Drug Guideline Title: Inotropes and Vasopressors

Summary: This guideline outlines the effects of inotropic and vasopressor agents

Approved by: ICU Director
Publication (Issue) Date: July 2013
Next Review Date: July 2016

Replaces Existing Drug Guideline: Inotropes and Vasopressors

Previous Review Dates: 2009

1. Introduction contains:
The risk addressed by this policy:

Patient Safety

The Aims / Expected Outcome of this policy:

Staff will have an improved understanding of the effects of inotropes and vasopressors and they will be administered safely and appropriately without any adverse side effects

Related Policies
- LH_PD2013_C03.01 Drug Administration
- LH_PD2010_C03.00 Drug Prescribing
- LH_PD2008_C03.12 Administration of IV Medication

2. Policy Statement:
- All care provided within Liverpool Hospital will be in accordance with infection control, manual handling and minimisation and management of aggression guidelines.
- Medications are to be prescribed and signed by a medical officer/authorised nurse practitioner (NP) unless required during an emergency.
- All drugs administered during an emergency (under the direction of a medical officer/authorised nurse practitioner) are to be documented during the event, then prescribed and signed following the event.
- Medications are to be given at the time prescribed (as close to the time as is possible when multiple drugs require ‘same time’ administration and, when the nurse is caring for more than one patient, recognition is given to a possible short delay to administration – antibiotics and other lifesaving drugs are to be prioritised) and are to be signed by the administering nurse.
- Parenteral medication prescriptions and the drug are to be checked with a second registered or endorsed enrolled nurse prior to administration. The “rights of drug administration” must be followed: right: patient, drug, dose, route, administration, time, reason for the drug, documentation, education and evaluation/outcome.
- Adverse drug reactions are to be documented and reported to a medical officer.
• Medication errors are to be reported using the hospital electronic reporting system: IIMS.
• Guidelines are for adult patients unless otherwise stated
• Inotropic and vasopressor therapy will be chosen for patient treatment according to the alpha/beta effects desired.
• All staff managing administration of inotropic drugs and vasopressor agents must complete the ICU competency assessment.

For the purposes of this Policy, an accredited RN is: a Registered Nurse (RN) who has completed the required self directed learning packages and has been accredited by a Clinical Nurse Educator / Consultant with the inotrope competency tool, to administer/titrate inotropic drugs when caring for an Intensive Care Unit (ICU) Patient. The Educator/Clinical Nurse Consultant may deem the nurse competent if the nurse has previous documented experience/qualifications.

3. Principles

Definitions:
Inotropes: These are agents that alter the force and strength of myocardial contractility.

Vasopressors: These are sympathomimetic drugs that mimic the effects of the sympathetic nervous system. They cause vascular smooth muscle vasoconstriction.

Background Information3,4
Inotropes and vasopressors have excitatory and inhibitory actions on the heart and vascular smooth muscle, as well as important metabolic, central nervous system and presynaptic autonomic nervous system effects3.

Catecholamines mediate their cardiovascular effects though α1, β1, β2 and dopaminergic receptors.

Adrenergic receptors can be desensitized and downregulated in certain conditions such as chronic heart failure3. The relative binding affinities of individual inotropes and vasopressors to adrenergic receptors can be altered by hypoxia and acidosis, which limits their clinical effect.

Receptor Stimulation1,3,4
α1 – Activation of α1 adrenergic receptors on arterial vascular smooth muscle cells results in smooth muscle contraction and increase in systemic vascular resistance (SVR). It results in peripheral vasoconstriction.

β1 – Stimulation of β1 adrenergic receptors results in enhanced myocardial contractility through Ca2+ mediated facilitation of the actin-myosin complex binding with troponin C. It also enhances chronicity through Ca2+ channel activation. It results in an increase in heart rate and contractility.

β2 – Stimulation of β2 adrenergic receptors on vascular smooth muscle cells through a different intracellular mechanism results in increased Ca2+ uptake by the sarcoplasmic reticulum and vasodilation. This causes bronchodilation and dilation of coronary arteries.

DA – Stimulation of dopaminergic receptors in the kidney and splanchnic vasculature results in renal and mesenteric vasodilation.

V1 - Stimulation of V1 receptors in the vascular smooth muscle mediates constriction.

