Drug Guideline  Prostacyclin_Nebulised

Summary:
This guideline outlines the use of nebulised prostacyclin with the AeronebSolo. It is used for short term treatment in pulmonary hypertension and for severe hypoxic respiratory failure.

There are two available preparations of prostacyclin:
- Iloprost (prostacyclin solution for inhalation) which is used as nebulised solution for intermittent therapy.
- Epoprostenol solution is used for the continuous nebulizer therapy

Note: Please refer to the guideline 'Epoprostenol' for detailed use of intravenous epoprostenol.

Approved by: ICU Medical Director
Publication (Issue) Date: September 2015
Next Review Date: September 2018
Replaces Existing Drug Guideline: none
Previous Review Dates: none

Background Information:

1. Introduction contains:
The risk addressed by this drug guideline:

Patient safety

The Aims / Expected Outcome of this drug guideline:

The use of nebulised prostacyclin is administered safely to patients by accredited nursing staff who comply with hospital and ICU guidelines and policies

Related Standards or Legislation

NSQHS Standard 1 Governance
National Standard 4 Medication Safety

Related Policies

LH_PD2013_C03.01 Drug Administration
LH_PD2013_C03.03 Drug Calculation Formulas
LH_PD2013_C03.00 Drug Prescribing
LH_PD2013_C03.12 Administration of Intravenous (IV) Medications
LH_PD2014_C03.58 Intravenous Epoprostenol Sodium - Administration for Rheu
2. **Policy Statement**

- All care provided within the Liverpool Health Service 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

3. **Guideline**

**Actions**

- Prostacyclin (epoprostenol and the inhalation solution iloprost) delivered via the Aeroneb Solo nebuliser device will only reach distal airways and alveoli, which are able to be ventilated. It therefore selectively dilates pulmonary arteries, which supply ventilated lung tissue, and has little effect on segments of non-ventilated lung. In doing so it increases blood flow to well ventilated alveoli and reduces shunt to improve arterial oxygenation.
- Epoprostenol is spontaneously hydrolysed at neutral pH to 6-keto prostaglandin-f1a. The in-vivo half-life of Epostrostenol is 6mins.
- When iloprost is administered via inhalation in patients with pulmonary hypertension peak serum levels are reached at the end of inhalation. These levels decline with half-lives between approximately 5 and 25 minutes

**Indications**

- In patients with severe hypoxic respiratory failure where pulmonary shunt is felt to be significant and conventional therapies are failing to reverse hypoxia.
- Nebulised prostacyclin / epoprostenol can also be used as a pulmonary artery vasodilator to aid in the treatment of severe pulmonary hypertension (PHT) and right ventricular dysfunction.

**Contraindications**

- Hypersensitivity (Absolute contraindication)
- Pregnancy (Relative: Prostaglandins may cause spontaneous abortion)
- High risk bleeding conditions where the effects of prostacyclin on platelets might increase the risk of haemorrhage (e.g. active peptic ulcers, trauma, intracranial haemorrhage). (Relative contraindication: Prostacyclin may impair platelet
aggregation although there is no clinical evidence that this occurs during continuous nebulisation). **Consider withholding other anticoagulation.**

**Precautions**
- The pulmonary vasodilatory effect of nebulised prostacyclin is of short duration (one or two hours).
- Inhalation might entail the risk of inducing bronchospasm, especially in patients with bronchial hyper-reactivity. Patients with concomitant acute pulmonary infections, COPD, and severe asthma should be carefully monitored.

**Significant interactions/Incompatibilities**
- Nebulised prostacyclin may increase the antihypertensive effect of vasodilating and antihypertensive agents.
- Because it inhibits platelet function, its use with anticoagulants (such as heparin, coumarin type anticoagulants), or other inhibitors of platelet aggregation (such as acetylsalicylic acid, nonsteroidal anti-inflammatory drugs, phosphodiesterase inhibitors and nitro vasodilators) may increase the risk of bleeding.

**Adverse effects**
- May cause mild systemic hypotension although this is unlikely with nebulised prostacyclin.
- Abrupt cessation of nebulised epoprostenol may result in rebound Pulmonary Hypertension.
- The epoprostenol dissolved in the glycine buffer and then mixed with 0.9% sodium chloride in the three way tap has a measured pH of 10.4. Nebulising this alkaline solution could possibly irritate the airway mucosa.

