THE EFFICACY OF STEROIDS IN THE TREATMENT OF BRONCHIOLITIS

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ABSTRACT

Objective: To determine the efficacy of steroids in the treatment of bronchiolitis.

Study Design: Randomised Controlled Trial (RCT)

Place and Duration of Study: The Department of Paediatrics, Military Hospital, Rawalpindi and the Department of Paediatrics, PNS Shifa Hospital, Karachi for six months, from Feb 2006 to Aug 2006

Patients and Methods: Ninety patients of bronchiolitis were sampled and randomly divided into three groups. Each group was given the same treatment protocol differing only in the steroid given (Group I - intravenous Hydrocortisone, Group II – nebulised Beclomethasone, Group III - no steroids). Data was compiled by means of a proforma. Outcomes were length of hospital stay (LOS), difference in clinical respiratory score (R), and time to become wheeze free (W).

Results: Mean LOS was lowest in Group II (p = 0.259). The mean duration to become wheeze free (W) was also lowest in Group II (p= 0.40). The biggest improvement in Respiratory Distress Assessment Instrument (RDAI) score at admission and discharge (R) was in Group I and least improvement in Group II (p=0.056).

Conclusions: Corticosteroids are not significantly effective in reducing length of hospital stay, duration of wheezing and improvement in clinical severity. However, inhaled steroids may possibly have a potential advantage over parenteral steroids.

Keywords: Bronchiolitis, Beclomethasone nebulizer, steroids.

INTRODUCTION

Bronchiolitis is a predominantly viral infection of the small airways causing significant morbidity and mortality, especially in infants[1], and is one of the commonest reasons for hospitalization[2]. Contemporary practice in the treatment of bronchiolitis in our region includes the use of corticosteroids, which is not evidence based. The least controversial aspect of its treatment is supportive management.[3]

The fine line between bronchiolitis and bronchial asthma tends to confound research and thus impedes efforts toward attaining a definite consensus treatment strategy. The inflammatory response to viral replication in the bronchiolar epithelium is characterized by necrosis and sloughing of the small airways epithelium, with edema and increased secretion of mucus by goblet cells, which occludes the flow of terminal airways. The combination of debris and edema produces critical narrowing and obstruction of small airways.[4] Bronchiolitis tends to be limited to the first two to three years of life, is not characteristically episodic (although recurrent infections may give the impression of episodicity), is usually associated with a fever (50% of cases) and does not have the characteristic airway reversibility to bronchodilators associated with bronchial asthma. On the other hand bronchial asthma is not age-limited, is characteristically episodic with airway reversibility to bronchodilators and usually occurs in an afebrile setting; though a precipitating bout of influenza or common cold may present with fever. Thus, recurrent bronchiolitis in early years may mimic bronchial asthma.

To further add to the grey area, the association of RSV bronchiolitis in early infancy with the subsequent persistence of long term wheezing and the possibility of its contribution towards the development of asthma is under evaluation and has been the subject of a number of trials. There are two hypotheses regarding the association between RSV infections in infancy and respiratory abnormalities later in life. One states that recurrent wheezing and subsequent airway dysfunction are caused by

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damage to the lung during an infant's viral infection. The other holds that genetics play a major role in predisposing infants to long-term respiratory abnormalities.[5] In other words the question is whether severe RSV infection during infancy causes the respiratory sequelae or inherent abnormalities predispose an infant to develop severe respiratory infection and sequelae, *i.e.* RSV is associated with the development of pulmonary sequelae.

This study was driven by the observation that a similar trend is prevalent in Pakistan where intravenous hydrocortisone (Solu-cortef) and nebulised Beclomethasone (Clenil) are routinely prescribed in the treatment of bronchiolitis. It was conducted to determine the efficacy of steroids in the treatment of bronchiolitis, to establish evidence for its use or otherwise.

