Randomised Controlled Trial

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# Effects of oral montelukast on pulmonary function and clinical symptoms in acute asthma exacerbations: a randomized, double-blind, placebo-controlled trial

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**Introduction:** Montelukast is a leukotriene receptor antagonist that helps treat chronic asthma and allergic rhinitis by reducing inflammation and bronchoconstriction. However, oral montelukast's effectiveness in managing acute asthma attacks has yet to be completely identified.

**Methods:** This randomized, double-blind, placebo-controlled trial investigated the efficacy of oral montelukast in acute exacerbations of asthma. Seventy patients between 18 and 65 years of age with a primary diagnosis of asthma attack were included in the study and were randomly assigned to receive 10 mg of montelukast orally daily or placebo. Symptoms, signs, forced expiratory volume in 1 second (FEV1), and peak expiratory flow rate (PEFR) were evaluated.

**Results:** Our findings showed a statistically significant difference between montelukast and placebo regarding $FEV_1$ (78.05 ± 7.84 vs. 72.05 ± 12.00, $P = 0.016$), PEFR (322.86 ± 28.95 vs. 290.86 ± 44.21, $P = 0.003$), and wheezing ($P = 0.022$) on the fifth day of treatment. Additionally, $FEV_1$ and PEFR values were compared in two subgroups of patients, ICS users (ICSU) and non-ICS users (NICSU), in both the montelukast and placebo groups. In the montelukast group, while PEFR improved significantly for day 5 in both the ICSU ($P = 0.007$) and NICSU ($P = 0.027$) subgroups, $FEV_1$ only improved in the ICSU ($P = 0.009$) subgroup compared to placebo.

**Conclusion:** The present study demonstrated that oral montelukast administered in acute asthma exacerbation could lead to better values of PEFR and $FEV_1$ on pulmonary function and improvement of wheezing in terms of symptoms.

**Keywords:** asthma exacerbation, clinical trial, forced expiratory volume in 1 second, leukotriene modifier, leukotriene receptor antagonists, montelukast, peak expiratory flow rate

## Introduction

Asthma is a chronic respiratory disease caused by airway inflammation, bronchial hyperresponsiveness, and reversible airflow obstruction that affects more than 300 million people worldwide. Acute asthma exacerbations, often referred to as asthma attacks, are among the most common and potentially fatal causes of emergency department visits[1]. Inhaled bronchodilators, such as short-acting beta-agonists (SABAs) and systemic corticosteroids, which suppress airway inflammation, are standard treatments for acute asthma exacerbations[2]. Asthma is associated with persistent airway inflammation characterized by the recruitment of T cells, mast cells, and eosinophils. These cells are capable of producing cysteinyl leukotrienes. The interaction of these mediators with type 1 cysteinyl leukotriene (CysLT) receptors, which are positioned on inflammatory and structural cells of the airways, contributes to inflammatory cell infiltration, initiation of contraction in bronchial smooth muscles, mucus secretion, and increased vascular permeability, all of which result in airway constriction[3].

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Leukotriene receptor antagonists (LTRAs) are a category of medications that specifically target leukotriene receptors. As a leukotriene receptor antagonist, montelukast has been found to help treat chronic asthma and allergic rhinitis[4]. Leukotrienes are potent mediators of inflammation and bronchoconstriction in asthma, and montelukast collaborates by blocking the activity of these leukotrienes. This decreases inflammation and bronchoconstriction, hence enhancing asthma control[5]. Montelukast has a rapid onset of action, with effects observed within 2 hours of oral tablet administration. The peak effect is reached within 3–4 h, and the duration of action is ~24 h. Montelukast is well absorbed after oral administration, with a bioavailability of ~64%. It is metabolized by CYP3A4 and CYP2C9 and excreted in the feces, with a half-life of nearly 3–6 h. Montelukast is typically administered orally, but granules for children and nebulizer administration are also available[6].

