Oxygen

Section: 1. Anaesthetics, preoperative medicines and medical gases > 1.4. Medical gases

EMLc | ATC codes: V03AN01

Indication	Respiratory failure as acute or chronic ICD11 code: CB41.2
Medicine type	Gas
List type	Core
Additional notes	For use in the management of hypoxaemia. No more than 30% oxygen should be used to initiate resuscitation of neonates less than or equal to 32 weeks of gestation.
Formulations	**Respiratory > Inhalation:**
EML status history	First added in 2017 (TRS 1006)
Sex	All
Age	Also recommended for children
Therapeutic alternatives	The recommendation is for this specific medicine
Patent information	Patents have expired in most jurisdictions Read more about patents.
Wikipedia	Oxygen
DrugBank	Oxygen

Expert Committee recommendation

The Expert Committee recommended extending the current listing of oxygen on the EML and EMLc to include management of hypoxaemia, in addition to its current listing as an inhalational medicine in general anaesthesia. The new listing is recommended to be in a new section, 1.4 Medical gases. In addition, the Committee considered that the current title of Section 1, “Anaesthetics”, is not truly representative of the medicines listed in the subsections and therefore recommended that Section 1 be renamed “Anaesthetics, preoperative medicines and medical gases”. The Expert Committee noted that use of oxygen in the management of hypoxaemia is recommended in numerous WHO and other guidelines, albeit on the strength of low- to very low-quality evidence in many cases. The Committee accepted that there are ethical issues associated with conducting randomized controlled trials (RCTs) of oxygen versus control in acute care settings, and that the lack of RCTs could contribute to the downgrading of the quality of the available evidence. Overall, the Committee considered that it was clinically appropriate to treat hypoxaemic patients with oxygen. The importance of pulse oximetry in the detection and treatment of hypoxaemia was also noted. The Committee noted the reports of unreliable and limited access to oxygen in many LMICs and considered that inclusion of oxygen on the EML and EMLc for the new indication could, together with other initiatives, contribute to improving the current situation.

Background

Oxygen has been included on the EML since 1979 and on the EMLc since 2007. It is currently included in Section 1 Anaesthetics > 1.1 General anaesthetics and oxygen > 1.1.1 Inhalational medicines.

Public health relevance

Clinical indications for oxygen treatment to reverse or prevent hypoxaemia include surgical anaesthesia, treatment of acute and chronic respiratory conditions, obstetrics, neonatal care, and emergency and critical care (1). Surveys in low- and middle-income countries (LMICs) have found that fewer than half of all health facilities have uninterrupted access to oxygen (2–4). It has been reported that lack of access to reliable oxygen supplies contributes to preventable deaths, particularly in LMICs. For example, it has been estimated that up to 122 000 deaths from childhood pneumonia could be prevented annually with the strengthening of oxygen supplies (5).

Benefits

The application identified numerous existing WHO guidelines in which recommendations are made relating to the use of oxygen (Annex 1 of the application). The rigorous review and decision-making processes of WHO guideline development were acknowledged and a review of GRADE tables from existing WHO guidance documents, insofar as they relate to oxygen use, was conducted. No additional systematic reviews were conducted for the application. WHO recommendations on oxygen use were strong, but based on low- or very low-quality evidence (observational evidence and consensus) in many cases (6–9). A meta-analysis of 13 studies involving 13 928 children with acute lower respiratory infection from LMIC found hypoxaemia (defined with oxygen saturation rate (SpO2) below 90%) to be associated with significantly increased risk of death (odds ratio (OR) 5.47; 95% confidence interval (CI) 3.93–7.63). Similarly, an increased risk of death was observed in meta-analysis of three studies involving 673 children with SpO2 less than 92% (OR 3.66; 95% CI 1.42–9.47) (10).

Harms

Hyperoxia – excess oxygen supply to, or concentration in, tissues and organs – can result in oxygen toxicity and organ damage. Patients at greatest risk of oxygen toxicity are preterm babies and patients sensitive to hypercapnic respiratory failure (11). It is necessary to balance risks of oxygen toxicity against risks associated with targeting lower oxygen saturations, including neurological damage and death, and to optimize therapeutic oxygen delivery to achieve adequate tissue oxygenation. Preterm infants are particularly sensitive to oxygen toxicity and are at increased risk of bronchopulmonary dysplasia, retinopathy of prematurity and subsequent blindness. Careful titration and monitoring of oxygen concentrations is important to prevent these events.

