Lower respiratory tract infection caused by respiratory syncytial virus. The short-term and the long-term efficacy of corticosteroids

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Treatment for bronchiolitis: the story continues

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For over 40 years respiratory syncytial virus (RSV) is recognised as the primary pathogen of respiratory tract infections in infants and young children.\(^1\) Annual outbreaks with a peak each winter cause a serious burden on health-care budgets in the Western World where RSV is the leading cause of hospitalisation for bronchiolitis and other forms of lower respiratory tract infections among children. In addition, the number of hospitalisations for bronchiolitis substantially increased in different parts of the world.\(^2,3\)

Despite decades of effort, no effective treatment is available for RSV bronchiolitis. This lack was recently once again confirmed by a paper of Abul-Ainin and colleagues.\(^4\) Although previously adrenaline nebulisation was considered to be better than other bronchodilators the investigators showed in a well-designed trial that adrenaline nebulisation is not superior to placebo or general supportive care. The available evidence on the efficacy of bronchodilator therapy in both ambulatory and hospitalised patients with bronchiolitis is conflicting. In part, this may be explained by great variability in design and intervention of the previous studies, as well as biased enrolment of subjects. These shortcomings have hampered the reliability of two meta-analyses that have been performed on the efficacy of bronchodilators in patients with bronchiolitis. Both meta-analyses demonstrated a statistically significant but clinically irrelevant beneficial effect.\(^5,6\)

A large amount of evidence has demonstrated that immunopathological mechanisms are, in part, responsible for the symptomatology of RSV bronchiolitis.\(^7\) Therefore corticosteroids may be an effective treatment. This idea has been subject of studies since the 1960s, but is controversial. Most of the well-designed studies were unable to demonstrate a benefit of either inhaled or systemic corticosteroids. However, a meta-analysis of systemic corticosteroids in infant bronchiolitis suggested a statistically significant beneficial effect in clinical symptoms.\(^8\)

Why are bronchodilators and corticosteroids, that are the cornerstone in the treatment of childhood asthma, at best marginally effective in infant bronchiolitis despite the pathological, inflammatory and clinical similarities between these two diseases? There might be several explanations.

First, other factors than bronchial constriction and airway inflammation that are related to the anatomy and immature physiology of the respiratory system in infants very likely play a role in the pathogenesis of bronchiolitis. Indeed it is well known that the risk for a severe course of RSV infection is increased in younger and smaller infants.

Second, RSV infections are mild and self-limiting in the majority of the cases. Only in few patients with their first RSV infection severe respiratory insufficiency develops necessitating admission for supportive therapy and monitoring. Most of the benefit occurs in patients in a severe course of RSV infection. In a randomised controlled trial corticosteroids seemed to be most effective in those patients who needed mechanical ventilation.\(^9\)

Finally, potential effective treatment for bronchiolitis may be obscured by the heterogeneity of the investigated populations. There is little uniformity in the definition
of bronchiolitis. In the United Kingdom and Australia bronchiolitis is strictly reserved to an acute upper respiratory tract infection preceding tachypnea and (non obligate) wheezing with widespread fine crepitations and sometimes expiratory ronchi on auscultation. In the US publications, however, the definition of bronchiolitis tends to be broader since all first-time wheezing associated with an respiratory tract infection in infants is included. The distinction that, based on the clinical presentation can made between RSV bronchiolitis and RSV pneumonia, where wheezing also may be present, complicates the situation. It is questionable if these old definitions still are sufficient for the description of patients that are studied in intervention trials. Apart from the entangling definitions, it is likely that RSV lower respiratory tract infection is not a uniform disease and that inter-individual differences in the balance between viral cytotoxic and disease augmenting immunological phenomena strongly determine the pathogenesis and therefore the response to certain forms of treatment. This may explain why bronchodilators and corticosteroids seem to be helpful only in limited groups of patients that yet need to be defined more precisely. In conclusion, in the treatment for bronchiolitis the story has not ended. Only precise and more differentiated description of patients in future intervention studies may help to identify the patient that will benefit from different treatment modalities. In addition, further insight in the differences of pathophysiology resulting in different clinical patterns of RSV lower respiratory tract infections is needed.
References

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Chapter 7  Treatment for bronchiolitis: the story continues