

## Nebulised Prostacyclin (nPGI<sub>2</sub>)

Under exceptional circumstances, for example contraindication to ECMO, short term-improvements in gas exchange and right ventricular function can be achieved by using recruitment manoeuvres, inhaled vasodilators, or high frequency oscillation depending upon local expertise and availability. <sup>1</sup>

Inhaled vasodilators in current clinical practice are inhaled nitric oxide (iNO) and nebulised prostacyclin (nPGI<sub>2</sub>).

There is no iNO within WAHT.

There is no high frequency oscillatory ventilator within WAHT.

nPGI<sub>2</sub> is available both on the Alexandra ITU and Worcestershire Royal ICU.

There have been two Cochrane reviews of nPGI<sub>2</sub>. The most recent review was in 2017.

**No current evidence supports or refutes use of nPGI<sub>2</sub> for patients with ARDS. <sup>2</sup>**

Before considering nPGI<sub>2</sub> every option for optimal mechanical ventilation must be explored.

In particular, prone ventilation must be considered and applied, if possible, before prescribing nPGI<sub>2</sub>.

Anecdotal evidence from Italy suggests that prone ventilation is a very effective therapy in COVID-19.

Anecdotal evidence from COVID-19 in Northern Italy suggests that iNO **may** be a useful rescue therapy in the most critically ill patients.

There is neither evidence nor comment on the use of nPGI<sub>2</sub> in COVID-19

**nPGI<sub>2</sub> must only be prescribed by, or on the instruction, of a Consultant in Intensive Care Medicine**

## Potential benefits of nPGI<sub>2</sub>

- Pulmonary vasodilation

Prostacyclin is metabolised from endogenous arachidonic acid via the cyclo-oxygenase pathway and is a potent vasodilator that has been identified as one of the most effective drugs for the treatment of pulmonary arterial hypertension.<sup>3</sup>

Nebulised prostacyclin has demonstrated greater selectivity as a pulmonary vasodilator compared to intravenous prostacyclin.<sup>4</sup>

With a reduction in pulmonary artery pressure there is potential to improve the performance of the right side of the heart.

- Improved oxygenation

Inhaled vasodilators may selectively dilate the pulmonary vasculature in ventilated lung areas improving V/Q matching and arterial oxygenation.

ARDS is heterogenous disorder and there are responders and non-responders to nPGI<sub>2</sub>. In responders there may be improvement in P<sub>a</sub>O<sub>2</sub> and P<sub>a</sub>O<sub>2</sub>/fiO<sub>2</sub>.

## Potential side effects of nPGI<sub>2</sub>

- Bronchospasm. A potential risk in asthma and COPD.
- Mucosal irritation. Epoprostenol solution is an alkaline solution with a pH of 10.4 for Mercury Pharma and 12 for proprietary Flolan.

**Proprietary Flolan must not be used for nPGI<sub>2</sub>**

- Systemic hypotension especially when administered with vasodilating and anti-hypertensive agents.
- Bleeding due to platelet inhibition. Caution must be exhibited with simultaneous administration of anticoagulants and antiplatelets.
- Rebound pulmonary hypertension and acute right heart failure on abrupt termination of nPGI<sub>2</sub>.

**nPGI<sub>2</sub> must not be terminated abruptly**

## Contra-indications to nPGI<sub>2</sub>

- Hypersensitivity (absolute)

- Pregnancy (relative)
- High risk bleeding conditions (relative)

#### Risks to Staff

- Insertion of the Aeroneb Solo nebuliser is an aerosol-generating procedure
- Changes of the respiratory filters is an aerosol-generating procedure

#### **PPE required**

#### **Current COVID-19 recommendations**

**gloves, gown, apron, eye shield, FFP3 mask or hood**

- Caution where pregnant staff involved in delivery of nPGI<sub>2</sub>

## Product and Dose of Epoprostenol for nPGI<sub>2</sub>

PGI<sub>2</sub> is supplied as a sodium salt of epoprostenol. It is reconstituted in 50 mL of glycine buffer diluent to a final concentration 500µg per 50ml (10000ng per ml)

Epoprostenol solution is an alkaline solution with a pH of 10.4 for Mercury product

**Proprietary Flolan must not be used for nPGI<sub>2</sub>**

Half-life approximately 3 minutes

Dose range 10 to 50 nanogramkg<sup>-1</sup>min<sup>-1</sup>

Start at 20 nanogramkg<sup>-1</sup>min<sup>-1</sup>

Increase by 10 nanogramkg<sup>-1</sup>min<sup>-1</sup> at 30 minute intervals for desired endpoint

