

Prophylaxis against RSV infection for high-risk infants

Aim

To provide guidelines for the use of respiratory syncytial virus immunoglobulin prophylaxis for infants being discharged home from hospital. Recommendations are for clinical use but may be useful for commissioning and for parent information.

Background

Respiratory syncytial virus (RSV) causes respiratory tract infections across all age groups, and in infants a specific recognisable syndrome: acute bronchiolitis. Over 80% of infants probably come into contact with RSV during their first winter, and 1-2% are hospitalised with acute bronchiolitis. Overall the disease has a low mortality, but among infants with bronchopulmonary dysplasia (i.e. severe chronic lung disease of prematurity) mortality in reported series has been around 30%. Infants with congenital heart disease are another recognized high risk group.

There is currently no effective active vaccine against RSV: an early vaccine in the 1960s was associated with *more* severe bronchiolitis. Passive immunity can now be provided using an intramuscular preparation of RSV-specific immunoglobulin: Palivizumab (tradename "Synagis"). This is given once a month during the bronchiolitis season (usually October to February in northern Europe).

A large randomised trial carried out in 139 centres in the US, UK and Canada demonstrated a significant (55%) reduction in hospitalisation of preterm infants due to RSV infection¹. Following this, the American Academy of Paediatrics recommended use of Palivizumab in all infants born below 36 weeks gestation. Understandably cost implications have led to a more cautious approach in the UK. Nevertheless, it has been suggested that use of Palivizumab in infants discharged home on oxygen with bronchopulmonary dysplasia would be cost-effective². Subsequently a further study³ has shown a reduction in hospitalization for infants with haemodynamically significant congenital heart disease.

Since 2002 the JCVI RSV sub-committee has continued to up-date advice on the use of RSV-specific immunoglobulin. Unfortunately the recommendations have been questioned⁴. In particular, the proportion of infants who would require treatment has been challenged (the JCVI suggested 0.3% but a London group estimated up to 1.1%), as have the cost per child of treatment and the cost-effectiveness estimates⁵. Another difficulty is the definition of chronic lung disease. The JCVI subgroup defined this as 28 days, but this would encompass many babies who ultimately have minimal lung disease. Concern has also been expressed that recent proposed recommendations have been too complicated and would therefore be implemented inconsistently. More recently evidence from two Health and Technology Assessments has been included.^{6,7}

Recommendations

In 2010 the JCVI has made further recommendations and clinicians have been asked by the Department of Health to implement these as soon as possible. The Surrey and Sussex Neonatal Network recommend that units within the network comply with this request.

The 2010 JCVI statement on RSV immunization is at www.dh.gov.uk/ab/JCVI/DH and the guidance on treatment can be found in the Green Book at: www.dh.gov.uk/greenbook.

Summary Recommendations:

1) Preterm infants with CLD (oxygen dependency for at least 28 days from birth) are eligible for RSV immunoglobulin.

It remains cost effective to immunize very preterm infants with CLD even if they have weaned off oxygen months before the onset of the RSV season. For instance a baby born at 24 weeks or less and considered to have CLD will qualify for immunization if his/her chronological age at the beginning of the RSV season is 6 to 9 months.

Table 1 shows a shaded area indicating the recommended and cost effective use of Palivizumab for preterm infants with CLD according to chronological age at the start of the RSV season (beginning of October).

Table 1 Chronological age (months)	Gestational age at birth (weeks)						
	≤24	24 - 26	26 - 28	28 - 30	30 - 32	32 - 34	≥35
1.0 to <1.5	✓	✓	✓	✓	✓	✓	
1.5 to 3	✓	✓	✓	✓	✓		
3 to 6	✓	✓	✓				
6 to 9	✓						
>9							

2) A preterm infant that does not fit into the criteria for Table 1 but has had an oxygen requirement at 36 weeks corrected age may receive RSV immunoglobulin for their first RSV season. This will be a consultant decision made in outpatients if respiratory progress is poor.

3) All infants with haemodynamically significant acyanotic congenital heart disease are eligible for RSV immunoglobulin for their first RSV season.

The Green Book has restricted eligibility in this section to preterm infants <32 weeks gestation. However, there seems to be sufficient evidence to provide term infants with prophylaxis as well.⁸

4) Children under 24 months of age who have severe combined immunodeficiency syndrome are eligible for RSV immunoglobulin

5) Long Term Ventilated (LTV) children aged less than 12 months at the start of the RSV season and LTV children with co-pathology (heart disease/pulmonary hypertension, oxygen dependency) less 24 months at the start of the RSV season are eligible for RSV immunoglobulins.

The Green Book also states that “Where clinical judgement or other individual patient circumstances strongly suggest that prophylaxis would prevent serious RSV infection in infants who are at particular risk of complications from RSV, use of RSV immunoglobulin could be considered during the RSV season”

Any requests for RSV prophylaxis outside the recommendations in bold type need to be discussed with Dr Seddon

Dosage and Duration

Palivizumab 15 mg/Kg, intramuscularly, once a month.

Maximum of 5 injections, October to February.

The protection will be offered during the first full winter season. Infants discharged part-way through their first winter will be considered for prophylaxis during the following winter if the above criteria still apply (e.g. still oxygen-dependent).

Cost

The cost of a 5 month course of treatment varies with size, from £1,800 for a 3.5Kg infant to £4,800 for a 10Kg infant. Cost savings are possible by grouping together infants and vial-sharing, but this has to be set against staff costs and potential risks of bringing infants up to hospital.

References

1. Impact - RSV Study Group. *Pediatrics* 1998; **102**:531-7
2. *Arch Dis Child* 2000; **83**: 122-7
3. *Arch Dis Child* 2004; **89**:673-8
4. *Arch Dis Child* 2005; **90**:F286-289
5. London New Drugs Group – APC/DTC Briefing Sept 2006: www.nelm.nhs.uk/search/product.aspx?id=9
6. *Health and Technology Assessment* 2008; 12;36 Immunoprophylaxis against RSV with Palivizumab in children.
7. *Health and Technology Assessment* 2010; Palivizumab for immunoprophylaxis of RSV bronchiolitis in high risk infants, additional subgroup analysis. www.hta.ac.uk/project/2056.asp
8. *Arch Dis Child* 2009; **94**:785-789

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