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ORIGINAL ARTICLE

Effect of montelukast on clinical score and cytokine levels of infants for clinically diagnosed acute bronchiolitis

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Abstract
Background: Acute bronchiolitis comprises a major cause for morbidity in infants with viral infection which induces an immune inflammatory response that may produce long lasting harmful effects. Currently, there is no effective therapy for bronchiolitis.
Objective: Our aim was to investigate the efficacy of five-day montelukast therapy in acute bronchiolitis management.
Methods: The study included 50 infants with acute bronchiolitis. The infants with first episode of acute bronchiolitis were randomly assigned to receive daily montelukast dose of 4 mg over five days after admission or no treatment. Plasma eotaxin, IL-4, IL-8 and IFN-gamma levels were evaluated before and after treatment by ELISA method. In the present study, the primary outcome measure was change in clinical severity score, whilst secondary outcome measures were changes in plasma eotaxin, IL-4, IL-8, IFN-gamma levels.
Results: No significant differences was found in clinical severity score with five-day montelukast treatment ($p > 0.05$, Mann–Whitney *U* test). There were no significant differences in plasma eotaxin, IL-4, IL-8, IFN-gamma levels between the groups ($p > 0.05$ Mann–Whitney *U* test). There was significant decrease in plasma IFN-gamma levels following five-day montelukast treatment ($p = 0.027$, Wilcoxon). There were no significant differences in plasma IL-4, IL-8, IFN-gamma levels between the groups after five-day montelukast treatment ($p > 0.05$, Wilcoxon). There was significant increase in eotaxin levels after five-day montelukast treatment ($p = 0.009$, Wilcoxon).
Conclusion: Our study showed that montelukast affected plasma IFN-gamma and eotaxin levels after five days of treatment. Further studies are needed to demonstrate effects of montelukast on chemokine levels in bronchiolitis.

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Introduction

Acute bronchiolitis is the most common infantile respiratory disease resulting in hospital admission and is associated with considerable morbidity.[1,2] Bronchiolitis symptoms generally result from airway inflammation. Cysteinyl leukotrienes (CysLTs) are released, and their levels are significantly elevated during viral airway infection in infants. Montelukast is a potent cysteinyl leukotriene (cysteinyl-LT) receptor antagonist, which exerts some anti-inflammatory effects.[3–6] Cysteinyl-leukotrienes represent a rational target for the treatment of acute bronchiolitis as they are potent pro-inflammatory mediators known to cause bronchial obstruction, mucosal oedema, eosinophil recruitment, and increased bronchial hyper-responsiveness.

The aim of this study was to evaluate the effects of montelukast on clinical course; in addition, it was also aimed to determine the effect on cytokines (plasma IL-4, IL-8, eotaxin levels, and on the production of IFN-gamma) in acute bronchiolitis.

Material and methods

Patients

This is a prospective, randomised study conducted in a tertiary healthcare facility. Inclusion criteria were patients aged 6 and 24 months with respiratory tract infection during the winter season. All patients were evaluated by the same physician. Infants with a first episode of wheezing were re-evaluated on the fifth day after discharge. The diagnosis of bronchiolitis was made based on clinical findings. Infants with cardiac disease, cystic fibrosis, or chronic neonatal lung disease associated with prematurity were excluded. Infants were also excluded if they needed intensive care, if they received corticosteroids in any form during current illness, or if they were treated with anti-asthma medications before presentation. The study was approved by the Erciyes University Hospital Ethics Committee. All parents gave written informed consent before participation.

Bronchiolitis diagnosis and treatment

All children admitted to hospital with bronchiolitis were treated according to the same clinical approach to minimise the variability of the results.

The patients were permitted to use short-acting beta-2 agonist (salbutamol) for treatment of respiratory symptoms as needed and oxygen, nutrition, and intravenous fluids according to the physicians' discretion. The infants received treatment at 3-, 4- or 6-h intervals based on respiratory rate and respiratory effort. All patients were responded to SABA treatment. Paracetamol was administered in case of fever. No patient was prescribed antibiotics.

Randomisation and investigational therapy

After obtaining written informed parental consent, patients were randomised to receive daily montelukast (4 mg granule for five days; $n = 25$) and no treatment ($n = 25$). Placebo was not used in the study. Before randomisation, subjects were stratified according to age (>6 months) and simple randomisation was used.[7] Detailed clinical data in the clinical pathway, including the duration of symptoms before presentation at the hospital, the medical history, previous medications, parental smoking history and family history of atopy were recorded. Physical examination findings were recorded at admission including respiratory rate and heart rate, whether infant is quiet, body temperature, respiratory effort, SpO_2 while breathing room air, presence or absence of wheezing or crackles on auscultation of the chest, and level of hydration. Each infant's condition was scored by using a validated score described by Wainwright[5] (Box 1). SpO_2, respiratory rate, and respiratory effort were observed at admission by the physician (Box 1). Follow-up evaluations including clinic score, pulse rate, oxygen saturation, and

Box 1: Calculation of the severity score

Respiratory-effort score

The physician examined the patient for intercostal recession, subcostal recession, substernal recession, tracheal tug, and nasal flaring and assigned a score of 0 (not present), 1 (mild to moderate), or 2 (severe) for each factor. Each score was then multiplied by a weighting factor, as follows: intercostal recession (−1), subcostal recession (−1), substernal recession (−1), tracheal tug (−1.5), and nasal flaring (−1.5). The weighted scores were then totaled to obtain a score for respiratory effort. Finally, infants with respiratory-effort scores of 0–4.9 were given a severity score of 1 (mild); those with respiratory-effort scores of 5.0–8.9 were given a score of 2 (moderate); and those with respiratory-effort scores of 9.0–12.0 were given a score of 3 (severe).

Oxygen saturation breathing ambient air

The infants received scores of 0, 1, or 2 for oxygen-saturation values of 95–100%, 90–94%, and less than 90%, respectively.

Respiratory rate compared with that of healthy infants of the same age

Those whose rates were within 2 SD of the mean for their age received a score of 0; those whose rates were 2–3 SD above or below the mean for their age received a score of 1; and those whose rates were more than 3 SD from the mean for their age received a score of 2.

Overall severity score

The above three scores were totaled for each infant, and the infant's condition was classified as mild (total score less than 2), moderate (total score 2–3), or severe (total score more than 3).