Review paper

The efficacy of mometasone furoate for children with asthma: a meta-analysis of randomized controlled trials

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Adv Dermatol Allergol 2021; XXXVIII (5): 740–745
DOI: https://doi.org/10.5114/ada.2020.93273

Abstract

Introduction: The influence of mometasone furoate for paediatric asthma remains controversial.
Aim: We conducted a systematic review and meta-analysis to explore the efficacy and safety of mometasone furoate for paediatric asthma.
Material and methods: We have searched PubMed, Embase, Web of science, EBSCO, and Cochrane library databases through October 2019 for randomized controlled trials assessing the effect of mometasone furoate versus placebo for paediatric asthma. This meta-analysis was performed using the random-effects model.
Results: Four RCTs were included in the meta-analysis. Overall, as compared to placebo for paediatric asthma, mometasone furoate is associated with substantially increased predicted forced expiratory volume in 1 s (FEV1) (mean difference (MD) = 7.53; 95% CI: 7.02–8.04; p < 0.00001), FEV1 (MD = 0.11; 95% CI: 0.10–0.12; p < 0.00001), and morning peak expiratory flow (AM PEF) (MD = 17.70; 95% CI: 9.91–25.49; p < 0.00001), but demonstrates no obvious effect on pharyngitis (RR = 0.96; 95% CI: 0.59–1.58; p = 0.89), upper respiratory tract infections (RR = 0.73; 95% CI: 0.50–1.05; p = 0.09), or adverse events (RR = 1.05; 95% CI: 0.84–1.31; p = 0.69).
Conclusions: Mometasone furoate may be effective and safe for paediatric asthma.

Key words: mometasone furoate, paediatric asthma, forced expiratory volume in 1 s, randomized controlled trials.

Introduction

Asthma has become one of the most common chronic medical conditions and about 300 million people globally are estimated to suffer from asthma [1–3]. Asthma is also regarded as the most common chronic disorder in children [4, 5]. This disease can result in considerable morbidity and remarkably reduced quality of life in paediatric populations, and hospitalizations and urgent medical care is sometimes required for these patients [6, 7]. Inhaled corticosteroid (ICS) is currently accepted as the most effective anti-inflammatory medications for the treatment of paediatric asthma and is recommended by international guidelines [8].

Mometasone furoate, a potent ICS has high binding affinity to the glucocorticoid receptor in order to inhibit production of inflammatory mediators and cytokines [9–12]. Mometasone furoate has the features of low systemic bioavailability by inhalation, and high plasma protein binding because of slow diffusion from the bloodstream into other tissues throughout the body [13]. In adults and children as young as aged 4 years, mometasone furoate is reported to have efficacy in improving the lung function, reducing symptoms, and reducing the frequency and severity of exacerbations [14–17].

Recently, several studies reporting mometasone furoate for paediatric asthma have been published, but their efficacy has not been well established.

Aim

With accumulating evidence, we therefore have performed a systematic review and meta-analysis of RCTs to compare the efficacy and safety of mometasone furoate versus placebo for paediatric asthma patients.

Material and methods

Ethical approval and patient consent were not required because this was a systematic review and meta-
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The systematic review and meta-analysis was conducted and reported in adherence to PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) [18].

Search strategy and study selection

Two investigators have independently searched the following databases (inception to October 2019): PubMed, Embase, Web of science, EBSCO, and Cochrane library databases. The electronic search strategy has been conducted using the following key words: mometasone furoate, and asthma, and paediatric or children. We have also checked the reference lists of the screened full-text studies to identify other potentially eligible trials.

The inclusion criteria were as follows: (i) population: children patients diagnosed with asthma; (ii) intervention treatments: mometasone furoate versus placebo; (iii) the study design was RCT.

Data extraction and outcome measures

We have extracted the following information: the author, number of patients, age, female, weight, duration of asthma and detailed methods in each group etc. Data have been extracted independently by two investigators, and discrepancies were resolved by consensus. We have also contacted the corresponding author to obtain the data when necessary.

The primary outcome was predicted forced expiratory volume in 1 s (FEV1) and FEV1. Secondary outcomes included morning peak expiratory flow (AM PEF), pharyngitis, upper respiratory tract infection, and adverse events.

