# Role of Mometasone Furoate Nasal Spray Combined with Montelukast Sodium in the Treatment of Adenoids Hypertrophy in Children

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## Abstract

**Background:** Adenoidectomy is currently considered the treatment of choice for children with severe symptoms caused by Adenoids Hypertrophy (AH). Non-surgical alternative treatment options are considered in less severe cases to avoid the untoward effect of surgery. This study was aimed to evaluate the efficacy and safety of Mometasone Furoate nasal spray combined with Montelukast Sodium in children with AH.

**Materials and methods:** This trial included 118 patients aged 3 to 13 years having symptomatic AH from the OPD of Otolaryngology and Head Neck Surgery of CMCH from May 2019 to April 2020. They were allocated to either Mometasone Furoate nasal spray combined with Montelukast Sodium (Group A: 59) or Mometasone Furoate nasal spray alone (Group B: 59) randomly for 8 weeks. Outcome measures were changes in the severity of symptoms and changes in the adenoid size from baseline. Out of 118 enrolled children, 109 children completed the study per protocol.

**Results:** The mean total clinical symptom score before and after treatment in group A was respectively 10.04 (±1.78) and 4.92 (±1.65). In group B the corresponding figures were respectively 9.42 (±1.33) and 5.48 (±1.36). Clinical symptom scores as well as Adenoidal-nasopharyngeal ratio dropped significantly in both groups without any statistical significance between two groups with 8 weeks of treatment.

**Conclusion:** Mometasone Furoate nasal spray with and without oral Montelukast Sodium showed similar efficacy in symptom alleviation and adenoid size reduction without any superiority of combination therapy.

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## Introduction

Adenoidal Hypertrophy (AH) a common disorder in children, presents with symptoms ranging from nasal obstruction to Obstructive Sleep Apnea Syndrome (OSAS). Growth of adenoids continue rapidly during infancy reaching a maximal size around the age of 7 years and tend to involute after puberty[1,3]. Surgery (Adenoidectomy) is considered the treatment of choice for symptomatic AH[1]. Because of surgical risks involved, younger age, adenoid as an immune organ, parents are often apprehensive and view adenoidectomy as their last option, which many pediatricians and general practitioners also endorse. So, conservative treatment has been tried for these children with AH[2].

There is now a reasonable amount of evidence that topical nasal steroid sprays can cause a reduction in adenoid size with improvement in the presence of middle ear fluid, audiometric thresholds, nasal obstruction, rhinorrhoea, cough, snoring, and sleep apnoea. It will probably find a role in clinical practice, although that role is still unclear[1]. Mometasone Furoate (MF) is an Inhaled Corticosteroid (ICS). MF has a higher binding affinity to corticosteroid receptors, poor systematic concentration (0.1%) and extensive first-pass metabolism on intranasal administration. MF had been reported previously not to cause any adverse tissue changes in the nasal mucosa of patients treated for long periods, it has no effect on growth in children, it has no impact on the hypothalamic-pituitary-adrenal axis, and the systemic availability of the drug after topical administration is lower than that of other steroids.[4] On the other hand, increased concentrations of Leukotrienes (LTs) in tonsils and upper airway condensate in children with OSAS, along with a relatively high abundance of LT receptors in these tissues, suggested that LT pathways may contribute to the proliferative status of adenotonsillar

tissues[5]. In several studies, both leukotriene antagonists and intranasal steroids separately provided a reduction in adenoid size, but they could not demonstrate the statistical superiority of one over the other. At this point, the question could arise as to whether the combined administration of both these medications would contribute to improvement[2]. This study examined the effects of intranasal mometasone with and without oral Montelukast Sodium on nasal obstruction symptom relief in children with AH.

**Material and methods**

This randomized controlled trial was conducted in the Department of Otolaryngology and Head Neck Surgery of Chittagong Medical College Hospital, Chattogram, Bangladesh from May 2019 to April 2020. Ethical clearance for the study was obtained from the Ethical and Review Committee of Chittagong Medical College.