Montelukast has been found to improve lung function, reduce the need for rescue medication, and reduce symptoms such as cough, wheezing, and dyspnea in patients with persistent asthma[4,7,8]. Despite the favorable effect of montelukast on the control of chronic asthma, its usefulness in managing acute asthma attacks is still being determined. Montelukast has been shown to have acute bronchodilator effects that may be helpful during an acute asthma attack. However, there is limited evidence that montelukast may effectively reduce the duration or severity of exacerbations and improve pulmonary function tests (PFT) with conflicting results. Therefore, more studies are needed to investigate this issue. For instance, Ramsay *et al.*[9] showed that Montelukast leads to higher PEFR and Chaudhury *et al.*[10] demonstrated that this intervention leads to improved PEFR and $FEV_1$, whereas Zubairi *et al.*[11] found no beneficial effects of Montelukast on PFT.

Also, previous studies were mainly conducted in children with adding 5 mg of montelukast to conventional drugs, which required more evidence of the drug's effectiveness in adults with other available doses. Due to the paucity of data regarding the use of LTRAs in an acute asthma attack, the present clinical trial aimed to evaluate the clinical effectiveness of 10 mg of oral montelukast in acute exacerbation of asthma by evaluating the drug's effects on pulmonary function and clinical symptoms.

## HIGHLIGHTS

- Montelukast is a leukotriene receptor antagonist that helps treat chronic asthma and allergic rhinitis by reducing inflammation and bronchoconstriction.
- This study was a randomized, double-blind, placebo-controlled trial that investigated the efficacy of 10 mg daily oral montelukast in acute exacerbations of asthma.
- The present study demonstrated that oral montelukast administered in acute asthma exacerbation could lead to better values of PEFR and $FEV_1$ on pulmonary function and improvement of wheezing in terms of symptoms in adults with bronchial asthma.

## Materials and methods

### *Study setting*

In this double-blind, randomized, placebo-controlled clinical trial, patients admitted with acute asthma exacerbation at the respiratory department of Imam Khomeini hospital, Sari, Iran, were enrolled. This is a 500-bed tertiary care hospital with a dedicated respiratory special care unit consisting of professionally trained physicians and nurses for managing pulmonary diseases.

### *Study subjects*

The minimum required sample size for each group was determined to be 35 participants. This calculation accounted for a 10% attrition rate, ensuring that the study would maintain sufficient power even with potential dropouts. The sample size was based on the mean and standard deviation of PEFR reported in the study by Ramsay *et al.*[9] using a two-tailed hypothesis with a significance level (α) of 0.05 and a power (β) of 0.2, corresponding to an 80% chance of detecting a statistically significant difference between the treatment and control groups if one exists. The formula used for the sample size calculation was:

$$n_1 = n_2 = \frac{\left(z_{\frac{\alpha}{2}} + z_{\beta}\right)^2 \left(\begin{smallmatrix} 2 \\ 1 \end{smallmatrix} + \begin{smallmatrix} 2 \\ 2 \end{smallmatrix}\right)}{(\mu_1 - \mu_2)^2} = 65, \alpha = 0.05,$$

$$\beta = 0.2, \quad _1 = 124, \quad _2 = 109, \ \mu_1 = 332, \ \mu_2 = 389.6$$

Inclusion criteria comprised of 1. Adults between 18 and 65 years of age, 2. Primary diagnosis of moderate or severe asthma attack, and 3. Known case of asthma under the care of a pulmonologist. The diagnosis was made based on clinical history, pulmonary function testing, and staging per GINA guidelines version 2021[12]. Patients with a lifetime smoking history of more than 20 pack-years, requiring mechanical ventilator support, female patients who were pregnant or lactating or patients unable to take adequate contraceptive precautions, patients who had previously taken LTRAs, phenytoin, rifampicin, phenobarbital, or oral corticosteroids more than five days during one month before hospital admission, ischemic heart disease with left ventricular failure, and patients with improved symptoms requiring discharge were excluded from the study. Additionally, patients who were unwilling to consent were excluded from the study.

### *Study design and measurements*

Enrollment was performed at the time of admission or first consultation evaluation by a pulmonologist. A checklist concerning baseline characteristics including age, sex, height, weight, BMI, presenting symptoms, past medical history, duration of asthma, current medications, history of smoking, presence of comorbidities such as diabetes, hypertension, ischemic heart disease, previous history of exacerbations, vital signs including blood pressure, pulse rate, respiratory rate, arterial oxygen saturation, and patients medications for asthma was used to record the relevant data on the admission day (day 0). The patient's signs and vital signs were also recorded on the third and fifth days after admission. After the initial assessment, patients were randomly allocated into two groups: placebo and intervention (Airokast 10 mg, Abidi Corporation, Iran).

