

## Role Of Montelukast In The Management Of Chronic Rhinosinusitis With Nasal Polyps

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### Abstract:

**Background:** Chronic rhinosinusitis with nasal polyps is a common medical problem; however, the management of nasal polyps has been a challenge for a long time. This study aims to evaluate the effect of adding montelukast to steroids in the management of nasal polyps.

**Patients and methods:** This study was a randomized controlled trial conducted at Otolaryngology department, Assiut University from January 2022 to January 2024. The study involved 60 patients who were diagnosed to have CRSwNP and divided into two groups. The first group (treatment group) received montelukast for three months in addition to oral steroids and INCS. The control group received oral steroids and INCS only.

**Results;** The study found that the treatment group showed significant improvement in many symptoms as nasal discharge, facial pain and sneezing over the control group. The treatment group showed more improvement in endoscopic evaluation of nasal polyps size, radiological changes assessment and quality of life score than the control group but the difference between the two groups was statistically insignificant.

**Conclusions:** The results of this study showed that montelukast has a positive role as an add-on therapy for patients with CRSwNP.

**Keywords:** Montelukast, Chronic rhinosinusitis, Nasal polyps

### Introduction

Nasal polyps (NP) represent benign swellings of the mucosal lining of the nose and paranasal sinuses. They are mostly associated with chronic rhinosinusitis with the term known as chronic rhinosinusitis with nasal polyps (CRSwNP).<sup>1</sup> Prevalence rates in the general adult population are likely to be between 2% and 4%.<sup>2-3</sup>

The aetiology of nasal polyps is not fully understood. They seem to be allergic in origin or arise due to chronic mucosal inflammation.<sup>1</sup> Polyp tissue is a mixture of loose connective tissue, edema, inflammatory cells, glandular cells, and capillaries. Most polyps are

ethmoidal; arising from the ethmoid sinus and extending into the nasal cavity.<sup>2</sup> Nasal obstruction, facial pain, nasal discharge (anterior/posterior or both) and hyposmia are the main symptoms of patients with nasal polyps.

Diagnosis of CRSwNP is based on symptoms and endoscopic findings, as well as sinus imaging (computed tomography [CT] scanning).<sup>4</sup>

Many current recent guidelines recommend long-term medical treatment with intranasal corticosteroid (INCS) sprays, with short courses of oral systemic corticosteroids as a first line treatment.<sup>5-6</sup> In case of failure of the

medical treatment after the initial 3 months follow-up, most clinicians suggest surgery for removal of polyps. However, the polyps' recurrence rate after endoscopic sinus surgery (ESS) in CRSwNP patients is still high.<sup>7</sup>

Studies have shown increased levels of leukotrienes (LTs) and their receptors in the tissue of nasal polyps. Leukotrienes are produced through arachidonic acid metabolism in inflammatory cells (eosinophils and mast cells). They bind to G-protein coupled receptors to initiate localized inflammation, including eosinophil infiltration, mucous secretion, collagen deposition, and release of cytokines. This action is prevented by blocking the receptor with an LT receptor antagonist, such as montelukast.<sup>8</sup>

Leukotriene's antagonists (LTAs) have shown efficacy in chronic inflammatory conditions such as allergic rhinitis, asthma, and aspirin-exacerbated respiratory disease (AERD), all diseases that often coexist with CRSwNP.<sup>9-12</sup> Some authors discussed the efficacy of montelukast in treating nasal polyps but the evidence of this topic is low and more studies are needed.<sup>13</sup>

The aim of this study is to evaluate the role of adding montelukast to oral steroids and INCS in the management of patients with CRSwNP and its effects on patient symptoms, nasal polyps' size, radiological changes and quality of life.

### **Patients and Methods**

This study was a prospective randomized controlled trial conducted at outpatient clinic of the otorhinolaryngology department, Faculty of Medicine, Assiut University Hospital, Egypt, from January 2022 to January 2024 after obtaining approval from the institutional ethics committee.

The study included 60 patients who were diagnosed after clinical and

radiological assessment to have CRSwNP.

#### **Inclusion criteria:**

- 1- Consecutive adult patients ( $\geq$ aged 18 years).
- 2- Bilateral nasal polyps confirmed by endoscopic examination and radiological evaluation.

#### **Exclusion criteria:**

- 1-Patients with CRS but without nasal polyposis.
- 2-Cases of unilateral nasal polyp.
- 3-Patients with history of previous surgical treatment.
- 4-Patient with bronchial asthma.
- 5- Pregnant patients.

