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Clinical and therapeutic variables influencing hospitalisation for bronchiolitis in a community-based paediatric group practice

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Abstract

Aim: To examine the effect of different clinical characteristics and different treatments on the hospitalisation of infants with bronchiolitis seen in an outpatient clinic setting.

Methods: The medical records of infants under 2 years of age who presented with a first episode of wheezing over a two-year period were reviewed retrospectively. Hospitalisation within ten days of evaluation was used as the primary outcome measure.

Results: Data from 320 patients were included. 17% were hospitalised. Age was lower in the hospitalised patients (4.9 months vs. 7.1, $p < 0.001$). Hospitalisation was higher in RSV-positive versus RSV-negative patients (38% vs. 10%, $p < 0.001$) and was higher in those children who had been exposed to tobacco smoke versus those who hadn't (24% vs. 12%, $p < 0.01$). Treatment with oral corticosteroids was associated with fewer hospitalisations in those patients with a family history of asthma or allergic rhinitis (9.7% vs. 24%, $p = 0.02$) and in RSV-negative patients (2.5% vs. 16.7%, $p < 0.05$).

Conclusion: Early treatment of bronchiolitis with oral corticosteroid in an outpatient clinic setting was associated with lower hospitalisation rates in patients with a family history of asthma or allergic rhinitis and in RSV-negative patients.

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Introduction

Bronchiolitis is the leading cause of hospitalisation in children during the first year of life with a rate of 31 per 1000, and treating children with bronchiolitis therefore represents a large proportion of health care cost.¹⁻⁵ Bronchiolitis is commonly treated with bronchodilators and systemic cortico-

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steroids in an attempt to alleviate symptoms, alter disease course, and to prevent hospitalisation. Most previous clinical trials on these two treatments have studied patients who were already hospitalised, with the duration of hospitalisation being used as the primary outcome measure.⁶⁻¹³ The effectiveness of both treatments has been strongly debated.¹⁴ Two recent studies looking at emergency room management with subsequent hospitalisation as one of the outcome measures showed systemic steroids to have a better effect on hospitalisation rates.^{15,16} Based on these studies, it has been proposed that early intervention could be contributing to the superior effect from steroids. There have been no previous studies conducted specifically in outpatient paediatric clinics where patients can present first and where there is greater potential for early intervention and possible prevention of hospitalisation.

In this study, we determined the effect of different patient characteristics and different treatments for bronchiolitis on hospitalisation rates for children under 2 years of age seen in a community-based paediatric clinic.

Methods

Study protocol

This retrospective study was conducted in a community-based paediatric group practice consisting of four full-time and two half-time paediatricians serving a population of roughly 60,000 in a rural community in the Midwestern area of the USA. Patients are evaluated in the outpatient clinic. If hospitalisation is needed, patients are admitted to the only regional hospital where all of the paediatricians have admitting privileges. Records of physician visits, emergency room visits and any hospitalisation are placed in the patients' clinic charts. The study was approved by the hospital's institutional review board.

All charts of patients seen in the clinic between September 2001 and April 2003 and given the ICD-9 codes for RSV bronchiolitis (466.11) and for non-RSV bronchiolitis (466.19) were retrieved and reviewed retrospectively for data gathering and analysis. Only patients less than 2 years of age with a first episode of wheezing were included. Hospitalisation within ten days was used as the outcome measure to determine the effects of different patient characteristics and different treatments. Patients who were directly admitted at first clinical evaluation were eliminated from the analysis of the effect of outpatient treatment on hospitalisation.

Data collected from charts included age at the time of diagnosis, sex, RSV status, tobacco smoke exposure, family history of allergic rhinitis or asthma, and prematurity. Data on the medications prescribed for patients, including albuterol and oral corticosteroid, were also collected. RSV testing was done on nasopharyngeal wash samples and performed at the regional lab using BD Directigen RSV test which is an enzyme immunoassay (EIA) rapid antigen test (Becton, Dickinson and Company). The decision to hospitalise was based on the treating physician's clinical judgment. Also, the decision to test for RSV, treat with oral steroids and bronchodilators, and the dose and duration of such treatment, were all determined by the treating physician.

Statistical analysis

Data analysis was performed using S-PLUS® 6.1 (Insightful Corp.), a statistical software for managing, analysing and graphing data. Categorical multivariables were analysed with contingency tables where Chi-square tests and Fisher's exact tests were performed to relate the hospitalisation rate to treatment with oral steroid and albuterol, gender, age, prematurity, RSV status, exposure to cigarette smoke, and family history of asthma or allergic rhinitis. Interaction between statistically significant variables was controlled using subgroup analysis where the effect of the other variable(s) was subtracted. A *p* value of 0.05 or less was used to reject the null hypothesis of no relationship of the tested variable on hospitalisation.