All patients in both groups received standard therapy for the management of acute attacks of bronchial asthma according to GINA guidelines, and any side effects caused by drugs were noted

for all patients[12]. These included parenteral steroids, inhaled short-acting beta$_2$ agonists with/or without anticholinergics every 4–6 h, depending on the severity of the attack, oxygen therapy, and other supportive treatments. Antibiotics were prescribed only if infection was suspected.

All included patients had moderate or severe exacerbations, according to GINA guidelines[12]. At the beginning of the study, PFT and post-bronchodilator spirometry after 2.5 mg salbutamol nebulization was performed using a handheld spirometer (spirojet) and peak flowmeter (Pasargadteb Irsa), and forced expiratory volume in 1 second ($FEV_1$) and peak expiratory flow rate (PEFR) were recorded. The PEFR was recorded every morning (~8–10 a.m.) on the same flowmeter by the chest physician and continued every morning until discharge. Lung function tests were repeated with the handheld spirometer on days 3 and 5. Detailed clinical and spirometric evaluations were performed at the end of the study period.

### *Randomization and blinding*

Patients were randomly allocated into two groups using block randomization with blocks of four to ensure balance in the number of participants assigned to each group at regular intervals throughout the study. The randomization sequence was generated using the Sealedenvelope website, a widely recognized and validated tool for clinical trial randomization, ensuring a rigorous and unbiased allocation process.

The study was designed as a double-blind trial, where neither the patients nor the investigators, including those responsible for data collection, analysis, and treatment administration, were aware of the treatment allocations. This double-blinding was crucial for minimizing bias and maintaining the objectivity of the trial outcomes. To preserve blinding integrity, the placebo and montelukast tablets were manufactured to be identical in appearance, taste, and packaging. Both the active drug and placebo were indistinguishable to the participants and investigators, reducing the risk of unblinding during the trial. Additionally, the allocation codes were securely stored and only revealed after the completion of the data analysis to further ensure that blinding was maintained throughout the study period.

### *Statistical analyses*

Fisher's exact or $\chi^2$ tests were used where appropriate to compare the qualitative variables between the two groups. Quantitative values such as $FEV_1$ and PEFR were compared between the intervention and control groups using analysis of variance (ANOVA) with adjustment for baseline characteristics in the case of a normal distribution and nonparametric equivalent tests, including the Friedman and Mann–Whitney U tests, where appropriate. The normal distribution of the data was assessed using the Kolmogorov–Smirnov test. All analyses were performed using SPSS version 24 for Windows. A $P$ value less than 0.05 was considered statistically significant. For descriptive analysis, mean ± standard deviation is reported for continuous variables and number (%) for categorical variables.

## Results

### *Baseline characteristics*

In this trial, 70 asthmatic patients with asthma exacerbation were randomly assigned into two groups of 35 patients to receive 10 mg oral montelukast (intervention group) or placebo, and any side effects caused by drugs were noted for all patients. Figure 1 shows a flow chart of the present study. The baseline characteristics of the patients and medications used for long-term care were not significantly different between the two groups (Table 1). Dyspnea, cough, and wheezing were the most common presenting symptoms in the patients admitted with acute asthma exacerbation. The prevalence of concurrent allergic rhinitis in the montelukast and placebo groups was 48.57% and 37.14%, respectively.