After fulfilling the inclusion criteria, 60 patients were included and subjected to:

#### **A. History taking with attention to:**

1. Personal data.
2. History of nasal symptoms and the duration of each symptom. All participants scored the main five sinonasal symptoms (nasal obstruction, anterior rhinorrhea, posterior rhinorrhea, loss of smell, and facial pain) from zero to four.
  - 0=Symptom-free/no symptom
  - 1= Mild symptom.
  - 2= Moderate symptom.
  - 3= Severe symptom.
  - 4= Very severe symptom.
 The total five-symptom score (T5SS) is then calculated by the sum of the score of the individual symptoms (0–20).
3. Other ENT symptoms.
4. General symptoms e.g., any allergic symptoms.
5. Medical history (including any systemic disease).
6. Current and previous medications.
7. History of previous nasal surgery.

**B. Examination:**

1. General examination.
2. Full ENT examination with special attention to: Nasal examination including nasal endoscopy with 4 mm 0`Karl Storz (Germany) nasal endoscope emphasis on;
  - Nasal masses and polyps.
  - Hypertrophy of the inferior or middle turbinates
  - Evidence of previous surgery.

**C. Investigations:**

CT of the nose and PNS axial, coronal and sagittal cuts without contrast, both bone and soft tissue windows, 2mm thickness.

**D. Management:**

Patients were divided into two groups of treatment (30 patients in each group) in a randomized manner. The study group received systemic steroids for 2 weeks (prednisolone 60 mg/day for five days then 40 mg/day for five days then 20 mg/day for five days) and fluticasone furoate nasal spray 100 micrograms (2 sprays) in each nostril twice daily plus oral montelukast (montelukast 10 mg, once a day) for three months. Subjects in control group received systemic and topical steroids in the same regimen without montelukast.

**E. Follow-up and reassessment:**

Follow-up of the patients was done every month for three months.

**Outcome Measures:****a. Primary (main):**

**Nasal polyp size score:** At every follow-up visit, each CRSwNP patient underwent nasal endoscopy using a 4 mm 0`Karl Storz nasal endoscope to score the polyp size (score from 0–3) in both nasal cavities using a Lildholdt scoring system (Table 1).<sup>14</sup>

Table 1: Lildholdt scoring system of endoscopic appearance of the nasal polyps.

Score	Endoscopic Appearance
0	No polyposis.
1	Mild (small polyps not reaching the upper edge of the inferior turbinate).
2	Moderate (medium polyps between the upper and lower edges of the inferior turbinate).
3	Severe (large polyps reaching the lower edge of the inferior turbinate).

Nasal polyps were also assessed radiologically by MSCT nose and PNS before and three months after the treatment. Modified Lund-Mackay (LMK) scoring system was used for staging the radiological findings. Modified Lund-Mackay (LMK) scoring system depends on that each sinus (maxillary, anterior ethmoidal, posterior ethmoidal, frontal, sphenoidal) is scored for opacification from 0-5:

- 0= no opacity
- 1= opacity < 25%
- 2= opacity (26-50%)
- 3= opacity (51-75%)
- 4= opacity (76-99%)
- 5= opacity (100%)

The ostiomeatal complex is scored 0 (no obstruction) or 2 (obstruction). Each side is graded separately, resulting in a maximum total score of 54.<sup>15</sup>

**B. Secondary:****1- Nasal symptoms:**

The total five-symptom score (T5SS) was used to evaluate the severity of patients' symptoms. This score was assessed before and three months after the treatment.

**2- Quality of life:**

Subjects completed the ICSD (International Classification of Sinus Disease)<sup>[16]</sup> questionnaire to assess the quality of life before and after treatment. The ICSD scores patients'

symptoms of facial pain and pressure; headache; nasal blockage or congestion; nasal discharge; disturbance of smell and over all discomfort from 0 to 10.<sup>16</sup>

### **Statistical analysis:**

Data were collected and analyzed by using SPSS (Statistical Package for the Social Science, version 20, IBM, and Armonk, New York). Shapiro test was done to assess normality of data. Quantitative data are expressed as mean  $\pm$  standard deviation (SD), range and compared with Student t test. Nominal data are implemented as frequency (percentage) and compared by Chi2 test. In each separate groups; paired t test was used to compare between baseline and follow up assessment of different scores. Level of confidence was kept at 95% and hence, P value was considered significant if  $< 0.05$ .

