NITRIC OXIDE

INDICATIONS

- Persistent pulmonary hypertension of the newborn in term and near term (>34 weeks) babies, proven on clinical grounds or by echocardiography [see **Persistent pulmonary hypertension of the newborn (PPHN)** guideline]
- Oxygen index >20
- Initiate treatment with nitric oxide (NO) only after discussion with on-call consultant
- Babies requiring NO should be referred to a NICU for ongoing management, in accordance with Toolkit principles

CAUTIONS

- Preterm baby
  - not effective as rescue therapy for very ill preterm babies (Cochrane review 2017)
  - early routine use does not prevent serious brain injury or survival without BPD (Cochrane review 2017)
  - may be beneficial in preterm babies with preterm prolonged rupture of membranes – discuss with consultant
- Grade 4 intraventricular haemorrhage (IVH)
- Recent pulmonary haemorrhage
- Platelets $<50 \times 10^9$/L

CONTRAINDICATIONS

- Congenital heart disease (especially circulations dependent on right-to-left shunting)

DOSE AND ADMINISTRATION

Starting NO

Preparation

- Ensure ventilation optimal and that other aspects of the **Persistent pulmonary hypertension of the newborn (PPHN)** guideline have been followed
- A sustained inflation immediately before starting NO can enhance response

Administration

- Document FiO_2 and SpO_2 immediately before starting NO
- Start NO at 10 ppm
- If no response (see below), increase to maximum of 20 ppm
- If still no response at 20 ppm, discontinue after trial of 1 hr
  - NO can be stopped abruptly without weaning if given for <4 hr
- Once responding, wean to 5 ppm as soon as possible, and within 2–24 hr of starting treatment

Definition of response to NO

- **Either** increase in postductal SpO_2 >20%, **or** increase in postductal PaO_2 >3 kPa occurring within 15 min of starting NO and while ventilator settings constant
- Approximately 30% of babies with PPHN do not respond to NO

Weaning

- If NO has been administered for ≥4 hr, wean gradually to prevent rebound
  - in ‘responders’, once FiO_2 <0.5, attempt to reduce dose
  - reduce NO to 5 ppm in decrements of 5 ppm every 1–2 hr. Then reduce by 1 ppm every 1–2 hr, and finally to 0.5 ppm for ≥1 hr before stopping. Reverse any reduction that causes SpO_2 to drop persistently by >5%
  - some babies will require low dose (<0.5 ppm) for some time (up to 24 hr) during weaning
    - may be necessary to temporarily increase FiO_2 by 0.1–0.2 to facilitate weaning
- If sustained and significant fall in SpO_2 occurs following reduction in dosage, increase dosage to previous level and continue to wean at half previous rate
- Once discontinued, wait ≥6 hr before removing NO circuit from ventilator

MONITORING

- Use SpO_2 to monitor response
- Blood gases 4-hrly
- Monitor methaemoglobin before starting NO, 1 hr after starting and then 12-hrly. Maximum proportion of total haemoglobin is reached after 8 hr
  - normal <1%
  - 2–3% is acceptable
  - 4% requires action: reduce NO and repeat in 1 hr
    - if still >4%, stop NO
    - if >6%, treat with methylthioninium chloride (methylene blue) 1 mg/kg IV over 1 hr
- NO inhibits platelet function and can trigger bleeding if baby has bleeding problem or thrombocytopenia. Check FBC daily while baby receiving NO