Results

Out of 367 patients initially reviewed, 40 patients were excluded from analysis because they were over 2 years of age, and seven other patients were excluded because of missing charts. Of the remaining 320 patients, 53 patients (17%) were hospitalised within ten days of presentation. 22 patients were directly admitted from clinic. Mean age at time of presentation was 6.8 months (range of 0.3-23.1). One hundred and eighty-nine patients (59%) were male, and 30 of them were hospitalised. One hundred and thirty-six patients (41%) were female, and 23 of them were hospitalised. The difference in hospitalisation rate between males and females was not significant (*p* value = 0.73).

Hospitalisation rate was associated with younger age at presentation, a history of passive

Table 1 Difference in hospitalisation rate between groups of patients with different demographic and clinical characteristics. 'n' = absolute number of patients in the 'hospitalised' and 'non-hospitalised' categories

Patient variables	Hospitalised (n = 53)	Non-hospitalised (n = 267)	P value
Age in months Mean (Range)	4.9 (0.3-19.6)	7.1 (0.5-23.1)	0.001
Gender (M:F)	1.3	1.4	0.92
RSV (+)	38%	10%	0.0003
Smoking exposure	24%	12%	0.013
Family history*	18%	16%	0.67

* Family history of asthma / allergic rhinitis.

smoke exposure, and a positive RSV rapid antigen test (see Table 1).

There was no significant difference in hospitalisation rate between the group of patients who had a positive family history of asthma or allergic rhinitis and the group of patients who did not (18% versus 16% respectively, $p=0.6$). There were 27 patients who had been born prematurely at between 29 and 36 weeks gestation. There was no statistical difference in hospitalisation rate between those children born prematurely and those born at full term (p value = 0.98). All patients born prematurely received anti-RSV antibody prophylaxis according to the American Academy of Pediatrics guidelines.

There were 254 patients (85%) who were treated with albuterol and 212 (71%) treated with oral corticosteroids. There was no significant difference

in the overall hospitalisation rate between the groups of patients who were treated with or without oral corticosteroids and with or without albuterol.

Further analysis was conducted to determine whether treatment with oral corticosteroids and albuterol was effective in certain subgroups of patients. Hospitalisation rate was found to be significantly lower in the corticosteroid-treated patients if they had a positive family history of asthma and/or allergic rhinitis or if they tested negative for RSV (Figure 1).

Discussion

In this retrospective study, we aimed to evaluate the variables and different treatment methods affecting hospitalisation of patients under 2 years of age presenting with a first episode of

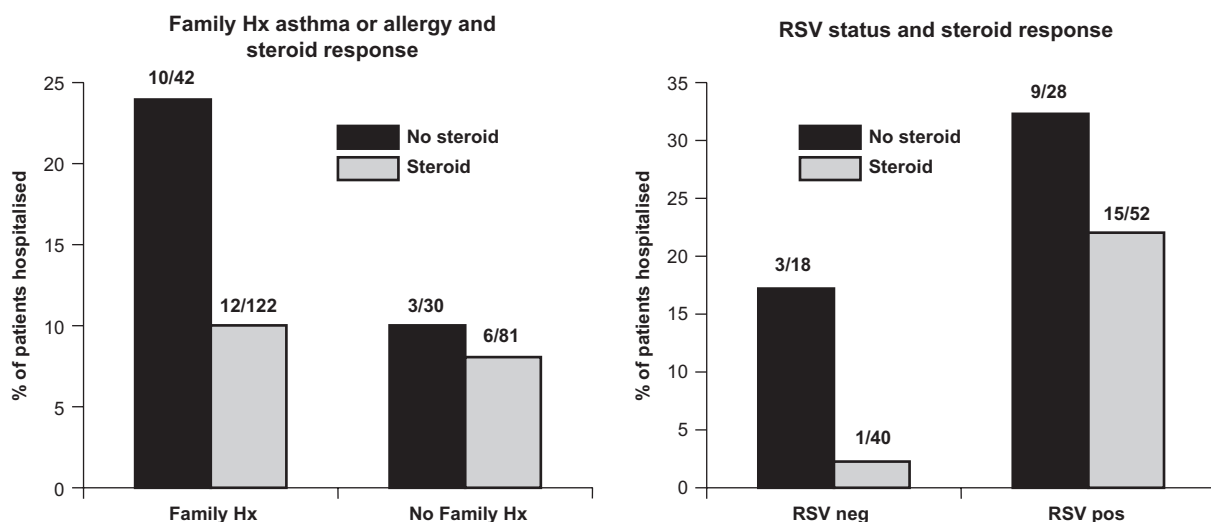


Figure 1 The effect of treatment with systemic corticosteroids on hospitalisation of bronchiolitis patients. (Numbers above each column represent the number of patients who were hospitalised over the total number of patients in each group)

bronchiolitis to a large primary paediatric outpatient clinic. Hospitalisation rate was higher among younger patients, RSV-positive patients, and patients with a history of smoke exposure.