### *Symptomatic assessments*

The severity of dyspnea was not statistically different between the Montelukast and placebo groups on days 3 and 5 ($P = 0.324$ and 1.000, respectively). Despite the trend toward improvement in other respiratory symptoms in the Montelukast group compared to placebo, only improvement in wheezing was statistically significant on day 5 ($P = 0.022$). Table 2 compares some of the signs and symptoms of the patients on days 0, 3, and 5 in the two study groups. No statistically significant difference was detected between the two groups regarding the level of consciousness and

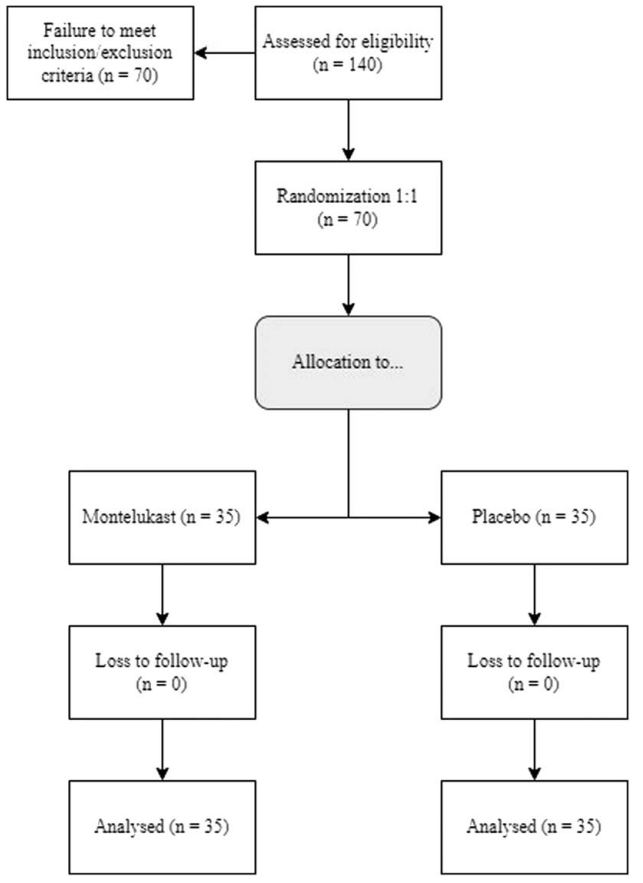


**Figure 1.** CONSORT flow chart of the study.

**Table 1**

**Baseline characteristics of the patients.**

| Variable | Montelukast | Placebo | *P* |
|---|---|---|---|
| *N* | 35 | 35 | |
| Age (year) | 59.84 ± 11.03 | 56.93 ± 12.4 | 0.329 |
| Sex, *n* (%) | | | |
| Male | 15 (42.86) | 13 (37.14) | 0.626 |
| Female | 20 (57.14) | 22 (62.86) | |
| BMI (kg/m$^2$) | 29.73 ± 5.32 | 28.60 ± 3.31 | 0.329 |
| Symptoms at presentation (yes/no), *n* (%) | | | |
| Dyspnea | 34 (97.14) | 35 (100) | 1.000 |
| Cough | 32 (91.42) | 32 (91.42) | 1.000 |
| Sputum | 16 (22.86) | 16 (22.86) | 1.000 |
| Wheezing | 26 (74.28) | 24 (68.57) | 0.597 |
| Duration of asthma exacerbation (days) | 9.66 ± 4.70 | 9.40 ± 4.43 | 0.815 |
| Coexisting allergic rhinitis (yes/no), *n* (%) | 17 (48.57) | 13 (37.14) | 0.334 |
| History of asthma attack (yes/no), *n* (%) | 31 (88.57) | 32 (91.43) | 1.000 |
| Asthma attack episodes (during the last year) | 1.76 ± 0.77 | 2.03 ± 1.07 | 0.294 |
| Smoking (yes/no), *n* (%) | 4 (11.43) | 3 (8.57) | 1.000 |
| Smoking history (pack/years) | 13.25 ± 8.88 | 15.00 ± 5.00 | 0.774 |
| Diabetes mellitus (yes/no), *n* (%) | 11 (31.43) | 6 (17.14) | 0.163 |
| Hypothyroidism (yes/no), *n* (%) | 11 (31.43) | 9 (25.71) | 0.597 |
| Cardiovascular disorders (yes/no), *n* (%) | 1 (2.86) | 3 (8.57) | 0.614 |
| Medications, *n* (%) | | | |
| SABA | 16 (45.71) | 20 (51.14) | 0.339 |
| SAMA | 5 (14.28) | 2 (5.71) | 0.428 |
| LABA | 24 (68.57) | 24 (68.57) | 1.000 |
| ICS | 27 (77.14) | 27 (77.14) | 1.000 |
| OCS | 0 | 2 (5.71) | 0.493 |

