Worcestershire Acute Hospitals NHS Trust

Administration of Peripheral Vasopressors for Critically Ill Patients

This protocol does not override the individual responsibility of health professionals to make appropriate decision according to the circumstances of the individual patient in consultation with the patient and /or carer. Health care professionals must be prepared to justify any deviation from this guidance.

INTRODUCTION

Vasopressor medications are used to treat hypotension in critically ill patients with shock. They increase systemic vascular resistance and aim to improve vital organ perfusion by restoring haemodynamic stability. Usually, these drugs are administered via a central venous catheter due to concerns about tissue damage in the event of extravasation. However, there is good evidence that demonstrates peripheral administration is feasible and safe. This guideline details the use of peripheral vasopressors as a bridging therapy in the critically ill patient prior to transfer to a critical care setting and establishment of central venous access.

THIS PROTOCOL IS FOR USE BY THE FOLLOWING STAFF GROUPS:

Critical Care Staff
Advanced Critical Care Practitioners

Lead Clinician(s)

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Approved by *ICM Forum* on:	20th May 2024
Approved by Medicines Safety Committee on:	10th July 2024
Review Date: This is the most current document and should be used until a revised version is in place	20th May 2027

Key amendments to this guideline

Date	Amendment	Approved by: (name of committee or accountable director)
May 2024	New document approved	ICM Forum

DETAILS OF PROTOCOL

Vasopressor	Presentation	Dilution	Recommended Dose
Adrenaline (direct acting sympathomimetic with alpha and beta-adrenergic activity)	Adrenaline 1mg/ ml (1:1000) for injection or infusion. Or 0.1mg/ml 1:10,000 for injection	For dilution with either 0.9% sodium chloride or 5% glucose to 16 microgram/ml i.e. 4mg 1:1000 (= 4ml) adrenaline with 246ml diluent.	Administer via an infusion pump at a rate of 210microgram/hr (13ml/hr of the standard concentration based on a 70kg patient at a recommended rate of 0.05microgram/kg/min). Then titrate to effect.
Noradrenaline (sympathomimetic with alpha and beta-adrenergic activity)	Noradrenaline 1mg/ml for injection or infusion.	For dilution with either 0.9% sodium chloride or 5% glucose to 16microgram/ml i.e. 4mg (= 4ml) noradrenaline with 246ml diluent.	Administer via an infusion pump at a rate of 210microgram/hr (13ml/hr of the standard concentration based on a 70kg patient at a recommended rate of 0.05microgram/kg/min). Then titrate to effect.
Metaraminol (sympathetic agent with direct and indirect effects on adrenergic receptors – predominant alpha activity)	Metaraminol 10mg/ml for injection or infusion	For dilution with either 0.9% sodium chloride or 5% glucose to 0.5mg/ml i.e. 20mg (= 2ml) metaraminol with 38ml diluent.	Administer via infusion pump at a rate of 1 to 20ml/hr of the standard solution.
Phenylephrine (sympathomimetic with direct effects on adrenergic receptors - predominantly alpha-adrenergic activity)	Phenylephrine pre-mixed 100microgram/ml or 10mg/mL solution for injection or infusion.	If pre-mixed phenylephrine 100microgram/ml not available, dilute with either 0.9% sodium chloride or 5% glucose to 100microgram/ml i.e. 50mg (5ml of 10mg/ml) with 495ml diluent.	Administer via an infusion pump typically at a rate of 10-40ml/hr of the standard solution. Titrate as required.

Vasopressor medications are used to treat hypotension in critically ill patients with various forms of shock but predominantly of a distributive nature. They increase systemic vascular resistance and aim to improve vital organ perfusion by restoring haemodynamic stability.