Additional evidence

N/A

Cost / cost effectiveness

The estimated cost per 1000 L of oxygen from cylinders is reported as US$ 10–30. From oxygen concentrators (devices that concentrate oxygen from ambient air), the estimated cost per 1000 L is US$ 2–8. No estimate of the cost of oxygen from pipeline systems was available. Total costs for oxygen supply will vary with the options for static or consumable sources, training and maintenance and other associated factors.

WHO guidelines

WHO’s 2016 Oxygen therapy for children: a manual for health workers (9) and 2012 Recommendations for management of common childhood conditions: newborn conditions, dysentery, pneumonia, oxygen use and delivery, common causes of fever, severe acute malnutrition and supportive care (8) make the following key recommendations in relation to oxygen therapy: • Pulse oximetry is recommended for determining the presence of hypoxaemia and for guiding administration of oxygen therapy to infants and children (strong recommendation, low-quality evidence). • If oximetry is not available, the following clinical signs could be used to determine use of oxygen therapy: central cyanosis, nasal flaring, inability to drink or feed (when due to respiratory distress), grunting with every breath, depressed mental state (drowsiness, lethargy) (strong recommendation, low-quality evidence) • In some situations, and depending on the overall clinical condition, children with the following less

specific signs may also need oxygen: severe lower chest wall indrawing, respiratory rate greater than 70/min, head nodding (strong recommendation, very low-quality evidence). • Effective oxygen delivery systems should be a universal standard of care and should be made more widely available (strong recommendation, expert opinion). • Children with hypoxaemia should receive appropriate oxygen therapy (strong recommendation, low-quality evidence). • Children with respiratory disease living at ≤2500 m above sea level should receive oxygen therapy if their oxygen saturation is ≤90% as measured by pulse oximetry (strong recommendation, very low-quality evidence). • In children living at high altitude (>2500 m above sea level), the normal oxygen saturation is lower than in those living at sea level. At high altitude, a lower level of saturation, such as SpO2 ≤ 87%, could be used as a threshold for giving oxygen (recommendation, very low-quality evidence). • Children with emergency signs (obstructed or absent breathing, severe respiratory distress, central cyanosis, signs of shock, coma or convulsions) should receive oxygen therapy during the resuscitation phase if their SpO2 is <94% (strong recommendation, very low-quality evidence). WHO's 2012 Guidelines on basic newborn resuscitation (7) make the following recommendation regarding ventilation of newborns: • In newly-born term or preterm (>32 weeks' gestation) babies requiring positive-pressure ventilation, ventilation should be initiated with air (strong recommendation, moderate-quality evidence). For preterm babies born at or before 32 weeks' gestation, it is preferable to start ventilation with 30% rather than 100% oxygen. If this is not possible, ventilation should be started with air. WHO's 2012 Prevention and control of noncommunicable diseases: guidelines for primary health care in low-resource settings (6) makes the following recommendation regarding use of oxygen in asthma and chronic obstructive pulmonary disease (COPD): • In the management of exacerbation of asthma, if available, oxygen should be administered to patients with acute severe asthma. This is in keeping with normal practice in high-resource settings where the decision to use oxygen is based on low oxygen saturation readings (strong recommendation, very low-quality evidence). • In the management of exacerbation of COPD, oxygen, if available, should be administered by a device that controls concentration to 24–28% (strong recommendation, very low-quality evidence).

Availability

Oxygen is available from cylinders, oxygen concentrators and central pipeline systems.

Other considerations

N/A

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7. Guidelines on basic newborn resuscitation. Geneva: World Health Organization; 2012 (http://www.who.int/maternal_child_adolescent/documents/basic_newborn_resuscitation/en/, accessed 31 January 2017).
8. Recommendations for management of common childhood conditions: evidence for technical update of pocket book recommendations. Geneva: World Health Organization; 2012 (http://www.who.int/maternal_child_adolescent/documents/management_childhood_conditions/en/, accessed 31 January 2017).
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