Quality assessment in individual studies

Methodological quality of the included studies was independently evaluated using the modified Jadad scale [19]. There are 3 evaluation items for Jadad scale: randomization (0–2 points), blinding (0–2 points), dropouts and withdrawals (0–1 points). The score of Jadad scale varies from 0 to 5 points. An article with Jadad score ≤ 2 is considered to be of low quality. If the Jadad score ≥ 3, the study is thought to be of high quality [20].

Statistical analysis

We estimated the difference (MD) with 95% confidence interval (CI) for continuous outcomes (predicted FEV1, FEV1, and AM PEF) and risk ratio (RR) with 95% CI for dichotomous outcomes (pharyngitis, upper respiratory tract infection, and adverse events). A random-effects model was used regardless of heterogeneity [21]. Heterogeneity was reported using the I² statistic, and I² > 50% indicated significant heterogeneity [21, 22]. Whenever significant heterogeneity was present, we searched for potential sources of heterogeneity via omitting one study in turn for the meta-analysis or performing subgroup analysis. All statistical analyses were performed using Review Manager Version 5.3 (The Cochrane Collaboration, Software Update, Oxford, UK).

Results

Literature search, study characteristics and quality assessment

A detailed flowchart of the search and selection results is shown in Figure 1. Two hundred and sixty-nine potentially relevant articles were identified initially. Finally, four articles that meet our inclusion criteria were included in the meta-analysis [14, 23–25].

The baseline characteristics of the four eligible RCTs in the meta-analysis are summarized in Table 1. The four studies were published between 2006 and 2017, and sample sizes ranged from 89 to 225 with a total of 704. Two studies report mometasone furoate 100 μg once daily [14, 25], while the other two studies report mometasone furoate 100 μg twice daily [23, 24].

Among the four studies included here, three studies report predicted FEV1 [14, 23, 25], two studies report FEV1 [14, 25], two studies report AM PEF [23, 25], three studies report pharyngitis and upper respiratory tract infection [14, 23, 24], and two studies report adverse events [14, 23, 25]. Jadad scores of the four included studies vary from 3 to 5, and all four studies are considered to be high-quality ones according to quality assessment.

![Figure 1. Flow diagram of the study search and selection process](image-url)
Primary outcomes: predicted FEV₁ and FEV₁

These outcome data were analysed using the random-effects model, and compared to the control group for paediatric asthma, mometasone furoate can significantly improve predicted FEV₁ (MD = 7.53; 95% CI: 7.02–8.04; \( p < 0.00001 \)) with no heterogeneity among the studies (\( I^2 = 0\% \), heterogeneity \( p = 0.66 \)) (Figure 2) and FEV₁ (MD = 0.11; 95% CI: 0.10–0.12; \( p < 0.00001 \)) with no heterogeneity among the studies (\( I^2 = 0\% \), heterogeneity \( p = 0.70 \)) (Figure 3).

Sensitivity analysis

No heterogeneity was observed for the primary outcomes, and thus we have not performed the sensitivity analysis by omitting one study in turn to detect the heterogeneity.

Secondary outcomes

In comparison with placebo for paediatric asthma, mometasone furoate demonstrates an increase in AM PEF (MD = 17.70; 95% CI: 9.91–25.49; \( p < 0.00001 \); Figure 4), but has no obvious impact on pharyngitis (RR = 0.96; 95% CI: 0.59–1.58; \( p = 0.89 \); Figure 5), upper respiratory tract infections (RR = 0.73; 95% CI: 0.50–1.05; \( p = 0.09 \); Figure 6), or adverse events (RR = 1.05; 95% CI: 0.84–1.31; \( p = 0.69 \); Figure 7).

Discussion

Inhaled corticosteroids are widely used to decrease the symptoms and the risk of asthma exacerbations, and initiation of ICS treatment or in combination with short-acting \( \beta_2 \)-agonists (SABA) is recommended in patients with the risk of exacerbations for inhibiting a long-term decline in lung function [26–29]. Mometasone furoate is a highly potent topical corticosteroid with negligible systemic bioavailability, and is available in a dry-powder inhaler for the treatment of asthma. Several trials found that mometasone furoate was efficacious and well tolerated in adolescent and adult patients who were receiving ICS maintenance therapy or only SABA [16, 30–32].