Typically, these agents were historically administered via a central venous catheter (CVC) into a central vein however recent literature has shown that peripheral administration is not only possible but also safe [1,2,3]. The most worrisome complication previously cited with administration via a peripherally inserted cannula (PVC) was extravasation. The above-mentioned literature however suggests that extravasation events are uncommon at only 3.4% and these events had no reported tissue necrosis or limb ischaemia. [1]

Whilst drugs such as metaraminol and phenylephrine have been used peripherally for a number of years, recent studies have shown that drugs such as adrenaline and noradrenaline are able to be used in dilute forms via PVC. [4] This may avoid at least the short-term risks associated with central venous access such as pneumothorax, arterial puncture and catheter related blood stream infection (CRBSI).

These drugs may otherwise be used as a bridge to stabilisation of the critically ill patient whilst waiting to transfer them to an appropriate place where central venous access can be gained. This may be in the emergency department, inpatient wards or other areas where patients may require stabilisation. Other indications may be peri-operative use by anaesthetic clinicians or where central venous access is proving difficult.

These guidelines are largely based on recommendations provided by the Intensive Care Society (ICS). [5] There is no formal consensus on concentrations and the ICS recommend agreeing a local policy with reference to available literature and current practice.

This trust may encounter children that require stabilisation before transfer to a tertiary centre with a paediatric ICU by the KIDS team and peripheral vasoconstrictors are frequently used for these children. [6] Please note that the concentrations in this guideline are different from the KIDS team guidance which can be found within the reference below.

Standards

The following are pre-requisites for providing peripheral vasopressors:

- Guidance on dilution, concentration and route of administration as detailed in this guideline must be followed.
- An infusion pump for the administration of vasopressor agents must be used.
- Vasopressor agents must only be administered by clinicians trained and competent in their use.
- Vasopressors should only be used in or on the transfer to an area capable of providing level 2 care (ICU, resus, theatres).
- PVCs should be of at least 20G (pink cannula).**
- PVCs being used for vasopressors should be sited proximal to the wrist and sites avoided that have required more than one attempt to secure access. Avoid sites of flexion in awake patients.**
- A second PVC should be sited as a back-up in case of primary cannula failure.
- Invasive blood pressure monitoring is recommended. If not possible then regular non-invasive monitoring must be employed.
- PVC should be monitored for signs of extravasation. If suspected extravasation then stop infusion, transfer to patent PVC and follow guidance in appendix 1.
- Where the infusion rate is greater than 50ml/hour, a CVC should be strongly considered.
- A peripheral vasopressor infusion should only be used for the minimum amount of time that it is required before either transitioning to a CVC or stopping due to clinical improvement.**
- All peripheral vasopressor infusions must be reviewed at 24 hours and the reason for continuing documented in the notes.**
- Adverse events should be documented in the patient's notes, and reported and investigated using the DATIX system.

**NB: Deviation from these standards significantly increases the risk of extravasation

Adrenaline

- Adrenaline is a direct-acting sympathomimetic agent with both alpha and beta-adrenergic activity. After stopping the infusion its effects on blood pressure cease after around 2-3 minutes.
- Presented as Adrenaline 1mg/mL (1:1000) solution for injection or 0.1ml/ml (1:10,000) solution for injection.
- For dilution with either 0.9% sodium chloride or 5% glucose to make a concentration of 16micrograms/ml i.e. 4mg 1:1000 (= 4ml) adrenaline with 246ml diluent.
- Administer via an infusion pump at a rate of 210microgram/hr (13ml/hr of the standard concentration based on a 70kg patient at a recommended rate of 0.05microgram/kg/min). Then titrate to effect.
- Administration can be either via a volumetric pump or via a syringe driver with the above concentration decanted to 50ml syringes.
- After discontinuation, the PVC should be flushed with 0.9% sodium chloride at the same rate the medicine was infused to avoid adverse haemodynamic effects. Giving adrenaline alongside other medications via a Y-connector should be avoided to minimise the risk of a bolus of adrenaline being delivered via siphoning.