### **Results**

#### **Baseline data of the studied groups:**

Mean age of the study group was  $43.43 \pm 13.16$  (years) with mean duration of symptoms was  $1.45 \pm 1.25$  (years). Majority of this group was males (63.3%) and came from rural areas (60%). Also, mean age of the control group was  $40.48 \pm 13.68$  (years) with mean duration of symptoms was  $1.68 \pm 1.06$  (years). Also, majority of this group was males (55.2%) and came from rural areas (56.7%).

A total of 7 (23.3%) and 8 (27.6%) patients of the study and control groups were hypertensive, respectively. Eleven (36.7%) patients of the study group and 8 (27.6%) patients of the control group were smokers. Both groups had insignificant differences as regard baseline data ( $p > 0.05$ ).

#### **Baseline symptoms among the studied groups:**

Both groups (study group and control group) had insignificant differences as regard different parameters of all symptoms ( $p > 0.05$ ). Also, mean T5SS at baseline was comparable in both groups ( $12.17 \pm 2.82$  vs.  $13.21 \pm 2.87$ ;  $p = 0.17$ ).

#### **Baseline Lildholdt scoring system, Modified Lund-Mackay score and ICSD score among the studied groups:**

At baseline, both groups had insignificant differences as regard nasal polyp size by Lildholdt scoring system ( $5.10 \pm 0.80$  vs.  $5.07 \pm 0.79$ ;  $p = 0.88$ ), radiological findings by Modified Lund-Mackay score ( $44.37 \pm 8.69$  vs.  $46.52 \pm 6.42$ ;  $p = 0.28$ ) and quality of life assessment by ICSD score ( $43.43 \pm 8.95$  vs.  $45.72 \pm 7.89$ ;  $p = 0.30$ ).

#### **Baseline and follow up evaluation in each separate group:**

After three months of treatment; both groups showed significant improvement in different scores of assessments in comparison to baseline data before the intervention ( $p > 0.05$ ).

#### **Follow up symptoms among the studied groups:**

During follow up; the study group had significantly lower anterior nasal discharge ( $1 \pm 0.69$  vs.  $2.17 \pm 0.93$ ;  $p < 0.001$ ), posterior nasal discharge ( $0.17 \pm 0.11$  vs.  $0.97 \pm 0.23$ ;  $p < 0.001$ ) and facial pain ( $1.20 \pm 0.88$  vs.  $2.4 \pm 1.22$ ;  $p < 0.001$ ) in comparison to the control group.

Also, the study group had significantly lower T5SS ( $6.40 \pm 1.88$  vs.  $10.24 \pm 2.89$ ;  $p < 0.001$ ) and sneezing ( $0.30 \pm 0.13$  vs.  $0.63 \pm 0.65$ ;  $p = 0.03$ ). Other parameters as nasal obstruction and loss of smell were insignificantly lower in the study group.

**Follow up Lildholdt scoring system, Modified Lund-Mackay score and ICSD score among the studied groups:**

During follow up; the study group had insignificantly lower Lildholdt scoring system ( $4.11 \pm 0.81$  vs.  $4.38 \pm 0.94$ ;  $p = 0.32$ ), Modified Lund-Mackay score ( $39.67 \pm 9.33$  vs.  $41.34 \pm 7.86$ ;  $p = 0.09$ ) and quality of life ( $37.03 \pm 8.33$  vs.  $38.93 \pm 8.57$ ;  $p = 0.11$ ) in comparison to the control group.

