NICE guidelines on bronchiolitis: a robust appraisal of current evidence

Bronchiolitis is common in infants. Oxygen therapy, fluids and occasionally respiratory support remain the mainstay of treatment. The NICE guidelines are expected to streamline the management of bronchiolitis and minimize potentially harmful interventions. Further research to find other useful therapies is necessary.

Bronchiolitis is defined as a lower respiratory tract infection affecting children under 2 years of age, peaking between 3 and 6 months (National Institute for Health and Care Excellence (NICE), 2015). It is the most common respiratory infection in infants, affecting approximately one in three infants in the first year of life, most commonly during the winter months (NICE, 2015). In hospitalized infants respiratory syncytial virus is the commonest organism detected in the nasopharyngeal aspirate. Other causative organisms include rhinovirus, parainfluenza virus, influenza virus, adenovirus, coronavirus, human bocavirus and human metapneumovirus (American Academy of Pediatrics Committee on Infectious Diseases; American Academy of Pediatrics Bronchiolitis Guidelines Committee, 2014; Datsopoulos, 2014). Co-infection with one or more respiratory viruses is common but the influence of co-infections on the severity of illness is unclear (Goka et al, 2014).

Current management of bronchiolitis

Clinical features of bronchiolitis include a prodrome of coryzal symptoms which progress over approximately 3–5 days to a cough, increased work of breathing and difficulty in feeding (NICE, 2015). On auscultation the presence of wheeze and crackles is consistent with the diagnosis. Clinicians should remain aware of the red flag signs and symptoms, which are shown in *Table 1*. Investigations are not routinely indicated. Infants with bronchiolitis are usually managed at home with advice on symptomatic management, such as regular small volume feeds, raising the head end of the bed, administration of antipyretics, and avoidance of exposure to tobacco smoke. Approximately 2–3% of infants with bronchiolitis require hospitalization, where they receive supportive care, such as oxygen and nasogastric tube feeding (NICE, 2015).

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Why the NICE guidelines on bronchiolitis became necessary

It is over 50 years since Reynolds and Cook (1963) wrote that 'oxygen therapy is vitally important in bronchiolitis and there is little convincing evidence that any other therapy is consistently or even occasionally useful'. The mainstay of treatment remains oxygen, fluids and, if necessary, respiratory support. More recently, various other treatment approaches including nebulized adrenaline with or without steroids (Hartling et al, 2011), nebulized hypertonic saline (Everard et al, 2014), or the use of high flow humidified oxygen (Franklin et al, 2015; Sinha et al, 2015) continue to be explored as potential therapeutic strategies (Datsopoulos, 2014) but have not been recommended for use in previous evidence-based guidelines (Scottish Intercollegiate Guidelines Network, 2006; Ralston et al, 2014). The NICE (2015) guidelines offer best practice advice on the care of children with bronchiolitis. It is expected that the guidelines should minimize variation in practice across the NHS. The Guideline Development Group also made recommendations for research, based on their review of evidence, to improve NICE guidance and patient care in the future.

There are a number of similarities and differences in the recommendations for management of bronchiolitis suggested by previous guidelines (Scottish Intercollegiate Guidelines Network, 2006; American Academy of

Table 1. Evolving red flag symptoms in bronchiolitis

Increased work of breathing, such as grunting, nasal flaring or marked chest recession, respiratory rate >70 per minute
Fluid intake of 50–75% of normal or less
No wet nappy for over 12 hours
Sign of exhaustion, e.g. waking only with prolonged stimulation
Any apnoeas or cyanosis, saturation <92% in air

From National Institute for Health and Care Excellence (2015)

Table 2. Comparison of recommendations between the National Institute for Health and Care Excellence, American Academy of Pediatrics and Scottish Intercollegiate Guidelines Network guidelines

