Section: ENT

Original Research Article

INTRANASAL FLUTICASONE FUROATE VERSUS INTRANASAL FLUTICASONE FUROATE WITH MONTELUKAST, LEVOCETRIZINE COMBINATION - A COMPARATIVE STUDY IN TREATMENT OF PATIENTS WITH CHRONIC ADENOIDITIS

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Abstract

Background: Chronic adenoiditis involves the enlargement of adenoids, leading to continuous or intermittent symptoms like nasal discharge, nasal blockage, snoring, mouth breathing, and dry mouth. The severity of these symptoms is linked to the extent of adenoid hypertrophy. When adenoid hypertrophy obstructs the nasal airway in children, it can cause severe complications such as enuresis, cognitive and physical developmental delays, and cardiorespiratory disorders. In our study we aim to assess the effectiveness and recurrence rates of combined therapy with intranasal fluticasone furoate alone versus intranasal fluticasone furoate in combination with montelukast and levocetirizine in treating chronic adenoiditis in children. **Materials and Methods:** The study involved 100 children aged 6 to 10 with symptoms of chronic adenoiditis, randomly divided into two groups. Group I (50 patients) received intranasal fluticasone furoate nasal spray, while Group II (50 patients) received a combination of intranasal fluticasone furoate nasal spray with montelukast and levocetirizine. Treatment lasted for 3 months, followed by a 3-month observation period post-treatment. Patients were evaluated based on symptom scores, the adenoid/nasopharyngeal ratio, and endoscopic grading of adenoid hypertrophy. **Result:** After 3 months of treatment, Group II showed significantly better scores for the main symptoms compared to Group I, with P-values of 0.001 for nasal discharge, 0.018 for mouth breathing, and 0.009 for snoring. The mean A/N ratio was 51.8 ± 10.3 in Group II, better than 56.78 ± 11.10 in Group I ($P < 0.001$). In terms of adenoid hypertrophy grading, a significant reduction in size was observed in 34 (68%) patients in Group II, compared to 18 (36%) patients in Group I ($P = 0.001$). After an additional 3 months of follow-up, the mean A/N ratio was 56.36 ± 10.05 in Group II, better than 64.24 ± 10.26 in Group I ($P < 0.001$). Recurrence occurred in 8 (23.5%) of the 34 improved cases in Group II, compared to 10 (55.5%) of the 18 cases in Group I ($P = 0.02$). **Conclusion:** Combining oral montelukast and levocetirizine with intranasal fluticasone furoate for the treatment of chronic adenoiditis resulted in better improvements and lower recurrence rates compared to using intranasal fluticasone furoate alone.

INTRODUCTION

Chronic adenoiditis involves the enlargement of adenoids, leading to continuous or intermittent symptoms like nasal discharge, nasal blockage, snoring, mouth breathing, and dry mouth. The severity of these symptoms is linked to the extent of adenoid hypertrophy.[1] When adenoid hypertrophy obstructs the nasal airway in children, it can cause severe complications such as enuresis, cognitive and physical developmental delays, and cardiorespiratory disorders.[2]

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Chronic adenoiditis with adenoid hypertrophy is diagnosed using lateral radiographs and nasal endoscopy. Adenoidectomy is the recommended surgical treatment, but it carries risks such as early or late bleeding (4%–5%), adenoid tissue recurrence (10%–20%), and postoperative respiratory issues (27%), as well as anesthesia-related risks.[3] Therefore, conservative treatments are often preferred for most patients with chronic adenoiditis and adenoid hypertrophy.[4]

Intranasal corticosteroids significantly impact the production and/or activity of various pro-inflammatory mediators in the nasal mucosa, reducing vascular permeability and edema. This anti-inflammatory effect may diminish the immune response in hypertrophied adenoid tissue.[5] Fluticasone, a potent corticosteroid administered intranasally, binds strongly to corticosteroid receptors, has low systemic absorption (0.1%), and undergoes extensive first-pass metabolism. At typical intranasal doses, it does not suppress the hypothalamic-pituitary axis.[6]

Levocetirizine, a third-generation antihistamine, and montelukast, a leukotriene receptor antagonist, exhibit significant synergistic anti-inflammatory effects across a range of signaling proteins, cell adhesion molecules, and leukocytes.[7]