PATIENTS AND METHODS

This randomized controlled trial was conducted, for the first four and a half months (Feb 2006 to June 2006), among indoor patients in the Department of Paediatrics , Military Hospital, Rawalpindi, and was completed in the Department of Paediatrics, PNS Shifa hospital Karachi (July 2006 to Sep 2006). Random purposive sampling method was used. Inclusion criteria included previously healthy children between 3 months to 2 years of both gender having the clinical features of bronchiolitis. Patients with recurrent episodes of wheezy ARI, pre-existing cardiac or pulmonary disease, family history of bronchial asthma / atopy and consolidation on the chest x-ray were excluded.

Ninety patients meeting the criteria were admitted for indoor management and after informed consent, were divided into one of the three groups by randomly picking up one of 90 sealed, unmarked envelopes that contained instructions pertaining to the group. Each group consisted of 30 patients each. Group 1 consisted of patients treated with intravenous (IV) Hydrocortisone sodium succinate (n = 30) in a dose of 5mg/kg/dose 6 hourly. Group 2 consisted of patients treated with nebulised Beclomethasone (n = 30) in a dose of 400-1000 µg 8 hourly. Group 3 consisted of patients not given steroids in any form (n = 30). All patients received a standard management protocol in addition to the above.

Baseline clinical parameters were recorded and treatment initiated as per protocol of each group i.e. intravenous Hydrocortisone (1), nebulised Beclomethasone (2) and no steroids, (3). Parameters of respiratory rate and presence of wheeze were monitored daily and scored according to a Respiratory Distress Assessment Instrument (RDAI) in which the minimum score was zero and maximum score was 17 based on clinical parameters of respiratory distress.[6]

Criterion for discharge was the normalization of the respiratory rate. Outcome measures were: Length of hospital stay (LOS), time taken to become wheeze free (W) and improvement in RDAI score at discharge compared to that at admission (R) which was calculated by subtracting the score at discharge from the score at admission.

The data was entered and analyzed in SPSS version 10.0. Frequencies and percentages were computed for the qualitative variable i.e. gender. Means and standard deviations were computed for quantitative variables. Analysis of variance (ANOVA) was applied to compare mean difference among independent groups for the variables length of hospital stay (in days) and duration to become wheeze free (in days). $P < 0.05$ was considered significant.

RESULTS

The average age of the patients was found to be 9.91± 5.76 (ranging from 3 to 24) months. Out of 90 patients, 67 (74%) were males and 23 (26%) were females showing an overall 3.2:1 male to female ratio. The mean lengths of hospital stay are shown in Table 1. The mean difference was not statistically significant among the groups (p= 0.259). The mean duration to become wheeze free (in days) is shown in Table 2. The mean difference was not statistically significant among the groups (p= 0.40). A comparison of means of respiratory distress assessment instrument (RDAI) score among groups is presented in Table 3. The

Table-1: Comparison of Mean Lengths of Hospital Stay Among Groups

	Length of hospital Stay (Days)		
	Mean ± SD	95% Confidence Interval for Mean	p-value
Group I (n=30)	4.7 ± 1.97	3.97 – 5.43	0.259
Group II (n=30)	4.13 ± 1.46	3.59 – 4.68	
Group III (n=30)	4.97 ± 2.43	4.06 – 5.87	

ANOVA used to compare mean difference among groups

Table 2: Comparison of mean duration to become wheeze free among groups

	Duration to become wheeze free (in days)		
	Mean ± SD	95% Confidence Interval for Mean	p-value
Group I (n=30)	4.03 ± 1.61	3.43 – 4.63	0.40
Group II (n=30)	3.50 ± 1.14	3.08 – 3.92	
Group III (n=30)	3.90 ± 1.90	3.19 – 4.61	

ANOVA used to compare mean difference among groups

Table 3: Comparison of mean of respiratory distress assessment instrument (RDAI) among groups

GROUPS	Initial RDAI Score On Admission Mean ± SD	Final RDAI Score On Discharge Mean ± SD	Difference between Initial and final RDAI scores (R)	*P* values for difference between groups
Group I (n=30)	9.67 ± 2.35	1.37 ± 1.30	8.3 ± 1.82	0.056
Group II (n=30)	8.37 ± 2.40	1.17 ± 1.09	7.2 ± 1.86	
Group III (n=30)	9.37 ± 2.27	1.37 ± 1.19	8.0 ± 1.72	

Repeated measure ANOVA used to compare mean difference between groups

mean difference was not statistically significant between the groups (p = 0.056).