		National Institute for Health and Care Excellence (2015)	American Academy of Pediatrics Committee on Infectious Diseases; American Academy of Pediatrics Bronchiolitis Guidelines Committee (2014)	Scottish Intercollegiate Guidelines Network (2006)
Admission criteria	Oxygen saturations (SpO_2)	SpO_2 <92%	Not discussed	SpO_2 <94%
	Respiratory rate	>60 per min	Not discussed	>60 per min
Investigations	Chest X-ray, bloods, blood gases	Not recommended routinely	Not recommended routinely	Not recommended routinely
	Nasopharyngeal aspirate	No clear guidance – may be helpful for cohorting	Recommended only if the infant is receiving palivizumab prophylaxis	Recommended in hospitalized infants for cohort arrangements
Management	Fluids	Suggest using nasogastric or orogastric tube for feeding. Intravenous fluids only if impending respiratory failure or not tolerating enteral feeds	If required suggest the use of nasogastric or orogastric tube or intravenous fluids	If required suggest the use of nasogastric or orogastric tube or intravenous fluids
	Antibiotics	Not recommended	May be justified in some children who require intubation and mechanical ventilation for respiratory failure	Not recommended
	High flow humidified oxygen	Discussed	Discussed	Not discussed
	Nebulized hypertonic saline	Not recommended	Recommended for hospitalized infants	Not discussed
	Nebulized bronchodilators (salbutamol, ipratromium, adrenaline)	Not recommended	Not recommended	Not recommended
	Use of paediatric early warning scores (PEWS) in monitoring	Widely used in UK clinical practice. Not recommended, suggests need for further evidence	Not discussed	Not discussed
	Limiting disease transmission	Not discussed	Provides strategies to limit disease transmission	Provides ward-based strategies for reducing and limiting disease transmission
Discharge criteria	Oxygen saturations	Has maintained SpO_2 > 92% in air for 4 hours, including a period of sleep	Not discussed	SpO_2 >94%
	Feeding	Is taking adequate oral fluids	Not discussed	>75% normal intake
	Clinical condition	Is clinically stable	Not discussed	Not discussed
Long-term prognosis	Complications	Not discussed	Not discussed	Discusses chronicity up to adulthood, mentions post-bronchiolitic wheeze
	Prevention in high risk infants with palivizumab	Not discussed	Recommends use in high risk groups (e.g. acyanotic congenital heart disease, chronic lung disease)	Recommends use in high risk groups (e.g. acyanotic congenital heart disease, chronic lung disease)

Pediatrics Committee on Infectious Diseases; American Academy of Pediatrics Bronchiolitis Guidelines Committee, 2014) and the NICE guidelines. These are highlighted in *Table 2*.

Advances in bronchiolitis management

This article discusses some recent advances in the management of bronchiolitis and their inclusion or not in the NICE guidelines.

Table 3. High priority research recommendations for future made by NICE (2015) guidelines

The clinical and cost effectiveness of oxygen saturation (SpO_2) measurement in primary care in children with bronchiolitis to help identify those who need admission to hospital should be assessed
The usefulness of routinely practiced paediatric early warning scores in infants with bronchiolitis in predicting deterioration needs to be assessed
The efficacy and cost effectiveness of combined bronchodilator and corticosteroid therapy, and nasal suction need to be assessed in multicentre randomized controlled trials

From National Institute for Health and Care Excellence (NICE) (2015)

Routine testing for respiratory syncytial virus

Cost effectiveness of routine testing for respiratory syncytial virus in nasopharyngeal aspirates was demonstrated in a case controlled study almost 2 decades ago, as this reduced use of unnecessary microbiological tests and antibiotics, and reduced the length of hospital stay (Woo et al, 1997). However, a more recent cohort study identified that one in three children had multiple viruses, and therefore challenged the effectiveness of the current respiratory syncytial virus-based cohorting practices, as recommended in different guidelines (Mansbach et al, 2012).