Use minimum effective dose

Remember to titrate down if possible

The syringe must be changed every 8 hours

**Do not abruptly terminate therapy**

**Wean nPGI<sub>2</sub> by 10 nanogramkg<sup>-1</sup>min<sup>-1</sup> at 30 minute intervals**

**Do not exceed 50 nanogramkg<sup>-1</sup>min<sup>-1</sup>**

## Dose of Epoprostenol weight versus infusion rate

Weight kg	Desired nebulisation rate in nanogramkg <sup>-1</sup> min <sup>-1</sup>				
	10	20	30	40	50
	Rate in mlhr <sup>-1</sup> nPGI <sub>2</sub> epoprostenol solution 500µg in 50ml				
30	1.8	3.6	5.4	7.2	9.0
35	2.1	4.2	6.3	8.4	10.5
40	2.4	4.8	7.2	9.6	12.0
45	2.7	5.4	8.1	10.8	13.5
50	3.0	6.0	9.0	12.0	15.0
55	3.3	6.6	9.9	13.2	16.5
60	3.6	7.2	10.8	14.4	18.0
65	3.9	7.8	11.7	15.6	19.5
70	4.2	8.4	12.6	16.8	21.0
75	4.5	9.0	13.5	18.0	22.5
80	4.8	9.6	14.4	19.2	24.0
85	5.1	10.2	15.3	20.4	25.5
90	5.4	10.8	16.2	21.6	27.0
95	5.7	11.4	17.1	22.8	28.5
100	6.0	12.0	18.0	24.0	30.0
105	6.3	12.6	18.9	25.2	31.5
110	6.6	13.2	19.8	26.4	33.0
115	6.9	13.8	20.7	27.6	34.5
120	7.2	14.4	21.6	28.8	36.0
125	7.5	15.0	22.5	30.0	37.5
130	7.8	15.6	23.4	31.2	39.0

**Do not abruptly terminate therapy**

**Wean nPGI<sub>2</sub> by 10 nanogramkg<sup>-1</sup>min<sup>-1</sup> at 30 minute intervals**

**Do not exceed 50 nanogramkg<sup>-1</sup>min<sup>-1</sup>**

Set up the Epoprostenol Infusion and Aerogen Solo nebuliser and Aeroneb controller

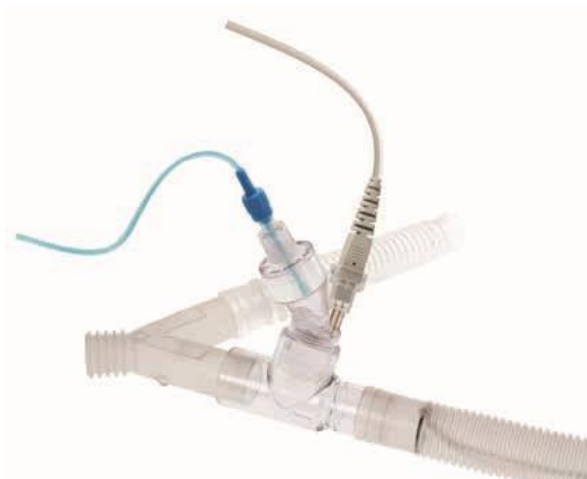
1. Remove the syringe cap from the medication filled syringe and attach the syringe end of the tubing onto the syringe.



2. Prime the tubing until the medication reaches the end of the tubing. Note: the tubing priming volume maximum is 3.65mL.



3. Unplug the tethered cap from the Aerogen Solo, do not remove it from the nebuliser. Screw the nebuliser end of the tubing onto the top of the nebuliser.



4. Insert the syringe filled with medication into the syringe pump. Turn on continuous mode on the controller. Press & hold the on/off button for 3 seconds from the off position to select continuous mode. Note: Medication is nebulised on a drop by drop basis. Observe continuous mode in action.



## Practical tips

- As in diagram 3, the Aerogen solo nebuliser must sit in the inspiratory limb of ventilator immediately before the Y piece.
- Modification of the standard circuit in use within WAHT is simply achieved by pulling elephant hose from the Y-piece. No knives or additional connectors are required. See picture 1 and 2.
- There must be no filter between the nebuliser and the patient.
- There must be a minimum of right angles in the breathing circuit between the nebuliser and the patient.
- The orientation of the Aerogen solo nebuliser is critical.
- The end of the infusion line must allow the epoprostenol to drip onto the nebulisation plate. See picture 1 and 2.

