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# BRONCHIOLITIS WITH MONTELUKAST;
## TO DETERMINE IMPROVEMENT IN SYMPTOMS IN 02 MONTHS TO 02 YEARS OLD CHILDREN.


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**ABSTRACT…Objectives:** To assess the efficacy of montelukast in children with bronchiolitis. **Study Design:** Experimental-Preventive. **Place and Duration of Study:** Pediatrics department Allied/DHQ hospital affiliated with Punjab Medical College, Faisalabad, from 1st Nov 2007 to 30th April 2008. **Patients and Methods:** One hundred children of bronchiolitis were studied in two equal groups, group A and group B. To group A montelukast along with symptomatic treatment was given. Group B was given only symptomatic treatment. The criteria of treatment efficacy was taken as number of symptoms free days and nights, bronchiodilator rescue therapy, duration of hospital stay and complications like worsening of symptoms, ventilatory support and side effects of drug therapy. **Results:** Symptoms free days were increased in group A as compare to group B (P value = 0.000) whereas duration of symptoms free nights were significant numerically but not statistically. There was a significant reduction in exacerbations (P = 0.046) and use of rescue therapy (beta 2-agonist) in group A. **Conclusions:** Leukotriene receptor antagonist (LRTA) reduced the duration and severity of lung symptoms in children with Bronchiolitis.



**Key words:**Bronchiolitis, Respiratory Syncytial Virus, Leukotriene Receptor Antagonist.


## INTRODUCTION

Bronchiolitis is an acute wheezing illness of children under 2 years of age with peak age of 1-3 months[1], having high seasonal prevalence, most frequently during winter and early spring[2]. Bronchiolitis is commonly, caused by respiratory syncyital virus[3], other agents include parainfluenza[4], adenovirus, mycoplasma and occasionally other viruses.

The inflammatory response to bronchiolitis includes obstruction, increased airway secretions, mucosal edema, and infiltration of inflammatory cells including eosinophilic granulocytes. Cysteinyl leukotrienes are released, known to cause inflammation and bronchial hyper responsiveness[5]. Montelukast is a specific leukotriene receptor antagonist. It has mild anti-inflammatory properties, exhibits bronchodilator effect and decreases the need for supplemental bronchodilators use. It is administered once daily and well tolerated in children[6]. It is also used in preventing bronchoconstriction in asthma[7], exercise induced asthma, allergic rhinitis and wheezing due to exposure to allergens, aspirin and cold. So far vastly studied in the world, very little data is available in Pakistan, so we conducted this study to assess the efficacy of Montelukast in treating airway hyper responsiveness in bronchiolitis.

## PATIENTS AND METHODS

Bronchiolitis was diagnosed on the basis of history and clinical examination and one hundred children between the ages of 2 months to 2 years without any sex discrimination were taken from both indoor and outpatient department of pediatrics Allied/DHQ hospital Faisalabad. Informed consent from parents and approval of ethical committee was taken. Children with known chronic illness like cystic fibrosis, Congenital heart disease, Congenital lung malformation, primary complex, post purtussis with recurrent aspiration syndrome, or diagnosed as having bronchiolitis and

having other systemic manifestations like encephalitis, myocarditis were excluded from the study.

Children were divided into two equal groups, group A and group B. To group A was given montilukast along with symptomatic treatment. Group B was given symptomatic treatment only. A specially designed profroma was prepared and filled. Follow-up was carried out weekly for 04 weeks period. Compliance was enforced by telephonic contact with family. The criteria of treatment efficacy was taken as number of symptoms free days and nights, bronchiodilator rescue therapy, duration of hospital stay and complications like worsening of symptoms, ventilatory support and side effects of drug therapy. Statistical analysis was performed using SPSS version 10. Study variables were age, gender, fever, cough, wheeze and respiratory distress. For quantitative data Mean and standard deviation were calculated. The t-test was applied to compare both groups. For qualitative data, frequency and percentage was calculated and chi square test applied. P-value $\leqslant$ 0.05 was considered as level of significance.

## RESULTS

We analysed the record of 50 children in group A (Montelukast given) and 50 children in group B (control).

Mean ages were 8.7±7.I months and 8.5±6.8 in group A and group B respectively (Table-I). Of the total patients, 60 were males (60%) and 40 were females (40%). Male to Female ratio was 1.5:1.