Nebulized hypertonic saline

The evidence base for use of nebulized hypertonic saline in acute bronchiolitis continues to come up with inconsistent results, with some in favour of its use (Zhang et al, 2013, 2015), and others concluding that claims that hypertonic saline achieves small reductions in length of stay must be treated with scepticism based on the 15 known trials of hypertonic saline. The findings appear highly dependent on trial design and local policies (Maguire et al, 2015). Maguire et al (2015) concluded that the possibility that nebulized hypertonic saline offers symptomatic relief cannot be ruled out but there are no conclusive data to support or deny this possibility. It is therefore understandable that the NICE guidance does not recommend the use of nebulized hypertonic saline to treat bronchiolitis in the current context of clinical practice in the UK.

Combined adrenaline and corticosteroids

Beneficial effects of combined adrenaline and corticosteroids were reported in subgroup analysis of a study (Plint et al, 2011). However, a larger study is needed to establish its usefulness in clinical practice (NICE, 2015). Similarly the use of other bronchodilators including magnesium sulphate (Modaresi et al, 2015) in acute bronchiolitis requires further evidence.

Oxygen saturation

A double-blind, randomized, equivalence trial assessed whether a more permissive strategy in the management of infants with bronchiolitis with regards to an oxygen saturation target of 90% or higher is as safe and clinically effective as one of 94% or higher. The primary outcome measure of time to resolution of cough was equivalent in both groups (Cunningham et al, 2015). Inclusion of the recommendation of this permissive strategy in future revision could have a significant effect in reducing the length of stay in infants needing hospitalization.

High-flow humidified oxygen

Newly-developed medical devices can now deliver high-flow humidified oxygen that is thought to provide more comfortable and effective delivery of gases while retaining airway humidity. The use of this medical device is becoming widespread but without demonstration of additional efficacy. The use of high-flow humidified oxygen is relatively expensive, it is not available in every unit, and can also give false reassurance to health professionals regarding oxygen delivery in sick infants who are beginning to decompensate, as highlighted in a pilot study from Bristol, UK (Hilliard et al, 2012). The NICE guidelines rightly recommend that research is needed to study the clinical and cost effectiveness of high-flow humidified oxygen *vs* standard supplemental oxygen. A multicentre study is recruiting patients for such a trial (Franklin et al, 2015).

Heliox

A Cochrane systematic review reported that the use of heliox reduced the length of treatment in infants with bronchiolitis requiring continuous positive airway pressure support for severe respiratory distress (Liet et al, 2015). This is not recommended in the NICE guidelines as the detailed appraisal of the available evidence was limited and contradictory, and further research is necessary.

Surfactant

A Cochrane systematic review with a total of 79 study participants identified favourable effects of surfactant administration in the management of critically ill infants with bronchiolitis who are mechanically ventilated. However, its translation into clinical practice needs further research because of the small pool of patients available from those studies (Jat and Chawla, 2015).

Respiratory syncytial virus vaccination

Significant progress has recently been made toward a respiratory syncytial virus vaccine (Neuzil, 2016) or specific anti-respiratory syncytial virus therapy. Hopefully the recommendations from this research will be available for appraisal when the NICE guidelines are next revised.

Conclusions

The NICE guidelines published in 2015 provide current best practice for managing infants with bronchiolitis in the UK. It is expected that these will help streamline the management pathway and prevent unnecessary and potentially harmful interventions. This is likely to be beneficial to both the patient and the NHS budget. Several

high priority research areas need to be assessed as a matter of urgency to provide evidence of other potentially useful treatments. **BJHM**

Conflict of interest: none.

KEY POINTS

- The National Institute for Health and Care Excellence guidelines are expected to rationalize and unify the management of infants with bronchiolitis across the UK.
- The management of bronchiolitis still remains largely supportive. A robust appraisal of the current evidence by the National Institute for Health and Care Excellence guidelines makes key recommendations in diagnosis, recognizing deterioration, and reducing unnecessary investigations and ineffective non-evidence based treatment as well as providing key safety information for parents.
- Clear admission and discharge criteria will help on-call emergency doctors and paediatric teams to decide the management pathway uniformly.

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