Leukotrienes, key inflammatory mediators in the respiratory system, are involved in the pathogenesis of childhood diseases such as asthma and are implicated in the inflammation process of adenoid hypertrophy.[8] Montelukast, an oral cysteinyl leukotriene receptor antagonist, is used to prevent asthma and allergic rhinitis and has been studied for treating adenoid hypertrophy based on the increased expression of cysteinyl leukotriene receptors in adenotonsillar tissues of children with sleep apnea.[9] Anti-inflammatory synergy between levocetirizine and montelukast in the downregulation of IL-4, IL-6, IL-8, TNF-alpha, GM-CSF, NF-kB, ICAM-1/sICAM-1, VCAM-1, and neutrophil/eosinophil quantity and migration.[10,11]

The aim of this study is to evaluate the role of combined therapy using montelukast and levocetirizine with intranasal fluticasone furoate compared to intranasal fluticasone furoate alone in treating chronic adenoiditis with adenoid hypertrophy, focusing on efficacy and recurrence rates.

MATERIALS AND METHODS

Patients: This prospective randomized study was conducted in a teritiary care teaching hospital April 2022 to March 2023. Written informed consent was obtained from the parents of the participating children. The study included 100 children aged 6 to 10 years with symptoms of chronic adenoiditis and adenoid hypertrophy, including nasal obstruction, persistent nasal discharge, mouth breathing, and snoring. Diagnosis was confirmed through lateral neck soft tissue radiographs and flexible endoscopy, including adenoid hypertrophy grades 3 or 4 on nasopharyngeal endoscopy and an adenoid/nasopharynx ratio (A/N ratio) > 50%.

Assessment and Evaluation: All patients underwent a comprehensive clinical assessment, including complete history taking, general and ENT examination. Symptoms such as nasal blockage, snoring, and mouth breathing were evaluated using a visual analog scale (VAS) from 0 to 10. Flexible fibro-optic endoscopic examination of the nose and nasopharynx was performed, and adenoid hypertrophy was graded according to Cassano's classification.[12]

Table 1: Cassano's Classification

Grade I	0%–25% obstruction
Grade II	25%–50% obstruction
Grade III	50%–75% obstruction
Grade IV	75%–100% with total choanal obstruction

Lateral neck radiographs were taken to assess airway patency, and the adenoid/nasopharyngeal ratio (A/N ratio) was measured as described by Fujioka et al.[13] In this approach, (A) denotes the distance from the most convex point of the adenoid shadow to a line running along the front edge of the basiocciput. (N) denotes the distance from the posterior edge of the hard palate to the front-lower edge of the spheno-basioccipital synchondrosis.

Treatment Groups: Patients were randomly assigned to two groups (50 patients each):

- Group I received fluticasone furoate intranasal spray (2 puffs, total 100 µg in each nostril, once daily) for 3 months.
- Group II received fluticasone furoate intranasal spray (2 puffs, 100 µg in each nostril, once daily) combined with montelukast and levocetirizine for 3 months.

Follow-Up: All patients were assessed after three months of treatment and again three months after discontinuing treatment to determine the recurrence rate. Evaluation included symptom assessment using the same 0 to 10 scale initially employed. Clinical examinations included flexible fiberoptic endoscopy of the nasopharynx and radiological examinations (X-ray) as conducted during the initial assessment.

Patients with chronic systemic steroid use, prior adenoidectomy, allergies to montelukast/ levocetirizine, fluticasone, syndromic conditions like Down syndrome, children with sleep apnea syndrome, and other complications of chronic adenoiditis were excluded from the study.

RESULTS

A total of 100 patients diagnosed with adenoid hypertrophy were enrolled and randomly divided into two groups. Group I included 50 patients who received fluticasone furoate, while Group II included 50 patients who received the combination therapy of fluticasone furoate, montelukast, and levocetirizine. Both groups were matched in age and sex, and there

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were no significant differences at the initial assessment regarding symptom scores, A/N ratio, and adenoid hypertrophy grades.

A total of 100 patients diagnosed with adenoid hypertrophy were included in this study and randomly divided into two groups. Group I comprised 50 patients who received combined therapy with fluticasone furoate intranasal spray and oral montelukast, while Group II comprised 50 patients treated only with fluticasone furoate intranasal spray. In Group I, there were 26 males and 24 females aged 6 to 12 years (mean age 7.8 ± 2.2 years), and in Group II, there were equal numbers of males and females with a mean age of 7.7 ± 2.1 years. [Figure 1] There were no significant differences between the groups in terms of age and sex distribution.