Treatment with oral corticosteroids did not significantly reduce hospitalisation rates except in the subgroup of patients with a positive family history of asthma and allergies. This suggests that the first episode of bronchiolitis is, in fact, a heterogeneous illness with a more favourable response to systemic steroids in patients who are predisposed to asthma. Previous studies evaluating the effect of systemic corticosteroids on bronchiolitis did not consider the heterogeneity of the illness and were mostly conducted on already-hospitalised patients using the duration of hospital stay as the primary outcome measure. The results of such studies were conflicting but have an overall modest positive effect.⁸

Most recently, Schuh *et al.* have evaluated the effect of corticosteroids in a double-blind randomised placebo-controlled study in patients presenting to the emergency room (ER) with bronchiolitis using subsequent hospitalisation as one of the outcome measures.¹⁶ They showed that oral dexamethasone given in the ER resulted in significant reduction of hospitalisation four hours later. It has been suggested that the use of high dose corticosteroid and the early implementation of therapy are the potential reasons for such a positive outcome.¹⁴ However, there was no randomisation or stratification of patients based on the patient's predisposition for asthma. Even though patients with recurrent wheezing were excluded in their study, this does not necessarily exclude patients with asthma who could have presented for the first time and who could have responded to corticosteroids more readily, therefore influencing the results towards a more positive effect. In fact, the corticosteroid-treated group in Schuh's study had a higher number of patients with a family history of atopy (30 out of 36 patients) compared to the placebo group (18 out of 34), which could account for the significant difference in overall steroid response between both groups.

The variability in response to steroids in bronchiolitis patients demonstrated in this study is also consistent with the observation that bronchiolitis is, in fact, a heterogeneous airway disease with either atopic or non-atopic airway inflammation.^{17,18} It is therefore to be expected that patients with a predisposition for atopic airway inflammation – as suggested by a family history of asthma and allergies – would respond more effectively to treatment with corticosteroids.

On the other hand, Oommen *et al.* studied the

efficacy of parent-initiated oral prednisolone for recurrent wheezing in children aged 1-5 years who were hospitalised with wheezing.¹⁹ No significant difference was found between the steroid-treated group and the placebo group. Even when study patients were stratified into two groups according to the presence of systemic eosinophil priming as defined by the level of serum eosinophil cationic protein and eosinophil protein X, prednisolone-treated patients were not significantly different than placebo patients in both strata. The outcome measure used in their study was respiratory symptom score rather than the requirement for hospitalisation.¹⁹

The potential drawbacks of the retrospective analysis conducted in this study include the lack of patient randomisation, and differences in the treatment dosages and length of treatments received by patients. Controlled trials specifically addressing this issue – a selective steroid effect which might reduce hospitalisation rates for bronchiolitis patients – is warranted.

There was no significant difference in hospitalisation rate between patients who were treated with albuterol and in patients who were not. However, these findings cannot be considered conclusive because of the small number of patients in the non-albuterol group and the greater variability between patients using inhaled medications. Controlled trials evaluating the effect of albuterol on bronchiolitis have shown conflicting results with a Cochrane review showing an overall modest positive effect.²⁰ The clinical effect of albuterol in the majority of studies, however, was short-term and was measured using clinical symptom scores or physiologic parameters which have doubtful validity as clinically relevant outcomes.

The reason for the higher hospitalisation rate among RSV-positive patients compared to the RSV-negative patients is not clear. This could be due to physician bias in that the physician hospitalised patients who had RSV-positive status because they were perceived to have worse disease. But it could be that RSV may cause a more severe form of bronchiolitis.²¹⁻²³ Furthermore, the better response of RSV-negative patients to steroid treatment as manifested in their lower rate of hospitalisation compared to RSV-positive patients supports the assumption that bronchiolitis is a heterogeneous airway disease with variable response to treatment and could suggest that RSV-negative bronchiolitis patients may be future asthma patients.

In this study, the higher hospitalisation rate among younger infants, and infants with a history of passive smoke exposure, is supportive of previous studies with similar conclusions.^{21,24}

The absence of any significant difference in hospitalisation rate between premature and full-term patients could be explained by the fact that all eligible premature patients received anti-RSV antibody prophylaxis according to the American Academy of Pediatrics guidelines.

Finally, we conclude that early intervention in an outpatient setting, and targeted treatment with corticosteroids to patients with a predisposition to asthma and to patients with non-RSV bronchiolitis, may have an impact in decreasing hospitalisation rates for infants with bronchiolitis. More prospective controlled studies which address this issue in the outpatient and community clinic setting are therefore needed.

Conflict of interest declaration

There are no conflicts of interest to declare.

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