Children with age between 3 and 13 years of either gender with a history of symptomatic AH for at least three months with no response to previous medical treatment and baseline Adenoidal-Nasopharyngeal Ratio (ANR) 50% or more diagnosed by X-ray Nasopharynx Lateral View, were included in the study.[6] Children with a history of the previous adenoidectomy, use of intranasal topical or systemic steroids in the last year, associated marked tonsillar hypertrophy, anatomical deformity of the nose or sinonasal disease, positive allergy or atopy against MF or Montelukast Sodium, chronic otitis media with effusion and Type-B tympanogram, indication for adenoidectomy for any other reason were excluded from the study. The informed written consent and assents were obtained from the guardians or legal relatives and the children (Where appropriate). One hundred and eighteen (59 in each treatment arm) patients were required to have an 80% chance of detecting, as significant at the 5% level, an increase in the primary outcome measure from 79.4% in the control group (Group B) to 94.1% in the experimental group (Group A).[6,7]

After consenting, eligible individuals were recruited consecutively and randomly assigned ina 1:1 ratio (Block size of two) with a computer-generated randomization list to one of the two treatment arms.[8]

Each of the selected patients of group A received a dosage-metered dose of 50 micrograms (Manual pumpspray) of MF nasal spray (Metaspray) on each nasal cavity once daily (In the morning) with oral Montelukast Sodium (4mg under 6 years of age and 5mg for 6 years of age or more, once daily at night) for 8 weeks. Patients of group B received a dosage-metered dose of 50 micrograms (Manual pump spray) of MF nasal spray (Metaspray) on each nasal cavity once daily (In the morning) for 8 weeks.

Patients were followed up over the phone at 2 weeks intervals and physically at 4 weeks and 8 weeks post-treatment. During over phone and physical follow up patients were enquired and examined for any adverse reaction.Patients were followed up for the outcome parameters.

Symptoms were assessed by Total Symptom Severity Scores-whole-number linear scale to grade their severity according to the following scale: 0=absent, 1=occasional, 2= frequent and 3= day time and night-time symptoms. All scores were summed to obtain an overall symptom score for each patient[4,9]. Objective assessment was done by determining the change in ANR measured according to the method described by Fujioka et al.[10] To assess the safety measures adverse events rate was calculated as the number of patients who experienced an adverse event following the initiation of treatment divided by the number of patients randomized into this group.Tolerability was evaluated by observing the withdrawal rate. Compliance with the administered drug was assessed bi-weekly over telephone interviews with parents.

Statistical analysis was carried out using SPSS (Statistical Package for Social Science) for Windows version 23 software. Data were presented as number (Percentage) for categorical data and as mean±SD for continuous data. The categorical data were tested between groups by Chi-square test/Fisher's exact test as appropriate. To compare mean between groups, independent sample t-test and comparison of mean difference within group paired sample t-test were used. A p-value $<0.05$ was considered statistically significant.

## Results

Out of 118 enrolled children, 109 children were available in the follow-up assessment (Lost to follow-up 9 children: 6 from Group A and 3 from Group B) and were included in the final analysis. Table I shows that both the groups were similar at baseline in terms of their demographic and clinical characteristics. The mean overall symptom scores were 10.04 for group A and 9.42 for group B (p=0.051).

**Table I** Baseline characteristics of the patients stratified by study groups

| Characteristics | Group A (n=53) | Group B (n=56) | p value |
|---|---|---|---|
| Age (Years) | 7.52 (±2.11) | 7.50 (±2.70) | 0.962* |
| Sex | | | |
| Male | 36 (67.9) | 40 (71.4) | 0.691† |
| Female | 17 (32.1) | 16 (28.6) | |
| Weight (Kg) | 18.53 (±5.49) | 19.21 (±6.39) | 0.556* |
| Height (cm) | 38.96 (±6.40) | 38.50 (±7.30) | 0.727* |
| Symptoms score | | | |
| Nasal obstruction | 2.38 (±0.53) | 2.27 (±0.49) | 0.244* |
| Mouth breathing | 2.32 (±0.80) | 2.21 (±0.79) | 0.471* |
| Rhinorrhea | 1.96 (±0.71) | 1.86 (±0.72) | 0.445* |
| OSA | 0.79 (±0.72) | 0.64 (±0.64) | 0.254* |
| Snoring | 1.70 (±0.69) | 1.54 (±0.76) | 0.257* |
| Night cough | 0.89 (±0.64) | 0.91 (±0.79) | 0.963* |
| Total symtomsscore | 10.04 (±1.78) | 9.42 (±1.33) | 0.051* |
| Obstruction ratio | 71.76 (±6.88) | 68.30 (±13.89) | 0.104* |

Group A: Mometasone Furoate nasal spray + Oral Montelukast Sodium, Group B: Mometasone Furoate nasal spray alone. Data are expressed as frequency (Percentage) or mean (±SD). *Independent sample t-test, †Chi-square test.