Our meta-analysis suggests that mometasone furoate can substantially improve predicted FEV₁, FEV₁, and AM PEF for children with asthma to a greater extent than placebo. In addition, mometasone furoate at a dose of 100 \( \mu \)g qd resulted in a significant improvement in quality of life compared to placebo, as evidenced by the Paediatric Asthma Quality of Life Questionnaire with Standardized Activities scores, with a difference of 0.22 points (\( p = 0.014 \)) [23]. Regarding the sensitivity analysis, although there is no significant heterogeneity analysis, different doses of mometasone furoate and treatment duration may have some impact on the pooling results.

In a 12-week, multicentre, double-blind, parallel-group, placebo-controlled study evaluating 2 dosing regimens

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| Author     | Mometasone furoate group | Control group |
|------------|--------------------------|---------------|
|            | Number | Age [years] | Female (n) | Weight [kg] | Duration of asthma [year] | Methods |
| Amar 2017  | 113    | 8.6 (1.9)   | 44        |            | –                     | Mometasone furoate delivered via a metered-dose inhaler 100 \( \mu \)g BID for 12 weeks |
| Skoner 2011| 44     | 6.3         | 16        | 5.4        | 25.4                  | Mometasone furoate 100 \( \mu \)g twice daily for 52 weeks |
| Meltzer 2007| 100   | 8.2 (0.2)   | 43        | 5.2 (1.1)  | 4.8 (0.3)            | Mometasone furoate 100 \( \mu \)g once daily by a novel dry-powder inhaler for 12 weeks |
| Berger 2006| 98     | 9.0 (1.8)   | 57        | 5.7 (0.7)  | 4.6 (0.9)            | Mometasone furoate 100 \( \mu \)g once daily for 12 weeks |

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Table 1. Characteristics of included studies
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| Study or subgroup | Mean difference | SE | Weight (%) | Mean difference IV, random, 95% CI | Mean difference IV, random, 95% CI |
|-------------------|-----------------|----|------------|------------------------------------|------------------------------------|
| Amar 2017         | 6.29            | 1.653 | 2.5       | 6.29 (3.05–9.53)                   |                                    |
| Berger 2006       | 6.5             | 2.071 | 1.6       | 6.50 (2.44–10.56)                  |                                    |
| Meltzer 2007      | 7.58            | 0.267 | 95.9      | 7.58 (7.06–8.10)                   |                                    |

Total (95% CI) 100 7.73 (7.02–8.04)

Heterogeneity: $t^2 = 0.00, \chi^2 = 2 (p = 0.66), I^2 = 0$

Test for overall effect: $Z = 28.80 (p < 0.00001)$

**Figure 2.** Forest plot for the meta-analysis of FEV$_1$

| Study or subgroup | Mean difference | SE | Weight (%) | Mean difference IV, random, 95% CI | Mean difference IV, random, 95% CI |
|-------------------|-----------------|----|------------|------------------------------------|------------------------------------|
| Berger 2006       | 0.125           | 0.038 | 1.7       | 0.13 (0.05–0.20)                   |                                    |
| Meltzer 2007      | 0.11            | 0.005 | 98.3      | 0.11 (0.10–0.12)                   |                                    |

Total (95% CI) 100 0.11 (0.10–0.12)

Heterogeneity: $t^2 = 0.00, \chi^2 = 0.15, df = 1 (p = 0.70), I^2 = 0$

Test for overall effect: $Z = 22.24 (p < 0.00001)$

**Figure 3.** Forest plot for the meta-analysis of FEV$_1$ (l)

| Study or subgroup | Mean difference | SE | Weight (%) | Mean difference IV, random, 95% CI | Mean difference IV, random, 95% CI |
|-------------------|-----------------|----|------------|------------------------------------|------------------------------------|
| Amar 2017         | 27.355          | 9.554 | 14.5      | 27.36 (8.63–46.08)                 |                                    |
| Meltzer 2007      | 16.06           | 0.804 | 85.8      | 16.06 (14.48–17.64)                |                                    |