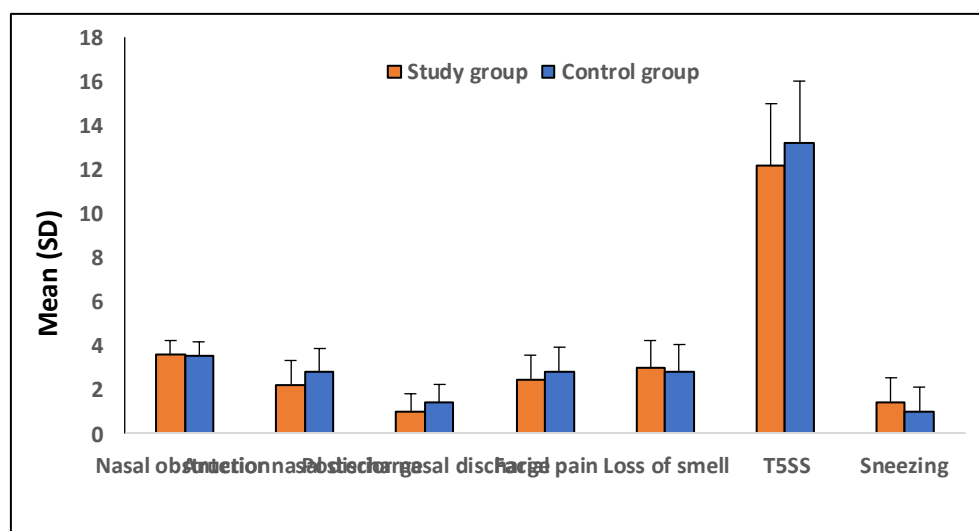
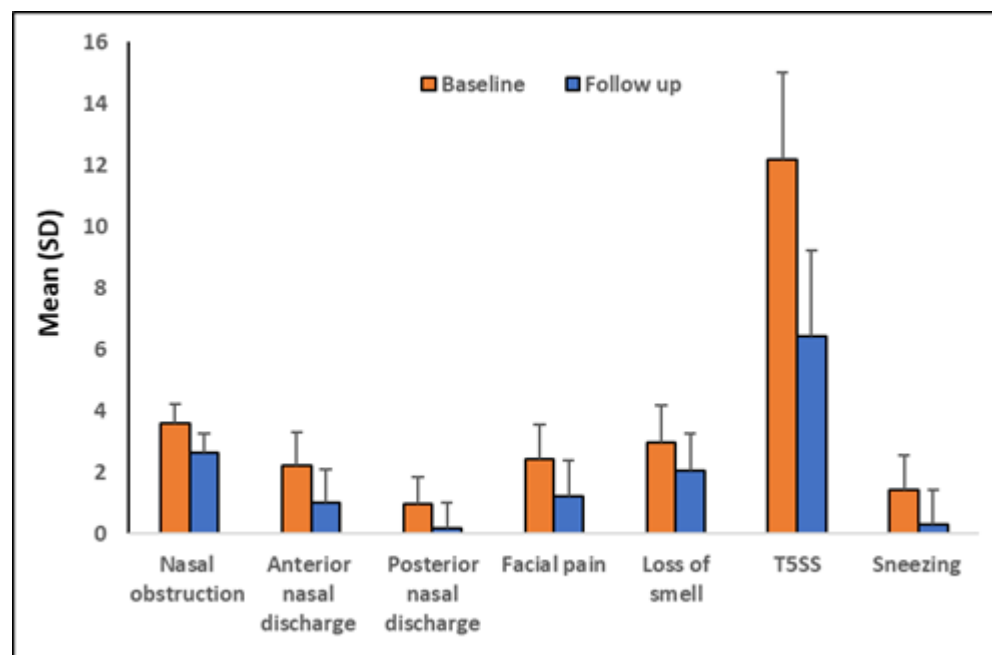
**Compliance and Tolerance**

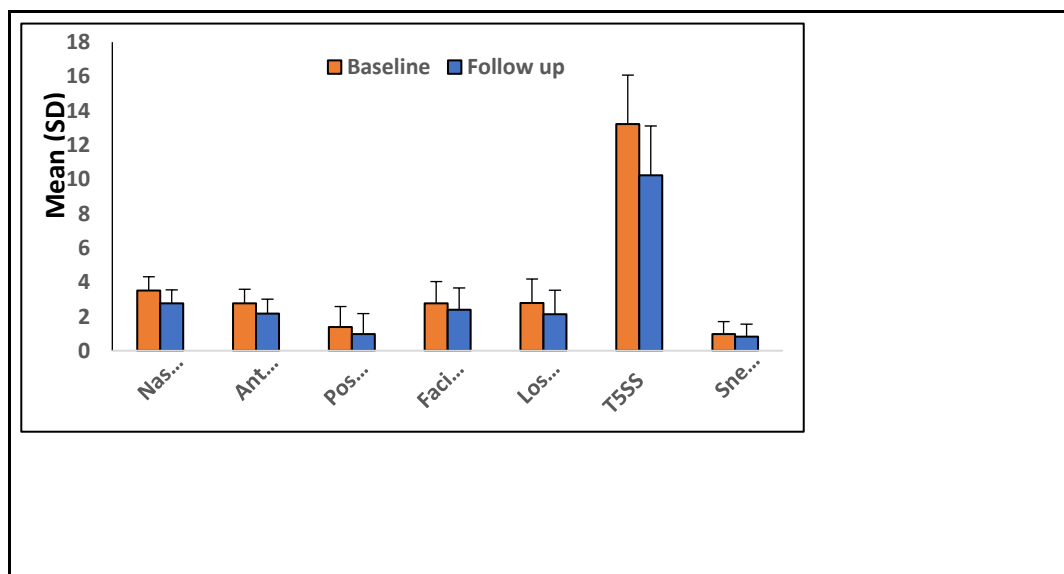
During the whole duration of the study (three months) all patients showed good compliance and tolerance. No major side effects detected in study populations. Two patients in the study group (6.6%) documented mild abdominal discomfort and only one patient of the control group (3.3%) documented nausea and abdominal discomfort.