DISCUSSION

The treatment of bronchiolitis in its acute phase is controversial, which is why there is no consensus evidence based treatment approach.[3] Other countries face the same dilemma. To review management practices for bronchiolitis in Ireland, a questionnaire was sent to all consultant pediatricians. Answers revealed that 90% of pediatricians felt that oxygen was necessary, 84% prescribed bronchodilators, only 2% prescribed oral steroids and 11% resorted to nebulised steroids.[7] In Belgium a similar survey showed bronchodilators (74.7%), physiotherapy (76.2%) and antibiotics (63.8%) were still largely prescribed in inpatient settings.[8] This illustrates the routine use of non-evidence based medications for bronchiolitis.

On our local and regional scenario, studies on bronchiolitis per se have been limited to a study on the clinico-epidemiological patterns. A multi-centre study in Bangladesh by Kabir et al, evaluated 348 children. concentrating on the clinico-epidemiological parameters with treatment options including antibiotics, oxygen and nebulised salbutamol and concluded that only hospitals outside the capital city used parenteral steroids but there is no data to suggest a comparative outcome.[9] A hospital based prospective study in Darjeeling, India by Das, also centered on the clinico-epidemiological aspects, concluding that the response to nebulised salbutamol was greater in the 06 month to 12 month age group.[10]

In Pakistan, a few efforts have been made to study bronchiolitis. Arif and Tajjamul (1998) studied the various parameters of its clinical presentation but treatment modalities were not touched upon in that study.[11] Rasul et al (2008) studied the role of antibiotics in bronchiolitis by similarly giving oral antibiotics, parenteral antibiotics and no antibiotics to the subjects of three groups and following their clinical parameters; the conclusion being that antibiotics did not affect the course of the

disease.[12] It is clear that the role of steroids in bronchiolitis remains unexplored locally. However, an article by Sethi and Nagar, from New Delhi, India has extensively reviewed the evidence base for various treatment modalities in bronchiolitis, from which it can be derived that steroids remain controversial. [13]

The results of our study show that the length of hospital stay is indeed lower in both steroid groups though not statistically significant (p = 0.259). The duration of wheezing was lowest in Group II whereas Group I showed the longest duration to become wheeze free although not statistically significant (p = 0.40). The course of the acute phase was measured by the difference between initial and final RDAI scores signifying the magnitude of improvement in clinical status. There was no significant difference among three groups having similar means and a p value of 0.056 which is statistically insignificant. This suggests that the clinical course of the disease remains the same whether steroids are used or not and that the improvement in clinical status is significant regardless of duration. In other words, the improvement in clinical status is part of the natural history of the disease and is unaffected by intervention with corticosteroids. These results indicate that both Hypotheses stand refuted.

The strengths of this study are: 1) It was interventional; 2) Randomization was achieved. The limitation of this study is that RSV confirmation of nasal washings was not done and would have greatly strengthened the diagnosis of bronchiolitis in RSV positive patients.

A review of the literature on bronchiolitis suggests that most studies and meta-analyses do not support the use of steroids in treatment of bronchiolitis.[14,15,16,17,18] Some studies , however, do show some beneficial effects.[19,20]A recent study by Somers et al (2009), attempted to evaluate the effect of parenteral dexamethasone on the cytokine concentrations in the tracheal aspirates of patients with RSV disease and correlate these with the clinical course. The conclusion was that the administration of dexamethasone did not have a consistent effect on the concentrations of pro-inflammatory cytokines in the tracheal aspirates of RSV infected patients. This study is significant as it attempts to explain the reasons for the lack of efficacy of steroids in the treatment of viral bronchiolitis.[21]

CONCLUSIONS

Bronchiolitis is a significant respiratory cause of hospitalization and morbidity in infants and young children. The mainstay of therapy is supportive management. Corticosteroids are not significantly effective in reducing length of hospital stay, duration of wheezing and improvement in clinical severity. It is recommended that further studies be done on a multicentre basis with larger samples to evaluate the significance of efficacy of steroids in the treatment of bronchiolitis.

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