**EQUIPMENT**

**Nebuliser Equipment** (see Appendix 1)
- Aeroneb® Pro-X Nebuliser (Control Module)
- Module/Nebuliser Control Cable
- AC / DC Adapter power cord
- Luer adapter for Aeroneb® (for continuous nebuliser)
- Universal Mounting Bracket
- Equipment Mount Adapter

**Nebuliser Consumables**
- Single patient use Aeroneb® Solo nebuliser
- T-piece
- Luer adapter (for continuous nebuliser)

**Infusion Equipment (for continuous nebulised therapy)**
- 1 Syringe driver
- 1 x 50ml blue Aerogen syringe
- 1 x IV extension tubing
- 3-way tap
- Prostacyclin medication (Epoprostenol (Flolan® is used for continuous therapy and iloprost solution for intermittent therapy)
- 1 x 50 mL vial of sterile glycine buffer solution and a filter unit (supplied with epoprostenol)

**Presentation**

**Intravenous**
- Vial containing sterile, freeze dried epoprostenol sodium equivalent to epoprostenol 500 microgram (500,000 nanograms), supplied with one 50 mL vial of sterile glycine buffer solution and a filter unit.
Nebuliser Solution
- Iloprost (as trometamol) 20 micrograms/2ml – solution for inhalation.

PROCEDURE / SET-UP
The Aeroneb solo nebuliser used with the Aeroneb Pro-X is a single use, general purpose nebuliser that can be set up as an intermittent or continuous nebuliser. It can be used for continuous nebulisation for up to 7 days.

Continuous Nebuliser Infusion set-up
1. Only the diluent (glycine buffer) supplied should be used for reconstitution of the freeze dried powder to maintain sterility of the drug.
2. Due to its short period of stability once reconstituted, preparation should only be carried out immediately prior to clinical use and NOT in advance.
3. Using the blue Aerogen 50ml syringe and the supplied filter reconstitute the 500 microgram vial of epoprostenol in the accompanying 50ml sterile glycine buffer to give a final volume of 500 micrograms in 50mL = 10 micrograms/mL.
4. Load the 50ml syringe (with the primed IV extension tubing attached) in a syringe driver.
5. Ensure the extension line is completely primed and there are no air bubbles.
6. Program prescribed infusion rate of Epoprostenol into the syringe driver.
7. This solution is only stable at room temperature for 8 hours. It must therefore be discarded after 8 hours and replaced with a fresh syringe.

Nebuliser Pro X set up

Figure 1: Nebuliser Control Module

1. Attach the universal mounting bracket to the side arm on the ventilator (see picture below)
2. Attach the control module to the universal mounting bracket.
3. Plug in A/C power cord
4. Plug in module Nebuliser Control Cable
**Nebuliser/Circuit Setup for the intubated and ventilated patient:**

1. The nebuliser should be inserted into a "WET" circuit.
2. Connect the nebuliser Solo unit to the T-Piece at the **inspiratory limb**, by pushing the nebuliser unit firmly onto the T-Piece. (Keep T-Piece clinically clean.)
3. Connect the Aeroneb® Pro-X control module to the nebuliser unit using the Module/Nebuliser control cable.

4. Insert the nebuliser into the ventilator circuit on the **inspiratory limb** immediately before the Y piece.
5. Ensure that Nebuliser bowl is on-top of the T-Piece and angle ventilator tubing so that the nebuliser is vertical and the drops slide onto nebuliser point - see picture (so it will be nebulised as soon as possible)
6. Twist the luer adaptor onto the top of the nebuliser, leaving the silicon plug in place (do not remove during continuous nebulisation).

7. Switch on the nebuliser before connecting the medication tubing.

8. Attach the primed Prostacyclin line to the luer adapter.

9. Never bolus an infusion while it is connected to the nebuliser – it will cause a pressure build up.

10. To turn on to the continuous mode hold blue "On" button for > 5 seconds until the continuous mode ∞ indicator lights up.