ICS, inhaled corticosteroid; LABA, long-acting beta agonist; OCS, oral corticosteroid; SABA, short-acting beta agonist; SAMA, short-acting muscarinic-antagonist.

vital signs, including respiratory rate ($P$ = 0.513, 0.526, and 1.000, on days 0, 3, and 5, respectively). No statistically significant difference was observed between the Montelukast and placebo groups regarding the frequency of attacks during the day ($P$ = 0.746, 0.747, and 0.461, respectively) or night ($P$ = 0.488, 0.961, and 0.994, respectively) on days 0, 3, and 5. Patients' use of accessory muscles and their lying position (can lie down, prefers to sit, must sit) were not significantly different between the two groups ($P$ = 0.493 and 0.473, respectively).

### *Pulmonary function tests*

The patients who received montelukast had a mean $FEV_1$ of 78.05 ± 7.84 and PEFR of 322.86 ± 28.95 l/min on day 5 compared with $FEV_1$ of 72.05 ± 12 and PEFR of 290.86 ± 44.21 l/min for the placebo group. There was a significant difference between both $FEV_1$ ($P$ = 0.016) and PEFR ($P$ = 0.003) values on the fifth day of treatment between the Montelukast group and the placebo group; however, this difference was not statistically significant on days 0 and 3 (Table 3).

To evaluate the bronchodilator effect of montelukast (independent of ICS), $FEV_1$ and PEFR values were compared in two subgroups of patients, ICS users (ICSU) and non-ICS users (NICSU), in both the montelukast and placebo groups. Regarding $FEV_1$, no differences were seen among NISCU on days 0, 3, and 5 (All P values > 0.05). However, among ICSU, $FEV_1$ was higher in the intervention group on day 5 ($P$ = 0.009) (Table 4). Regarding PEFR, both ICSU and NICSU showed significant improvements on day 5 (ICSU: 321.48 ± 32.21 vs. 291.48 ± 46.21, $P$ = 0.007, NICSU: 237.50 ± 20.52 vs. 288.75 ± 39.43, $P$ = 0.027) (Table 4).

**Table 2**

**Patient symptomatic improvements at presentation, on day 3, and day 5 compared between the intervention and control groups.**

| Variables | Montelukast ($n$ = 35) | Placebo ($n$ = 35) | *P* |
|---|---|---|---|
| Severity of dyspnea on day 3, *n* (%) | | | |
| Walking | 27 (77.14) | 24 (68.57) | 0.420 |
| Rest | 8 (22.86) | 11 (31.43) | |
| Severity of dyspnea on day 5, *n* (%) | | | |
| Walking | 35 (100) | 34 (97.14) | 1.000 |
| Rest | 0 | 1 (2.86) | |
| Friedman test *P* value | 0.000 | 0.000 | |
| Talking status on day 0, *n* (%) | | | |
| Full-sentence | 12 (34.29) | 8 (22.86) | 0.290 |
| Broken sentences | 23 (65.71) | 27 (77.14) | |
| Words | 0 | 0 | |
| Talking status on day 3, *n* (%) | | | |
| Full-sentence | 28 (80) | 26 (74.29) | 0.569 |
| Broken sentences | 7 (20) | 9 (25.71) | |
| Words | 0 | 0 | |
| Talking status on day 5, *n* (%) | | | |
| Full-sentence | 35 (100) | 34 (97.14) | 1.000 |
| Broken sentences | 0 | 1 (2.86) | |
| Words | 0 | 0 | |
| Friedman test *P* value | 0.000 | 0.000 | |
| Wheezing on day 0, *n* (%) | | | |
| End expiration | 0 | 0 | 0.759 |
| Whole expiration | 7 (20) | 6 (17.14) | |
| Expiration and respiration | 28 (80) | 29 (82.86) | |
| Wheezing on day 3, *n* (%) | | | |
| End expiration | 7 (20) | 5 (14.29) | 0.509 |
| Whole expiration | 28 (80) | 29 (82.86) | |
| Expiration and respiration | 0 | 1 (2.86) | |
| Wheezing on day 5, *n* (%) | | | |
| End expiration | 33 (94.29) | 26 (74.29) | 0.022 |
| Whole expiration | 2 (5.71) | 9 (25.71) | |
| Expiration and respiration | 0 | 0 | |
| Friedman test *P* value | 0.000 | 0.000 | |