**Table 2: Baseline data of the studied groups**

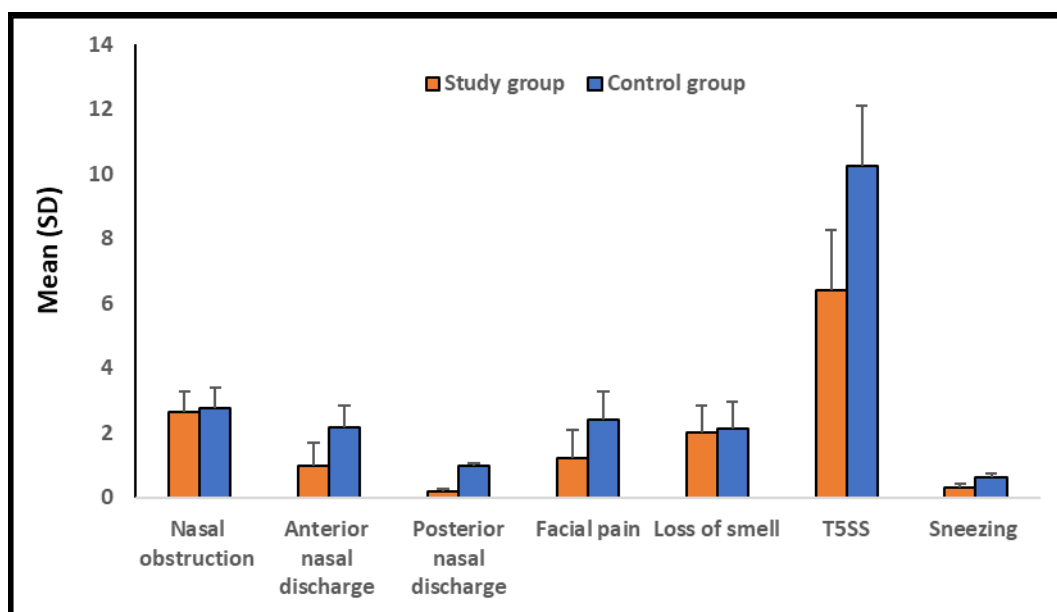
	Study group (n= 30)	Control group (n= 30)	<i>P</i> value
Age (years)	43.43 ± 13.16	40.48 ± 13.68	0.41
Sex			0.12
Male	19 (63.3%)	16 (55.2%)	
Female	11 (36.7%)	13 (44.85%)	
Residence			0.56
Rural	18 (60%)	17 (56.7%)	
Urban	12 (40%)	13 (43.3%)	
Hypertension	7 (23.3%)	8 (27.6%)	0.46
Smoking	11 (36.7%)	8 (27.6%)	0.32
Duration of symptoms (years)	1.45 ± 1.25	1.68 ± 1.06	0.46

Data expressed as frequency (percentage), mean (SD). *P* value was significant if < 0.05

**Figure 1: Baseline symptoms among the studied groups****Figure 2: Baseline and follow up symptoms in the study group**



**Figure 3:** Baseline and follow up symptoms in the control group.



**Figure 4:** Follow up symptoms among the studied groups.

## **Discussion:**

Chronic rhinosinusitis with nasal polyps is one of the most common rhinological problems; however, the mechanisms that underlie polyp formation and the reason for their recurrence are still not clear. Also, the management of nasal polyps has been a challenge for a long time.<sup>7</sup>

In recent years, large number of studies discussed the leukotrienes and their role in the pathogenesis of many diseases as asthma, allergic rhinitis and nasal polyps. Many researches focused on montelukast as a potent leukotrienes antagonist and proved its efficacy in the treatment of asthma and allergic rhinitis.<sup>17-19</sup> But the efficacy of montelukast in nasal polyps is still not well fulfilled.