11. Commence infusion at the prescribed rate.

12. Check that droplets are forming. Check that the drug is being nebulised by observing that a fine mist is being delivered into the circuit

   ➢ Above two points should be checked 15 minutely for the first hour followed by hourly checks by RN for remaining time of continuous infusion.

   ➢ For infusion rates > 12 mL/hr, checking for mist should be performed every 15 minutes throughout the time of infusion at this rate.

**Note:**
- If the Control Module is turned off or is unplugged, when it is turned back on it defaults to the intermittent mode unless you hold down the blue button for > 5 seconds to return it to Continuous ∞ Mode.
- The Nebuliser bowl can be accessed from the Luer connection without any leaking from the Ventilator circuit.

**Nebuliser /Circuit Setup for the Non-Intubated and Ventilated patient:**

The ultrasonic nebuliser must face upwards to work effectively.

To supply oxygen to the patient, use the venturi connector with oxygen tubing. **Do not use a combination of high flow nasal oxygenation and the nebuliser.** The high flow could limit the amount of drug being delivered via the mouth. **However,** if the patient has high oxygenation requirements, it may be necessary to combine the two methods.

The patient places the end of the flex tube in their mouth and inhales the nebulised solution. A face mask should not be used - it can irritate skin and eyes.

**For Non-intubated and ventilated patients, only intermittent dose of Iloprost can be used.**
Dose for Intermittent and Continuous nebulised prostacyclin

**Intermittent Prostacyclin**
- Use Iloprost (solution for inhalation)
- **Preparation** is 20micrograms /2mL
- **Dose is 5micrograms every 2 hours** (intermittent dose is delivered over 30 minutes).

**Administration**
- Dilute 20 micrograms in 10mL 0.9% sodium chloride = final concentration 2micrograms /mL.
- Insert 5micrograms (2.5ml) of the diluted solution into the nebuliser cup and close the stopper. The nebuliser and T-piece should have been inserted into the inspiratory limb of the ventilator circuit (as per nebuliser circuit set up above). OR see set up for the non-intubated ventilated patient.
- Turn on the control module and select the 30min cycle.

**Note:** Maximum volume that can be inserted into the nebuliser cup for a 30 minute cycle is 6mL.

**Continuous Prostacyclin**
- Using the blue Aerogen 50ml syringe and the supplied filter reconstitute the 500 microgram vial of epoprostenol in the accompanying 50ml sterile glycine buffer to give a **final volume of 500 micrograms in 50mL = 10 micrograms/mL**
- The dose range for nebulised epoprostenol is 10 to 50 nanogram/kg/min.
- **Commence infusion at 20 nanogram/kg/min.**
- If necessary, the dose may be increased by 10 nanogram/kg/min at 30 minute intervals until desired effect is achieved (monitor carefully for side effects such as bleeding and hypotension).
- Once there is significant improvement in arterial oxygenation the infusion can be decreased by 10 nanogram/kg/min to identify the minimum effective dose.
- **Maximum rate should not exceed 50 nanograms/kg/min.**

**Table: Epoprostenol infusion rate**

<table>
<thead>
<tr>
<th>Weight (kg)</th>
<th>Concentration (500microgram/ 50ml = 10micrograms/ml)</th>
<th>Dose in nanograms /kg/min (ng/kg/min)</th>
<th>Infusion rate in mL/ hr</th>
</tr>
</thead>
<tbody>
<tr>
<td>40 kg</td>
<td>10 micrograms/mL</td>
<td>20 ng/kg/min 30 ng/kg/min 40 ng/kg/min 50 ng/kg/min</td>
<td>4.8mL/ hr 7.2mL/ hr 9.6mL/ hr 12mL/ hr</td>
</tr>
</tbody>
</table>
Weaning Infusion for continuous nebulised prostacyclin
- It should be weaned slowly under close medical supervision, with the dose being decreased no faster than 10 nanograms/kg/min every 30 minutes.
- Exception to slow weaning may be made by ICU consultant or senior registrar in cases of bleeding or other major complications.
- Rapid cessation may result in rebound pulmonary hypertension.