### *Adverse effects and safety profile*

No adverse effects were documented in either the montelukast group or the placebo group during the study period. The treat-

**Table 3**

**$FEV_1$ and PEFR comparison between the montelukast and placebo groups on days 0, 3, and 5.**

| Variable | Montelukast ($n$ = 35) | Placebo ($n$ = 35) | *P* |
|---|---|---|---|
| $FEV_1$ | | | |
| On day 0 | 57.74 ± 10.89 | 58.51 ± 12.75 | 0.786 |
| On day 3 | 71.74 ± 10.14 | 68.91 ± 14.09 | 0.339 |
| On day 5 | 78.05 ± 7.84 | 72.05 ± 12.00 | 0.016 |
| ANOVA *P* value | 0.000 | 0.000 | |
| PEFR | | | |
| On day 0 | 217.14 ± 29.85 | 237.43 ± 45.20 | 0.030 |
| On day 3 | 268.00 ± 31.13 | 268.86 ± 46.44 | 0.928 |
| On day 5 | 322.86 ± 28.95 | 290.86 ± 44.21 | 0.003 |
| ANOVA *P* value | 0.000 | 0.000 | |

$FEV_1$, forced expiratory volume in 1 second; PEFR, peak expiratory flow rate.

**Table 4**

**$FEV_1$ and PEFR comparison between the montelukast and placebo groups on days 0, 3, and 5 in the ICSU and NICSU subgroups.**

| | ICSU | | | NICSU | | |
|---|---|---|---|---|---|---|
| Variable | Montelukast | Placebo | *P* | Montelukast | Placebo | *P* |
| $FEV_1$ | | | | | | |
| On day 0 | 57.85 ± 11.78 | 58.03 ± 14.03 | 0.958 | 57.37 ± 7.78 | 60.12 ± 7.35 | 0.480 |
| On day 3 | 72.11 ± 11.09 | 68.33 ± 14.77 | 0.293 | 70.50 ± 6.41 | 70.87 ± 12.15 | 0.940 |
| On day 5 | 79.14 ± 8.40 | 71.29 ± 12.51 | 0.009 | 74.37 ± 4.06 | 74.62 ± 10.44 | 0.951 |
| PEFR | | | | | | |
| On day 0 | 217.78 ± 31.78 | 237.41 ± 45.19 | 0.071 | 215.00 ± 23.90 | 237.50 ± 48.32 | 0.258 |
| On day 3 | 267.78 ± 34.34 | 270.74 ± 46.65 | 0.791 | 268.75 ± 18.07 | 262.50 ± 48.32 | 0.737 |
| On day 5 | 321.48 ± 32.21 | 291.48 ± 46.21 | 0.007 | 237.50 ± 20.52 | 288.75 ± 39.43 | 0.027 |

FEV1, forced expiratory volume in 1 second; ICSU, ICS users; NICSU, non-ICS users; PEFR, peak expiratory flow rate.

ment was well-tolerated by all patients, with no significant differences in safety profiles between the two groups.

## Discussion

The present study aimed to evaluate the clinical efficacy of 10 mg of oral Montelukast in acute asthma exacerbation by evaluating the effects of the drug on pulmonary function and clinical symptoms. Groups were matched for baseline characteristics. Our findings showed a trend toward improved signs and symptoms in the montelukast group compared to the placebo group. However, only improvement in wheezing on day 5 was statistically significant. Regarding pulmonary function, there was a significant difference between the $FEV_1$ and PEFR values on day 5 between the montelukast and placebo groups. Furthermore, while PEFR was significantly improved in both ICSU and NICSU subgroups in the montelukast group on day 5, $FEV_1$ was only improved in the ICSU subgroup compared to placebo. The combined use of montelukast and ICS may lead to a synergistic effect, enhancing overall asthma control. This synergy could explain why montelukast might be more effective in patients already using ICS, as it complements the anti-inflammatory effects of ICS by addressing an additional pathway of inflammation[13].

