

Business Unit Sign Off	**Group:SMBU2** **Date:21/7/2023**
Divisional Sign Off	**Group:Medicine Division** **Date:June 2023**
Date of Upload	February 2024
Review Date	July 2026
Contact for Review	Dr Lisa Crowley

6. Appendices

Appendix 1

Noradrenaline Algorithm 15mg / 297ml Glucose 5%



Appendix 2

Metaraminol Algorithm 50mg / 250ml sodium chloride 0.9%