**The top of the nebuliser may be rotated into the correct orientation**

**The Drager 'wet circuit' filter is to be used on the expiratory limb of the ventilator. The Drager 'wet circuit' filter will last for 7 days without needing changing. See picture 3 below.**

**If standard 'red safestar' filters are used on the expiratory limb, they very rapidly become saturated with water and need very regular monitoring/changing (sometimes multiple times a day).**

## How to set up Expiratory Valve and Heated Filter

01

Remove the water trap container from the expiratory valve



02

Attach the expiratory filter to the expiratory valve



03

Insert the expiratory valve with the attached expiratory filter into the device





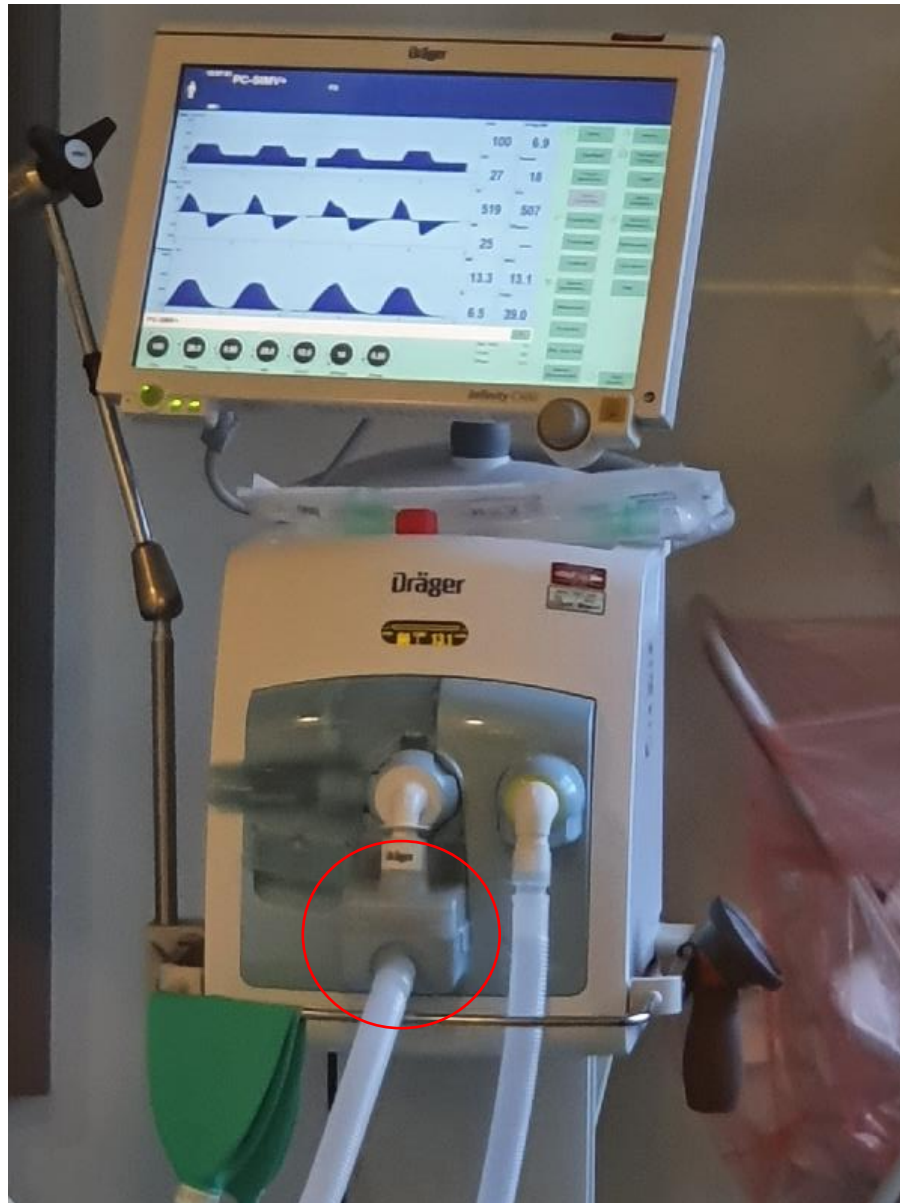
Picture 1 Aeroneb solo in correct position and orientation



Picture 2 Aeroneb solo in correct position and orientation close up



Picture 3 'Dräger Wet circuit filter on expiratory limb of circuit. Current local practice is to place a red safe-star filter on the inspiratory limb in addition to the wet circuit expiratory filter – it is unlikely to become blocked with water and so this would be reasonable practice.



## Bibliography

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