Although many studies have shown the beneficial effects of oral montelukast in treating chronic asthma, the literature regarding the effectiveness of this treatment in acute asthma exacerbations is controversial. In a randomized, double-blind, placebo-controlled trial including 27 children with moderate acute asthma exacerbations, oral administration of 5 mg of montelukast did not significantly improve pulmonary function, similar to other homogenous studies[14,15]. In contrast, a separate randomized, double-blind crossover trial with 279 children revealed that the addition of 5 mg of montelukast to standard therapy had a borderline effect on pulmonary function and a considerable improvement on exacerbation days, which was supported by the results of other similar trials[16,17]. Many of these controversial results in the reports of PFTs (including $FEV_1$) may be explained by the timing of the test (whether it was at the peak medication effect) and the severity of airway obstruction (the effects of LTRA are more significant in patients with more severe airway obstruction).

What drives clinicians and scientists to use LRTAs in asthmatic patients while ICS medications lead to better pulmonary function is the possibility that the adaptations resulting from the use of LRTAs may make the outcomes of ICS medications unnecessary in addition to the potential excessive clinical benefits caused by the addition of LRTAs to ICS. Table 5 presents an overview of similar articles and their results found during the literature review.

**Table 5**

**An overview of the methods and results of similar studies.**

| Study | Design | Sample size | Intervention | Results |
|---|---|---|---|---|
| Ramsay *et al.*[9] 2010 | DBRCT | 73 | 10 mg Oral Montelukast | • Significantly higher PEFR<br>• Nonsignificant difference in $FEV_1$ and RV |
| Chaudhury *et al.*[10] 2017 | SBRCT | 160 | 10 mg Oral Montelukast | • Significantly higher PEFR and $FEV_1$<br>• No difference regarding relapse rates |
| Zubairi *et al.*[11] 2013 | DBRCT | 100 | 10 mg Oral Montelukast | • Nonsignificant difference in PEFR, $FEV_1$, and Length of Hospitalization |
| Adachi *et al.*[18] 2012 | DBRCT | 242 | 7 mg and 14 mg IV Montelukast | • Significantly higher $FEV_1$ in both intervention groups compared to placebo |
| Camargo *et al.*[17] 2010 | DBRCT | 571 | 7 mg IV Montelukast | • Significantly higher $FEV_1$ |
| Bjermer *et al.*[19] 2003 | DBRCT | 1490 | 10 mg Oral Montelukast compared with salmeterol | • Salmeterol significantly increased $FEV_1$ and PEFR compared to Montelukast<br>• Montelukast significantly reduced Eosinophil counts |
| Ferreira *et al.*[20] 2001 | DBRCT | 20 | 10 mg Oral Montelukast | • Nonsignificant improvement in emergency room stay and PEFR |
| Cýlý *et al.*[21] 2003 | SBRCT | 70 | 10 mg Oral Montelukast and 1 mg IV Prednisolone | • Significant improvement in PEFR compared to placebo<br>• Nonsignificant improvement in PEFR compared to Prednisolone<br>• Significantly less SABAs required compared to both Placebo and Prednisolone |

$FEV_1$, forced expiratory volume in 1 second; PEFR, peak expiratory flow rate; RV, residual volume.

Ramsay *et al*.[9] conducted DBRCT on 73 adults with acute asthma attacks. The intervention consisted of 10 mg oral Montelukast. Their findings showed that this intervention led to a statistically significant improvement in PEFR compared to placebo on the first day after treatment (389.6 ± 109.7 vs. 332.3 ± 124.9). Likewise, the results of the present study also showed that PEFR increased significantly with 10 mg oral Montelukast compared to placebo. However, in this study, this improvement was achieved on day 5. Moreover, consistent with our findings, their results demonstrated that PEFR improved in both ICSU and NICSU subgroups taking montelukast.

In a DBRCT study conducted on 20 patients with acute asthma attacks by Ferreira *et al*.[20], the findings did not favor 10 mg montelukast treatment. Their results showed that although the length of stay in the emergency room and improvement in PEFR were better in the montelukast group than in the placebo group, this difference was not statistically significant. The discrepancy between our findings and their results could be due to the smaller sample size and the significant difference between prescribed asthma medications in their study.