Average duration of wheeze and dyspnoea was 8 ±1.6 days in group A as compared to 11±1.7 days in group B. (p value = <.001). Average duration of cough was 9.1±1.3 days in group A as compared to 15±1.7 days in-group B (p value =<.001). During 28-days treatment and follow-up period, children in group A were free of day time symptoms on 12.50±2.8days, and group B was symptom free on 10.02 ±1.73 days (p value=<.001) which is highly significant. Duration of symptom free nights in-group A and B was 8.96±1.86 nights and 8.32±2.13 nights respectively (p=0.113) which is not significant. (Table-III).

**Table-I. Clinical Parameters on Admission**

| Parameter | Group A | Group B |
|---|---|---|
| No of patients enrolled | 50 | 50 |
| Age (Month) | 8.7±7.1 | 8.5±6.8 |
| Gender | | |
| Male | 31(62%) | 29(58%) |
| Female | 19(38%) | 21(42%) |
| Fever | 35(70%) | 40(80%) |
| Cough | 39(78%) | 40(80%) |
| Wheeze | 30(60%) | 32(64%) |
| Respiratory distress | 47(94%) | 48(96%) |
| Weight | 8.5±2.25 | 8.7±2.33 |

There was a significant reduction in exacerbations (withdrawal due to symptom severity or attending emergency department or readmission due to lung symptoms) in treatment group A. Exacerbations occurred in 2 children in-group A and in 8 children in-group B (p=0.046). (Table-III)

Use of rescue therapy (beta2 agonist) was significantly reduced in-group A. Only 5 children (10%) in group A, used rescue therapy as compared to 16 children (32%) in-group B. (p=0.007). (Table-III).

**Table-II. Treatment given during hospital stay**

| Treatment | Group A | Group B |
|---|---|---|
| Duration of stay | 7.84±1.7 | 8.32±1.5 |
| Oxygen dependant days | 2.88±1.04 | 2.98±1.2 |
| % use of beta 2 agonists | 10% | 32% |
| Corticosteroids | 04% | 16% |
| Ventilator support | 0% | 0.02% |

There was no significant difference in duration of hospital stay and oxygen dependant days between the two groups, Group A had average duration of hospital stay of 7.84±1.7 days and Group B having average duration of

**Table-III. Clinical outcome during 4-wk treatment period**

| Parameter | Group A | Group B |
|---|---|---|
| Symptom free days | 12.50±2.81 | 10.02±1.73 |
| Symptom free nights | 8.96±1.86 | 8.32±2.13 |
| Duration of wheeze and dyspnoea | 8±1.6 | 11±1.7 |
| Duration of cough | 9.1±1.3 | 15±1.7 |
| Use of beta 2 agonists | 10% | 32% |
| Patients with exacerbation | 2 | 8 |
| Patients returning for follow up | 86% | 88% |

stay of 8.32±1.5 days (p value=0.138) which is not statistically significant. Group A was oxygen dependent for 2.88±1.04 days and group B for 2.98±1.2 days (p=0.665), which is not significant. (Table-II).

Follow-up was better in-group B as compared to group A, 43 children (86%) returned for follow-up in group A and 44(88%) returned for followup in-group B (control). (Table-III).

## DISCUSSION

Current therapeutic options for bronchiolitis are few — primarily antiviral drugs, bronchodilators, and corticosteroids — and all are controversial. No one is routinely recommended. Yet one or more of these agents, as well as antibiotics, are administered to as many as 50 to 80% of infants with bronchiolitis. Part of the rationale for their use is their acknowledged benefit of diminishing the respiratory distress from other obstructive airway illnesses. Cysteinyl-leukotrienes are released during RSV infection and may contribute to the inflammation and variation of severity of symptoms. Cys-LTs are therefore rational targets for treatment of bronchiolitis and this concept is the basis of use of anti leukotriene drugs in bronchiolitis.

In our study treatment with LRTA showed significant improvement in lung symptoms. Symptom free days and nights were increased, cough and wheeze was reduced and use of rescue therapy/ emergency department attendance was reduced significantly. There was no significant difference in duration of hospital stay and oxygen dependent days, which suggest that treatment affects reactive airway symptoms secondary to bronchiolitis rather than acute inflammatory changes. This may also be due to the fact that montelukast takes some time for therapeutic action. The suffering of mothers and caretakers is reduced to a great extent even by the small improvements so we recommend the use of Montelukast in children with bronchiolitis. The numerical values were in favour of active treatment, which supports general conclusion of a beneficial effect of LRTAs in bronchiolitis.