Noradrenaline

- Noradrenaline is a direct-acting sympathomimetic agent with both alpha and beta-adrenergic activity. After stopping the infusion its effects on blood pressure cease after around 1-2 minutes.
- Presented as Noradrenaline 1mg/mL solution for injection.
- For dilution with either 0.9% sodium chloride or 5% glucose to make a concentration of 16micrograms/ml i.e. 4mg (= 4ml) noradrenaline with 246ml diluent.
- Administer via an infusion pump at a rate of 210microgram/hr (13ml/hr of the standard concentration based on a 70kg patient at a recommended rate of 0.05microgram/kg/min). Then titrate to effect.
- Administration can be either via a volumetric pump or via a syringe driver with the above concentration decanted to 50ml syringes.
- After discontinuation, the PVC should be flushed with 0.9% sodium chloride at the same rate the medicine was infused to avoid adverse haemodynamic effects. Giving noradrenaline alongside other medications via a Y-connector should be avoided to minimise the risk of a bolus of adrenaline being delivered via siphoning.

Metaraminol

- Metaraminol is a sympathetic agent with direct and indirect effects on adrenergic receptors. It has both alpha- and beta-adrenergic activity, the former being predominant. The effects of metaraminol are similar to those of noradrenaline but it is much less potent.
- Presented as Metaraminol 10mg/ml for injection or infusion.
- For dilution with either 0.9% sodium chloride or 5% glucose to 0.5mg/ml i.e. 20mg (= 2ml) metaraminol with 38ml 0.9% diluent.
- Administer via infusion pump at a rate of 1 to 20ml/hr of the standard solution.
- After discontinuation, the PVC should be flushed with 0.9% sodium chloride at the same rate the medicine was infused to avoid adverse haemodynamic effects.
- Use with caution in patients on digoxin since the combination can cause ectopic arrhythmic activity.

Phenylephrine

- Phenylephrine is a sympathomimetic agent with mainly direct effects on adrenergic receptors. It has predominantly alpha-adrenergic activity.

- Presented as Phenylephrine pre-mixed 100microgram/ml or 10mg/mL solution for injection or infusion.
- If pre-mixed Phenylephrine 100microgram/ml is not available, dilute with either 0.9% sodium chloride or 5% glucose to 100microgram/ml i.e. 50mg (5ml of 10mg/ml) with 495ml diluent.
- After discontinuation, the PVC should be flushed with 0.9% sodium chloride at the same rate the medicine was infused to avoid adverse haemodynamic effects.
- Metabolised by monoamine oxidase therefore contraindicated in patients on monoamine oxidase inhibitors.

DEFINITIONS/ ABBREVIATIONS

CVC	central venous catheter
PVC	peripheral venous catheter
CRBSI	catheter related blood stream infection
MECU	medical enhanced care unit
SOP	standard operating procedure
ICS	Intensive Care Society

APPENDIX 1: Management of extravasation event:

1. Stop the infusion immediately and disconnect the line from the PVC.
2. Attempt to aspirate 3-5mL from the PVC if able.
3. Remove the cannula and apply a dressing to the removal site.
4. Mark the extravasation area if possible, in order to allow monitoring of any developing injury.
5. Elevate the affected limb if able to do so to reduce swelling.
6. Consider application of a topical vasoactive agent to encourage local blood flow (Glyceryl trinitrate 4mg/g rectal ointment has been used by other UK centres)
7. Administer analgesia if required.
8. Seek advice from a surgeon or your local tissue viability service if concerned, and / or consider a referral to the plastics team at University Hospitals Birmingham.
9. Document the incident and report via DATIX.

Monitoring Tool

This should include realistic goals, timeframes and measurable outcomes.

How will monitoring be carried out?

Who will monitor compliance with the guideline?

Page/ Section of Key Document	Key control:	Checks to be carried out to confirm compliance with the policy:	How often the check will be carried out:	Responsible for carrying out the check:	Results of check reported to: *(Responsible for also ensuring actions are developed to address any areas of non-compliance)*	Frequency of reporting:
	WHAT?	**HOW?**	**WHEN?**	**WHO?**	**WHERE?**	**WHEN?**
	These are the 'key' parts of the process that we are relying on to manage risk. We may not be able to monitor every part of the process, but we MUST monitor the key elements, otherwise we won't know whether we are keeping patients, visitors and/or staff safe.	What are we going to do to make sure the key parts of the process we have identified are being followed? (Some techniques to consider are; audits, spot-checks, analysis of incident trends, monitoring of attendance at training.)	Be realistic. Set achievable frequencies. Use terms such as '10 times a year' instead of 'monthly'.	Who is responsible for the check? Is it listed in the 'duties' section of the policy? Is it in the job description?	Who will receive the monitoring results? Where this is a committee the committee's specific responsibility for monitoring the process must be described within its terms of reference.	Use terms such as '10 times a year' instead of 'monthly'.