Cýllý *et al*.[21] evaluated the efficacy of 10 mg oral montelukast treatment in 70 patients with acute asthma attacks in a randomized, single-blind placebo-controlled trial (SBRCT) with three groups: montelukast plus IV prednisolone (MP), IV prednisolone (Pr), and placebo. Their findings showed that the MP and Pr groups had a significantly higher PEFR than the placebo group, and the MP group required fewer SABAs than the other two groups. Nevertheless, although MP had better PEFR results than Pr, this difference was not statistically significant.

The findings of the SBRCT trial by Chaudhury *et al*.[10] on 160 patients (72 montelukast 10 mg oral and 82 placebo) showed that this intervention resulted in a significantly better $FEV_1$ and PEFR. However, no difference was observed regarding vital capacity and recurrence rates; their results were consistent with ours.

The results of the present study demonstrated statistically significant improvements in $FEV_1$ and PEFR among patients receiving montelukast. While these improvements are promising, it is important to consider their clinical significance in patient outcomes and their quality of life (QOL). Although our study did not directly assess the impact of montelukast treatment on QOL, enhancements in PFTs (as observed in the present study) may lead to better overall physical function and reduced symptoms. Consequently, improvements in $FEV_1$ and PEFR are likely to contribute to an enhanced QOL. Also, Improvements in FEV1 and PEFR might lead to better asthma control, fewer exacerbations, and reduced healthcare utilization, all of which are clinically meaningful outcomes for patients[22]. However, there is a paucity of data to fully address this issue. Thus, we suggest that future studies include validated quality of life questionnaires, such as the Asthma Quality of Life Questionnaire (AQLQ) or the St. George's Respiratory Questionnaire (SGRQ), to provide a more direct measurement of how improvements in PFTs translate to daily living and overall well-being.

Concerning some discrepancies between the current study's findings and previous studies, further investigations with larger sample size are recommended. A multi-center study involving a larger sample size across different geographic regions and ethnicities would strengthen the external validity of our results. Moving forward, we encourage future multi-center studies in diverse global settings to further validate and expand upon our findings. These efforts could provide a more comprehensive understanding of the effectiveness and generalizability of montelukast in managing acute asthma exacerbations worldwide.

Also, we recognize that the chosen PFT measurement intervals (days 0, 3, and 5) may represent a limitation of our study. More frequent measurements could have provided a clearer picture of the treatment's efficacy over time and offered a more detailed trend analysis of $FEV_1$ and PEFR. Future research could address this by implementing more frequent monitoring to provide a more detailed assessment of the treatment's efficacy over time.

## Conclusion

The present study's findings showed that using oral montelukast in acute exacerbation of asthma could lead to better values of PEFR and FEV1 in terms of pulmonary function and improvement of wheezing in terms of symptoms in adults with bronchial asthma.

## Ethical approval

This study was conducted without commercial input or involvement in the design, implementation, analysis, or reporting. This study was approved by the Research Ethics Committee of Mazandaran University of Medical Sciences (Ethics Approval Code: IR.MAZUMS.IMAMHOSPITAL.REC.1396.3092). All procedures performed in this study were in accordance with the ethical standards of the Institutional Research Ethics Committee of Mazandaran University of Medical Sciences and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

## Consent for participation

Written informed consent was obtained from all participants before entering the study.

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## Author contribution

M.A., S.A. and M.F. designed the research. M.A., A.S., S.A. and M.F. collected data. J.Y.C. analyzed data. All authors were involved in performing the research. E.G., M.A. and H.M. wrote the paper.

## Conflicts of interest disclosure

The authors declare no conflicts of interest.

## Research registration unique identifying number (UIN)

Iranian Registry of Clinical Trials IRCT20171227038108N1

Clinical trial registration: This study was registered with the Iranian Registry of Clinical Trials (IRCT20171227038108N1).

## Guarantor

Dr Hossein Mehravaran.

## Data availability statement

The data are available upon reasonable request from the corresponding author. Trial protocol can be accessed at https://en.irct.ir/trial/28836.

## Provenance and peer review

Not commissioned, externally peer-reviewed.

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