Similar to baseline (Pretreatment) there were no signi cant differences between the two groups regarding symptoms such as rhinorrhea, mouth breathing, cough, snoring, nasal obstruction, and obstructive sleep apnea 8 weeks after treatment. The mean overall symptom scores after 8 weeks were 4.92 for group A and 5.48 for group B (p=0.056). The obstruction ratio was reduced in both groups with 8 weeks of treatment. However, no statistically significant difference was found after 8 weeks (p=0.095).

**Table II** Mean symptom score and obstruction score between two groups after 8 week

| Symptoms | Group A(n=53) | Group B(n=56) | p value* |
|---|---|---|---|
| Nasal obstruction | 1.15 (±0.66) | 1.14 (±0.48) | 0.942 |
| Mouth breathing | 0.92 (±0.65) | 1.04 (±0.85) | 0.446 |
| Rhinorrhea | 0.96 (±0.76) | 1.27 (±0.59) | 0.020 |
| Obstructive Sleep Apnea | 0.28 (±0.46) | 0.38 (±0.52) | 0.331 |
| Snoring | 0.98 (±0.57) | 1.13 (±0.66) | 0.228 |
| Night cough | 0.62 (±0.49) | 0.54 (±0.57) | 0.397 |
| Total symtoms score | 4.92 (±1.65) | 5.48 (±1.36) | 0.056 |
| Obstruction ratio | 57.04 (±6.90) | 59.71 (±9.40) | 0.095 |

Data are expressed as Mean (±SD). * Independent sample t-test.

In Group A, after 8 weeks of treatment, there were statistically significant reductions in symptom scores for nasal obstruction, mouth breathing, rhinorrhoea, night cough, snoring, and OSA (p= <0.001). The mean decrease in total symptom score was 5.11.In Group B, after 8 weeks of treatment, there were statistically significant reductions in symptom scores for nasal obstruction, mouth breathing, rhinorrhoea, night cough, snoring, and OSA (p= <0.001). The mean decrease in total symptom score was 3.95 (p=<0.001).

**Table III** Mean changes in the symptom scores before and after treatment in both groups

| Parameters | Study groups | | | |
|---|---|---|---|---|
| | Group A (n=53) | | Group B (n=56) | |
| | Mean (±SD) | P value‡ | Mean (±SD) | p value‡ |
| Nasal obstruction | 1.23 (±0.64) | <0.001 | 1.13 (±0.57) | <0.001 |
| Mouth breathing | 1.39 (±0.74) | <0.001 | 1.18 (±0.86) | <0.001 |
| Rhinorrhea | 1.00 (±0.68) | <0.001 | 0.59 (±0.57) | <0.001 |
| OSA | 0.51 (±0.54) | <0.001 | 0.27 (±0.49) | <0.001 |
| Snoring | 0.72 (±0.53) | <0.001 | 0.41 (±0.63) | <0.001 |
| Night cough | 0.26 (±0.49) | <0.001 | 0.38 (±0.49) | <0.001 |
| Total symptom score | 5.11 (±1.83) | <0.001 | 3.95 (±1.38) | <0.001 |
| Obstruction ratio | 14.72 (±2.23) | <0.001 | 8.59 (±2.08) | <0.001 |

‡Paired sample t-test. OSA: Obstructive Sleep Apnea.

Though the mean value of percentage reduction of total symptom score was comparatively higher in Group A than Group B (50.62±14.12 versus 45.69±12.32 respectively) it was not statistically significant (p=0.059).Similarly, the mean value of percentage reduction of ANR was comparatively higher in Group A than Group B (20.12±10.11 versus 16.73±9.26 respectively) but not statistically significant (p=0.071).

**Table IV** Comparison of the mean percentage reduction of total clinical symptom score and obstruction score between two groups

| Parameters | Group A (n=53) | Group B (n=56) | p value* |
|---|---|---|---|
| Total symptom score | 50.62±14.12 | 45.69±12.32 | 0.059 |
| Obstruction ratio | 20.12±10.11 | 16.73±9.26 | 0.071 |

Data are expressed as Mean (±SD). * Independent sample t-test.

The subjects in this study well tolerated both regimens. Adverse events were headache, burning sensation in the nasal cavity, and epistaxis. All these events were mild and resolved with reassurance. In cases of epistaxis, MF spray was stopped for 1 to 2 days and restarted with special advice to spray away from the nasal septum (Table V).

**Table V** Comparison of adverse events between two groups

| Adverse events | Group A (n=53) | Group B (n=56) | p value# |
|---|---|---|---|
| Headache | 3 (5.66) | 0 (0) | 0.874 |
| Burning sensation in nasal cavity | 4 (7.55) | 2 (3.57) | 0.845 |
| Epistaxis | 2 (3.77) | 3 (5.36) | 1.0 |

Data are expressed as frequency (Percentage) # Fisher exact test.