Total (95% CI) 100 17.70 (9.91–25.49)

Heterogeneity: $t^2 = 17.83, \chi^2 = 1.39, df = 1 (p = 0.24), I^2 = 28$

Test for overall effect: $Z = 4.45 (p < 0.00001)$

**Figure 4.** Forest plot for the meta-analysis of AM PEF (l/min)

| Study or subgroup | Mometasone furoate group | Control group | Weight (%) | Risk ratio, IV, random, 95% CI | Risk ratio, IV, random, 95% CI |
|-------------------|--------------------------|---------------|------------|--------------------------------|--------------------------------|
| Amar 2017         | 0                        | 109           | 2.8        | 0.20 (0.01–4.19)               |                                |
| Berger 2006       | 9                        | 98            | 31.2       | 1.01 (0.42–2.44)               |                                |
| Skoner 2011       | 15                       | 48            | 66.2       | 1.00 (0.55–1.84)               |                                |

Total (95% CI) 255 255 100 0.96 (0.59–1.58)

Total events 24 25

Heterogeneity: $t^2 = 0.00, \chi^2 = 1.04, df = 2 (p = 0.59), I^2 = 0$

Test for overall effect: $Z = 4.45 (p = 0.089)$

**Figure 5.** Forest plot for the meta-analysis of pharyngitis

| Study or subgroup | Mometasone furoate group | Control group | Weight (%) | Risk ratio, IV, random, 95% CI | Risk ratio, IV, random, 95% CI |
|-------------------|--------------------------|---------------|------------|--------------------------------|--------------------------------|
| Amar 2017         | 2                        | 109           | 2.4        | 2.04 (0.19–22.14)              |                                |
| Berger 2006       | 11                       | 98            | 26.5       | 0.69 (0.34–1.42)               |                                |
| Skoner 2011       | 19                       | 48            | 71.1       | 0.71 (0.46–1.10)               |                                |

Total (95% CI) 255 255 100 0.73 (0.50–1.05)

Total events 32 42

Heterogeneity: $t^2 = 0.00, \chi^2 = 0.74, df = 2 (p = 0.69), I^2 = 0$

Test for overall effect: $Z = 1.71 (p = 0.09)$

**Figure 6.** Forest plot for the meta-analysis of upper respiratory tract infections
of mometasone furoate DPI (100 μg every evening and 100 μg twice daily) in 296 children aged 4 to 11 years with asthma, predicted FEV\(_1\), were 4.73 and 5.52 percentage points for mometasone furoate at a dose of 100 μg daily and 100 μg twice daily, respectively. Both of these two doses demonstrated an important improvement in lung function to a higher extent than placebo. However, the difference of two doses was not significant [14]. In one RCT involving children with asthma included in this meta-analysis, all three doses of mometasone furoate treatment (50 μg BID, 100 μg BID, 200 μg BID) demonstrated statistically significant differences of predicted FEV\(_1\), compared to placebo. Mometasone furoate at doses of 100 μg BID and 200 μg BID induced the efficacy by increasing predicted FEV\(_1\), approximating a five percentage-point difference compared to placebo, and the 50 μg BID mometasone furoate demonstrated the sub-maximal efficacy. Mometasone furoate 100 μg BID [23]. This revealed the effect of various doses of mometasone furoate on treatment efficacy, and 100 μg BID may be the ideal dose of mometasone furoate for the treatment of paediatric asthma.

Similar incidences of pharyngitis, upper respiratory tract infections and total adverse events were observed in mometasone furoate and placebo groups based on the results of this meta-analysis. There are several potential limitations. Firstly, our analysis is based on four RCTs, and more RCTs with a large sample size should be conducted to explore this issue. Next, different doses of mometasone furoate and treatment duration may have some influence on the pooling results. Finally, some unpublished and missing data may lead to some bias for the pooled effect.

Conclusions

Mometasone furoate may provide treatment efficacy for children with asthma.

Conflict of interest

The authors declare no conflict of interest.

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