REFERENCES

[1] D. H. Tian, C. Smyth, G. Keijzers, S. P. Macdonald, S. Peake, A. Udy and A. Delaney, "Safety of peripheral administration of vasopressor medications: A systematic review," Emergency Medicine Australasia, vol. 32, no. 2, pp. 220-227, 2020.

[2] S. Hodzic, D. Golic, J. Smajic, S. Sijercic, S. Umihanic and S. Umihanic, "Complications Related to Insertion and Use of Central Venous Catheters (CVC)," Medical Archives, vol. 68, no. 5, pp. 300-303, 2014.

[3] The Association of Anaesthetists of Great Britain & Ireland, "Safe vascular access 2016," The Association of Anaesthetists of Great Britain & Ireland, London, 2016.

[4] C. Permipikul, S. Tongyoo, T. Viarasilpa, T. Trainarongsakul, T. Chakorn and S. Udompanturak, "Early Use of Norepinephrine in Septic Shock Resuscitation (CENSER). A Randomized Trial.," American Journal of Respiratory and Critical Care Medicine, vol. 199, no. 9, pp. 1097-1105, 2018.

[5] Intensive Care Society, "Vasopressors in the adult ICU V1.1" 2020, Intensive Care Society, available from https://www.ics.ac.uk/Society/Guidance/PDFs/Vasopressor_Agents_in_Adult_ICU

[6] KIDS NTS, Guideline for peripheral use of agents with inotropic and vasopressor properties in patients without available central access in emergency situations, available from https://kids.bwc.nhs.uk/wp-content/uploads/2021/11/Peripheral-inotropes-vasopressors.pdf

Contribution List

This key document has been circulated to the following individuals for consultation.

Designation
ICU Consultants via ICM forum
Ruth Coxhead – ICU pharmacist
Keith Hinton – ICU pharmacist

This key document has been circulated to the chair(s) of the following committees / groups for comments.

Committee
ICM forum
Medicines safety committee

Supporting Document 1 - Equality Impact Assessment Tool

To be completed by the key document author and included as an appendix to key document when submitted to the appropriate committee for consideration and approval.

Please complete assessment form on next page;

Herefordshire & Worcestershire STP - Equality Impact Assessment (EIA) Form
Please read EIA guidelines when completing this form

Section 1 - Name of Organisation (please tick)

Herefordshire & Worcestershire STP		Herefordshire Council		Herefordshire CCG	
Worcestershire Acute Hospitals NHS Trust	x	Worcestershire County Council		Worcestershire CCGs	
Worcestershire Health and Care NHS Trust		Wye Valley NHS Trust		Other (please state)	

Name of Lead for Activity	**Dr Sian Bhardwaj**

Details of individuals completing this assessment	**Name**	**Job title**	**e-mail contact**
	Sian Bhardwaj	**Consultant in Anaesthsia and Intensive Care Medicine**	**sian.bhardwaj@nhs.net**
Date assessment completed	**18/6/24**		

Section 2

Activity being assessed (e.g. policy/procedure, document, service redesign, policy, strategy etc.)	**Title:** Administration of Peripheral Vasopressors for Critically Ill Patients			
What is the aim, purpose and/or intended outcomes of this Activity?	Safe stabilisation of shocked patients prior to establishment of central venous access and admission to ICU			
Who will be affected by the development & implementation of this activity?	❑	Service User	❑	Staff
	x	Patient	❑	Communities
	❑	Carers	❑	Other _____
	❑	Visitors	❑	
Is this:	❑ Review of an existing activity x New activity ❑ Planning to withdraw or reduce a service, activity or presence?			