This study tested the effect of adding montelukast to oral and nasal steroids for patients with CRSwNP. The study involved 60 patients divided into two groups: the first group received montelukast in addition to oral and nasal steroids while the second group received oral and nasal steroids only.

After three months of treatment, both groups showed significant improvement in comparison to baseline data on symptoms, endoscopic score, radiological score and quality of life assessment.

The study group showed significantly lower anterior nasal discharge ( $p < 0.001$ ), posterior nasal discharge ( $p < 0.001$ ), facial pain ( $p < 0.001$ ) and sneezing ( $p = 0.03$ ) in comparison to the control group. This was in line with Rosemary et al.[20] who conducted a similar study and found that the group who received montelukast had significantly lower facial pain ( $P = 0.048$ ), and sneezing ( $P = 0.03$ ) but no significant difference was recorded in nasal discharge ( $P = 0.10$ ). Mostafa et al.[21] reported that patients who used montelukast showed more improvement in post-nasal discharge and headache than patients who used nasal steroids.

According to the baseline data of this study, nasal obstruction was the most common symptom (100%) with the highest score of severity ( $3.57 \pm 0.63$  in the study group and  $3.52 \pm 0.79$  in the control group). After treatment, nasal obstruction and loss of smell were insignificantly lower in the study group. Rosemary et al.[20] detected no significant differences between the two groups in nasal blockage ( $P = 0.31$ ) and alteration in smell ( $P = 0.89$ ).

Also, Vento et al.<sup>22</sup> in an open pilot study documented no significant improvement in sense of smell, nasal itching or nasal blockage for patients who used montelukast. Vuralkan et al.<sup>23</sup> reported a significant difference ( $p <$

$0.05$ ) of montelukast over INCS in improvement of smell.

The results of this study showed that T5SS was significantly lower in the study group ( $6.40 \pm 1.88$  vs.  $10.24 \pm 2.89$ ;  $p < 0.001$ ) but the quality-of-life score (ICSD) was insignificantly lower ( $37.03 \pm 8.33$  vs.  $38.93 \pm 8.57$ ;  $p = 0.11$ ). Kieff et al.<sup>24</sup> detected a significant improvement in symptom score in patients with CRSwNP after montelukast therapy.

Schäper et al.<sup>25</sup> showed significant improvement in symptoms with patients who received montelukast over placebo. Zahide et al.<sup>26</sup> discovered that adding montelukast to steroids for patients with nasal polyps and asthma improved the quality of life.

On the other hand, Gerven et al.<sup>27</sup> recommended not to use montelukast as they found no significant differences between patients who used INCS and patients who used INCS plus montelukast regarding symptoms and radiological evaluation.

For objective evaluation, this study used Lildholdt scoring system and Modified Lund-Mackay score. The results found that the study group had an insignificantly lower Lildholdt scoring system ( $p = 0.32$ ) and Modified Lund-Mackay score ( $p = 0.09$ ) than the control group. Also, Gerven et al.<sup>27</sup> found no difference in nasal polyp score and radiological score between patients who used INCS plus montelukast and patients who used INCS alone.

Nonaka et al.<sup>28</sup> found that patients with CRSwNP and asthma treated with a combination of intranasal corticosteroid and montelukast showed significant reduction in nasal polyps size after both 6 months ( $p < 0.01$ ) and 12 months of treatment ( $p < 0.01$ ). CT score was significantly improved after 1 year of treatment.

Rasp et al.<sup>29</sup> conducted a systematic review in 2010 involved nine studies



and gave class IB recommendation for the use of montelukast in the prevention of nasal polyp recurrence.

Another systematic review was done by **Jennifer et al.**<sup>30</sup> in 2013 evaluated leukotriene antagonists in nasal polyps. It involved 12 studies and found that leukotriene antagonists showed significant improvement in symptoms in comparison to placebo. But no significant difference was found when comparing leukotriene antagonists with INCS.

### **Conclusion:**

The results of this study showed that adding montelukast to steroids therapy has a positive role for patients with CRSwNP.

### **Recommendations:**

More studies with longer duration of treatment and longer duration of follow-up are recommended to exactly confirm the role of montelukast in nasal polyps.

**Funding support:** Our study did not receive any funding support.

**Conflicts of interest:** No

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