V2 – Stimulation of V2 receptors in the renal collecting duct, enhances the permeability of the collecting duct and mediates water reabsorption.
Commonly used sympathomimetic drugs and their mechanism of action: 1,2,3

**Adrenaline**: sympathomimetic amine with high affinity for β₁, β₂ and α₁. β effects are more pronounced at a small dose and α₁ effects at a higher dose.

**Noradrenaline**: sympathomimetic amine with potent α₁ effects and modest β-agonist activity.

**Metaraminolol**: sympathomimetic amine with positive inotropic effect on the heart and peripheral vasoconstriction.

**Dobutamine**: synthetic catecholamine with strong β₁ and β₂ effects. Its cardiac β₁ effect makes it a potent inotrope, however it has weak chronotropic activity. Vascular smooth muscle binding results in combined α₁ adrenergic agonism and antagonism as well as β₂ stimulation with a net vascular effect of mild vasodilation.

**Milrinone**: phosphodiesterase inhibitor (PDI). Phosphodiesterase 3 is an intracellular enzyme associated with the sarcoplasmic reticulum in cardiac myocytes and vascular smooth muscle that breaks down cAMP into AMP. Milrinone is a PDI that increases the level of cAMP by inhibiting its breakdown. This leads to increased myocardial contractility. It is also a potent inotrope and vasodilator.

**Vasopressin**: exerts its circulatory effect on V₁ receptors causing constriction of vascular smooth muscle. Its V₂ effects increase renal collecting duct permeability and mediate water reabsorption.

**Levosimendan**: calcium sensitizing agent. It has dual mechanism of action that includes calcium sensitization of contractile proteins and the opening of ATP dependant potassium channels. Calcium dependant binding to troponin C enhances ventricular contractility without increasing intracellular Ca+ concentration or compromising diastolic relaxation. The opening of potassium channels on vascular smooth muscle leads to arteriolar and venous vasodilation. This promotes myocardial protection during ischemia.

**Table: Inotrope / vasopressor, clinical indication, receptor binding**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Clinical Indication</th>
<th>α₁</th>
<th>β₁</th>
<th>β₂</th>
<th>DA</th>
<th>V₁ / V₂</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adrenaline</td>
<td>Shock (cardiogenic, vasodilatory), cardiac arrest, bronchospasm / anaphylaxis, symptomatic bradycardia</td>
<td>++++</td>
<td>+++++</td>
<td>+++</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Noradrenaline</td>
<td>Shock (cardiogenic, vasodilatory), low cardiac output with low SVR</td>
<td>++++</td>
<td>+++</td>
<td>++</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Dobutamine</td>
<td>Low cardiac output (decompensated HF, cardiogenic shock, sepsis induced myocardial dysfunction)</td>
<td>+</td>
<td>+++++</td>
<td>+++</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Dopamine</td>
<td>Shock (cardiogenic, vasodilatory), heart failure</td>
<td>+++</td>
<td>+++++</td>
<td>++</td>
<td>++++</td>
<td>N/A</td>
</tr>
<tr>
<td>Isoprenaline</td>
<td>Heart block &amp; Bradyarrhythmias</td>
<td>0</td>
<td>+++++</td>
<td>+++++</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>Phenylephrine</strong></td>
<td>Hypotension (vagally mediated, medication-induced) Increase MAP with Aortic stenosis and hypotension</td>
<td>++++</td>
<td>0</td>
<td>0</td>
<td>N/A</td>
<td>N/A</td>
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<tr>
<td><strong>Metaraminol</strong></td>
<td>Acute Hypotension</td>
<td>++++</td>
<td>+</td>
<td>0</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>Milrinone</strong></td>
<td>Low cardiac output (decompensated heart failure)</td>
<td>Phosphodiesterase inhibitor - ↑ cAMP</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Vasopressin</strong></td>
<td>Shock (cardiogenic, vasodilatory), cardiac arrest</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>++++</td>
</tr>
<tr>
<td><strong>Levosimendan</strong></td>
<td>Decompensated heart failure</td>
<td>Calcium sensitising agent</td>
<td></td>
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</tr>
</tbody>
</table>

- **α and β receptor activity:**
  
  \[ + \text{ to } ++++ \text{ is minimal to maximal.} \]

4. **Performance Measures**

All incidents are documented using the hospital electronic reporting system: IIMS and managed appropriately by the NUM and staff as directed.

5. **References / Links**


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**Endorsed by:** A Prof. Michael Parr, ICU Director