Compliance in our study was fairly good because of meticulous follow up. Long term follow up i.e one month after the end of LRTA treatment was not possible, but chronic treatment for persistent wheeze or asthma like symptoms after bronchiolitis should be studied. There were no reported side effects in our study but side effects are rare with montelukast, it would need a larger sample size to reach a significant conclusion. Other factors influencing the outcome measures like age, gender, family history of allergy and exposure to tobacco were addressed by randomizing the subjects and thus reducing the chance of confounding by the above mentioned and other unknown factors. The advent of cysteinyl leukotriene receptor antagonists and leukotriene synthesis inhibitors makes them attractive candidates for reducing the short- and long-term respiratory morbidity after a lower respiratory infection caused by RSV. Studies support recent reports on the beneficial effects of CysLT receptor antagonist in human trials and provide a model for investigating the role of CysLTs in bronchiolitis[8]. Montelukast is an oral leukotriene receptor antagonist for the treatment of asthma, seasonal allergic rhinitis (hay fever) and virus induced wheezing[9]. The safety and effectiveness of montelukast has been demonstrated in children as young as 6months of age. The FDA approved it in 1998[10-12].

Montelukast shows benefit in preventing recurrence of wheezing in post bronchiolitic children, known as virus induced wheezing. Montelukast can be used in infants with bronchiolitis to improve quality of life and increase in

| Procedure | Percentage |
|---|---|
| (R) Hemicolectomy | 26% |
| Anastomosis in multiple structures | 23% |
| Stricturoplasty | 13% |
| Ileostomy | 09% |
| Adhesiolysis | 17% |
| Conservatively managed | 12% |

symptoms free days. Any medication in a form of oral therapy is, therefore, a convenient way to administrate to very young children. Studies show that cysteinyl leukotrienes produced by both bronchial epithelial cells and macrophages are increased in the wheezing disease induced by viral bronchiolitis. For years, it has been noted that respiratory syncytial virus (RSV) bronchiolitis in infants and young children has been linked to increased respiratory symptoms lasting up to 11 years of age and perhaps even to asthma. Montelukast is used to prevent asthma attacks.

As other studies are concerned Bisgaard H evaluated role of montelukast in babies 3-36 months with RSV bronchiolitis. They were treated with 5 mg montelukast for 28 days and had fewer symptoms than the placebo group, particularly cough, It has been proven useful in increasing the number of symptom-free days and delaying the recurrence of wheeze in the month following a diagnosis of respiratory syncytial virus-induced wheezing in these children[13].

Bissgaard H an colleagues in another study evaluated that children aged 2-5 years with frequent episodic asthma, primarily involving viral induced attacks in this age group, regular therapy with daily montelukast for 12 months reduced the rate of asthma exacerbations by 31% over placebo, delayed the time to the first exacerbation by 2 months, and lowered the need to prescribe inhaled corticosteroids as preventive therapy in the management of children with virus-induced wheezing[14].

Fam J evaluated efficacy of montelukast as an acute episode modifier in children aged 2-14 years (85% children <6 years) with virus-induced wheezing where it was prescribed at the onset of a viral infection in children with an established pattern of viral induced episodes of wheeze in the preceding year. In this study, emergency department visits were reduced by 45%, visits to all health care practitioners were reduced by 23%, and time of preschool/school and parental time off work was reduced by 33% for children who took montelukast for a median of 10 days[15].

In another double blind randomized study Nanulescu M and colleagues evaluated the efficacy of montelukast in infants and small children. In the study group (20 children) treated with montelukast, 5 mg/day for 3 months. The frequency of bronchial obstruction episodes in the 6 months following the start of therapy was significantly lower ($p = 0.001$) than the 6 months before treatment (1.25 +/- 1.41 versus 3.79 +/- 2.41). In the control group (18 children) treated with placebo, the frequency of the bronchial obstruction episodes decreased (from 3.04 +/- 1 to 2.41 +/- 1.5) in the two analyzed periods, but the differences were not statistically significant ($p = 0.067$). Another study was a case series reporting 3 cases with virus associated brochiolitis/wheezing who responded poorly to inhaled steroids and bronchiodilators but addition of Montelukast was associated with marked clinical improvement within one week but these cases were very heterogenous, differed from simple virus induced acute bronchiolitis and use of multiple drugs including montelukast did not enable any firm conclusion[16].

## CONCLUSION

On the basis of our experience we conclude that the use of Montelukast in bronchiolitis in children improves day and night time symptoms and reducing duration of illness. This treatment modality may help us reducing the disease burden and removing the problem like drug resistance and opportunistic infections.

However like any good study, it has raised further questions on the issue, which should be addressed by larger trials including appropriate duration, interaction with other drugs and possible adverse effect by using the therapeutic doses.

In our study we could not study the relationship between bronchiolitis and long term respiratory sequelae like virus induced exacerbation of asthma and perhaps other chronic obstructive airway diseases in children. This is an area that definitely requires further research.



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