## Discussion

The present study has investigated the efficacy of combination therapy of Mometasone Furoate nasal spray with Oral Montelukast Sodium and Mometasone Furoate nasal spray alone in treating AH in children.The present study demonstrated that, with the 8 weeks of treatment of MF nasal spray, a significant reduction in the ANR improves the symptoms of snoring, mouth breathing, and nasal congestion. In a similar study,significant improvements were found in nasal obstruction outcomes, snoring, total nasal symptoms, pure tune audiometry, otitis media with effusion, and quality of life with MF nasal spray in adenoid hypertrophy in children.[9]

Regarding the combination regimen (MFnasal spray plus Oral Montelukast Sodium) the decline of total symptom score and adenoid size was more pronounced after 8 weeks of treatment. The difference was not statistically significant. A study compared intranasal Mometasone Furoate and Oral Montelukast Sodium in patients with nasal polyposis and reported no statistically significant difference between either preparation in reducing symptoms, although they found intranasal steroids were more efficient in the prevention of polyp recurrence[11]. Another study on patients with seasonal allergic rhinitis reported that the effectiveness of INC in symptom reduction was statistically significant compared with oral Montelukast Sodium.[12] At this point, the question could arise as to whether the combined administration of both these medications would contribute to improvement.

In a study with 22 patients, a combination of Budesonide and oral Montelukast Sodium was administered for 12 weeks for OSAS due to residual adenoid tissue following adenotonsillectomy and a significant improvement in the Apnea-Hypopnea Index was found.[13] According to our results, the combination therapy effectively reduces adenoid size, but statistical superiority over Mometasone Furoate alone could not be established. Similarly, another study reported that combined therapy has no superiority over single-therapy treatment.[14] In contrast to our findings, three recent studies published from China claimed that the clinical efficacy of MF nasal spray combined with Oral Montelukast Sodium in the treatment of AH in children is significant, which can effectively reduce the ANR, improve the symptoms of snoring, mouth breathing, nasal congestion, improve the quality of life of patientsand the effectivity ratio was higher than single-drug treatment, which was worthy of applying on clinic.[7,14,15]

To date, no standard indications regarding the dosage and duration of topical intranasal steroid therapy for the treatment of AH have been established. Compared with the previous trials, a lower daily steroid dose in each nostril was chosen to be administered in the present study for eight weeks. Only five cases of mild episodic epistaxis were observed, which was resolved after one to two days of stopping nasal spray.[7,4] Also, three cases of mild headache and six cases of burning sensation in the nasal cavity were observed, which were resolved by simple reassurance. This demonstrated the safety of intranasal MF administration. Liming et al reported in their meta-analysis that there were no significant adverse reactions or events associated with the use of oral Montelukast Sodium and nasal ICS in children. The reported reactions were mild (Nausea, headache, and epistaxis)[16].

## Limitations

Patients were selected from a single institution, so there is a chance of the sample being non-representative.There was no placebo group in our study, and the sample size was relatively small. Moreover, the observation period was only 8 weeks, so we do not know the long-term effects.It was an open-label study. So, there was a chance of allocation bias and assessment bias might. We did not perform polysomnography as a pre and post-treatment tool to evaluate the efficacy of the drugs for OSAS.

## Conclusion

In conclusion according to results of the present study, Mometasone Furoate nasal spray was successful in the treatment of adenoids hypertrophy in children. Combination therapy of Mometasone

Furoate nasal spray and oral Montelukast Sodium was also effective at reducing adenoids size and symptom scores but statistically significant superiority over Mometasone Furoate nasal spray alone could not be established.

**Recommendation**

Both treatment methods may separately be an alternative option to surgery depending on treatment adherence by the patients. Larger studies are warranted to assess the superiority of combination therapy over single drug therapy and for dosage and duration of use in a double-blind placebo-controlled design, and identi cation of factors that could be used to select non-responders are warranted.

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**Contribution of authors**

MUF-Conception, design, data collection, manuscript drafting & final approval.
MMA-Interpritation of data, critical revision & final approval.
KKU-Data analysis, critical revision & final approval.
MC-Data collection, drafting & final approval.
SMAS-Data collection, analysis, drafting & final approval.
SB-Data analysis, interpritation of data & final approval.
SB-Data collection, manuscript drafting & final approval.

**Disclosure**

All the authors declared no competing interest.

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