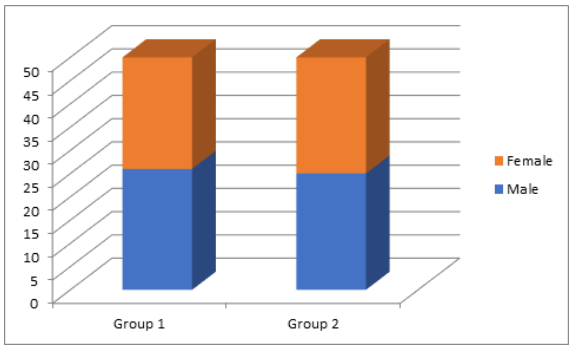

Figure 1: Distribution of patients based on sex in 2 groups

Baseline scores for the main symptoms (rhinorrhea, mouth breathing, and snoring) showed no statistically significant differences between Group I and Group II (P-values were 0.412, 0.441, and 0.501, respectively). Similarly, there was no significant difference in the baseline adenoid-to-nasopharynx (A/N) ratio between the two groups (P = 0.173), with mean ratios of 64.78 ± 4.01 in Group I and 66.21 ± 6.41 in Group II.

Initial grading of adenoid hypertrophy via endoscopic examination also did not differ significantly between the groups. In Group I, 90% had grade 3 and 10% had grade 4 hypertrophy, compared to 80% with grade 3 and 20% with grade 4 in Group II (P = 0.101).

After 3 months of treatment, Group I showed significantly greater improvement in symptoms (rhinorrhea, mouth breathing, and snoring) compared to Group II, with P-values of 0.001, 0.018, and 0.009, respectively. Group I also demonstrated a more favorable improvement in the A/N ratio (mean 51.8 ± 10.3) compared to Group II (mean 56.78 ± 11.10), with a statistically significant difference (P < 0.001). Endoscopic grading after treatment showed significantly better outcomes in Group I compared to Group II (P = 0.005).

During the 3-month observation period after treatment cessation, Group I maintained better symptom scores compared to Group II, with statistically significant differences (P < 0.001) for all symptoms. Group I also exhibited a more favorable A/N ratio (mean 56.36 ± 10.05) compared to Group II (mean 64.24 ± 10.26), with a significant difference (P < 0.001). Similarly, adenoid hypertrophy grading by endoscopic examination favored Group I over Group II (P < 0.001).

Analysis of A/N ratio changes within each group over the study period (baseline, after 3 months of treatment, and after 3 months of observation) revealed statistically significant differences (P < 0.001) in both groups.

Assessment of adenoid grade changes over the study period showed that in Group I, a significant proportion of grade 3 cases reduced to grade 2 (71.11%), and some grade 4 cases also improved. However, in Group II, fewer grade 3 cases reduced to grade 2 (45.0%), and there were more recurrent cases (55.5%) compared to Group I (23.5%). These findings underscored the superior effectiveness of treatment in Group I (P = 0.001) and the higher recurrence rate in Group II after treatment cessation (P = 0.02).

DISCUSSION

Adenoidectomy is widely used for treating adenoid hypertrophy, but adenoid tissue can regrow after infections or chronic allergic reactions, and the surgery carries risks such as hemorrhage, infections, and palate dysfunction, in addition to general anesthesia risks. These complications and the recurrence of adenoid tissue have led to a preference for more conservative treatments using anti-inflammatory and anti-allergy medications.[14]

Fluticasone furoate is a new, potent intranasal corticosteroid with high receptor affinity and low systemic exposure. Intranasal administration allows for high drug concentrations with rapid onset of action directly in the target organ, minimizing systemic effects. Fluticasone furoate's high receptor affinity and low equilibrium dissociation constant make it more effective than other corticosteroids like mometasone furoate, fluticasone propionate, beclomethasone, ciclesonide, and budesonide.[15]

Cysteinyl-leukotriene receptor-1, which mediates the inflammatory pathway, is overexpressed in adenotonsillar tissues of children with adenoid hypertrophy. Thus, anti-inflammatory agents with a safe therapeutic profile may provide an alternative to adenotonsillectomy.[16]

CONCLUSION

Our comparative study suggests that combining oral montelukast and levocetirizine with intranasal fluticasone furoate offers benefits over using intranasal fluticasone furoate alone in treating adenoid hypertrophy. Combined therapy resulted in better subjective and objective improvements after 3 months of treatment and lower recurrence rates 3

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months after stopping treatment compared to single therapy with intranasal fluticasone furoate alone.

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