What information and evidence have you reviewed to help inform this assessment? (Please name sources, eg demographic information for patients / services / staff groups affected, complaints etc.	Literature review and consideration of national guidelines
Summary of engagement or consultation undertaken (e.g. who and how have you engaged with, or why do you believe this is not required)	ICM forum Medicines safety committee
Summary of relevant findings	As in this guideline

Section 3

Please consider the potential impact of this activity (during development & implementation) on each of the equality groups outlined below. **Please tick one or more impact box below for each Equality Group and explain your rationale**. Please note it is possible for the potential impact to be both positive and negative within the same equality group and this should be recorded. Remember to consider the impact on e.g. staff, public, patients, carers etc. in these equality groups.

Equality Group	Potential positive impact	Potential neutral impact	Potential negative impact	Please explain your reasons for any potential positive, neutral or negative impact identified
Age		x		
Disability		x		
Gender Reassignment		x		
Marriage & Civil Partnerships		x		
Pregnancy & Maternity		x		
Race including Traveling Communities		x		
Religion & Belief		x		
Sex		x		
Sexual Orientation		x		
Other Vulnerable and Disadvantaged Groups (e.g. carers; care leavers; homeless;		x		

Equality Group	Potential positive impact	Potential neutral impact	Potential negative impact	Please explain your reasons for any potential positive, neutral or negative impact identified
Social/Economic deprivation, travelling communities etc.)				
Health Inequalities (any preventable, unfair & unjust differences in health status between groups, populations or individuals that arise from the unequal distribution of social, environmental & economic conditions within societies)		X		

Section 4

What actions will you take to mitigate any potential negative impacts?	Risk identified	Actions required to reduce / eliminate negative impact	Who will lead on the action?	Timeframe
	Harm due to extravasation.	*Highlighting practice which can increase the risk in Standards section of guideline.*		
How will you monitor these actions?	**Review of Datix submissions relating to protocol non-adherence or complications from any peripheral vasopressor therapy.**			
When will you review this EIA? (e.g in a service redesign, this EIA should be revisited regularly throughout the design & implementation)	**At ICM Forum routinely every 6 months, but sooner if any significant extravasation incident(s).**			

Section 5 - Please read and agree to the following Equality Statement

1. Equality Statement

1.1. All public bodies have a statutory duty under the Equality Act 2010 to set out arrangements to assess and consult on how their policies and functions impact on the 9 protected characteristics: Age; Disability; Gender Reassignment; Marriage & Civil Partnership; Pregnancy & Maternity; Race; Religion & Belief; Sex; Sexual Orientation

1.2. Our Organisations will challenge discrimination, promote equality, respect human rights, and aims to design and implement services, policies and measures that meet the diverse needs of our service, and population, ensuring that none are placed at a disadvantage over others.

1.3. All staff are expected to deliver services and provide services and care in a manner which respects the individuality of service users, patients, carers etc, and as such treat them and members of the workforce respectfully, paying due regard to the 9 protected characteristics.

Signature of person completing EIA	Sian Bhardwaj
Date signed	18/6/24
Comments:	
Signature of person the Leader Person for this activity	
Date signed	
Comments:	

Supporting Document 2 – Financial Impact Assessment

To be completed by the key document author and attached to key document when submitted to the appropriate committee for consideration and approval.

	Title of document:	Yes/No
1.	Does the implementation of this document require any additional Capital resources	
2.	Does the implementation of this document require additional revenue	
3.	Does the implementation of this document require additional manpower	
4.	Does the implementation of this document release any manpower costs through a change in practice	
5.	Are there additional staff training costs associated with implementing this document which cannot be delivered through current training programmes or allocated training times for staff	
	Other comments:	

If the response to any of the above is yes, please complete a business case and which is signed by your Finance Manager and Directorate Manager for consideration by the Accountable Director before progressing to the relevant committee for approval