Clinical Considerations
- Vital signs should be monitored while initiating nebulised prostacyclin. In patients with low systemic blood pressure, care should be taken to avoid further hypotension.
- Should signs of pulmonary oedema occur when nebulised prostacyclin is administered in patients with pulmonary hypertension, the possibility of associated pulmonary veno-occlusive disease should be considered. The treatment should be stopped.
- The Prescription for the continuous nebulised infusion of Epoprostenol should be charted on the ICU flow chart with other continuous infusions.
- The filters on the expiratory limb of the ventilator circuit need to be changed every 4 hours as they will develop a coating and may then become partially blocked leading to an elevated PEEP.
- The Epoprostenol should not be rapidly ceased as it may result in rebound pulmonary hypertension.
- Refer to Appendix 2 for Troubleshooting checklist.

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
1. MIMS Online, CIAP: NSW Health Department, Copyright MIMS Australia Pty Ltd 2013. [http://www.mims.hcn.net.au/](http://www.mims.hcn.net.au/).
9. Lowson SM. Inhaled alternatives to Nitric Oxide. Anaesthesiology 2002;96(6):1504-1513

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Appendix 1

Figure 1. Aeroneb Solo System

1. Aeroneb Solo With Plug
2. T-Piece (Adult)*
3. Aeroneb Pro-X Controller
4. Controller Cable
5. AC/DC Adapter
6. Universal Mounting Bracket & Equipment Mount Adapter
7. Continuous Nebulization Tube Set*
8. Aeroneb Solo Adapter*

Appendix 2
Aeroneb Solo - Controller Checklist

1. Connect the control module to the AC/DC adapter and attach it to an AC power source. Ensure AC/DC light is on.

2. Connect the nebulizer unit to the control module using the control module cable.

3. Press and release the on/off button and ensure the 30 Min mode light is on.

4. Verify that the green 30 Min indicator light illuminates. If using in continuous mode, ensure that continuous mode light is illuminated.

Aeroneb Solo - Nebulizer Orientation

For optimum use of the Aeroneb Solo please ensure it is in the optimum orientation at all times, in both continuous and intermittent settings.
### Troubleshooting

**Aeroneb Solo**

If you experience any difficulty using the Aeroneb Solo nebulizer please contact your local Aerogen representative.

<table>
<thead>
<tr>
<th>IF IT HAPPENS</th>
<th>IT COULD MEAN</th>
<th>TRY THIS</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Aerosol being produced in intermittent mode.</td>
<td>Air is trapped between the medication and the aperture plate.</td>
<td>Tap the nebulizer to dislodge the air.</td>
</tr>
<tr>
<td>No Aerosol being produced in continuous mode.</td>
<td>The feed system is not operating.</td>
<td>Check the feed system. \nCheck the feed rate does not exceed the maximum input feed rate of 12ML per hour.</td>
</tr>
<tr>
<td>Medication is left in the nebulizer unit after nebulization.</td>
<td>Nebulizer was not turned on or connected to power.</td>
<td>Ensure that nebulizer is connected to power and turned on. \nRecharge battery.</td>
</tr>
<tr>
<td>Rechargeable battery is depleted.</td>
<td>A 30 minute cycle was selected when connected to the continuous feed system.</td>
<td>Run a continuous cycle.</td>
</tr>
<tr>
<td>The fault indicator light illuminates.</td>
<td>The control module cable is incorrectly connected to the nebulizer, or electronics are malfunctioning.</td>
<td>Verify that the control module cable is correctly connected to both the nebulizer unit and the control module.</td>
</tr>
<tr>
<td>Battery will not recharge or battery light flashes while connected to AC/DC adapter.</td>
<td>It may be time to replace the battery.</td>
<td>Contact your local Aerogen sales representative with the serial number of your controller, located on the back of the unit.</td>
</tr>
<tr>
<td>The 30 Min or Continuous light illuminates but aerosol is not visible.</td>
<td>No medication in the nebulizer unit.</td>
<td>Refill medication through filler cap in the nebulizer unit.</td>
</tr>
<tr>
<td>30 Min or Continuous indicator does not light when on/off power button is pressed.</td>
<td>Air is trapped between the medication and the aperture plate.</td>
<td>Tap the nebulizer to dislodge the air.</td>
</tr>
<tr>
<td>There is no power to the system.</td>
<td>Rechargeable battery is depleted.</td>
<td>Recharge battery.</td>
</tr>
</tbody>
</table>

**Contact Information**

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