Omalizumab is effective in nasal polyposis with or without asthma, a real-life study

Tuğba Songül Tat, MDa,b

ABSTRACT

Background: Chronic rhinosinusitis with nasal polyposis (CRSwNP) can be recalcitrant in some patients despite medical therapies and surgery and has higher morbidity. Omalizumab is a new treatment option for patients with CRSwNP. The aim of this study is to evaluate the efficacy and safety of omalizumab (anti-IgE antibody) in patients with CRSwNP.

Methods: The efficiency and adverse effects of omalizumab were evaluated based on the data extracted from medical records of patients with CRSwNP. Patients were evaluated monthly for efficacy and adverse reactions. Treatment efficacy was evaluated by visual analog scale (VAS) for rhinorrhea, postnasal drip, sneeze, smell, and nasal stuffiness complaints, sinonasal outcome test-22 (SNOT-22), and nose obstruction symptom evaluation (NOSE) score.

Results: 17 patients with CRSwNP formed our cohort. The mean (SD) age, weight, and total IgE level were 41.9 (9.4) years, 78.6 (15) kg, and 198.8 (169.2) IU/mL, respectively. 3 patients had mild, 6 had moderate and 1 had severe asthma as comorbidity. The mean (SD) duration of omalizumab treatment and polypectomy numbers were 9.2 (13.3) months and 2.9 (1.5), respectively. All patients had at least one polyp surgery. All sinonasal outcome parameters were significantly improved by the omalizumab treatment, also in subgroups with and without asthma. The median changes from baseline at the last visit date for omalizumab treatment were as follows: SNOT-22 score decreased from 98 to 19, NOSE score decreased from 100 to 20, the VAS for postnasal drip, rhinorrhea, nasal stuffiness, smell and sneeze decreased from 8 to 2, 8 to 2, 10 to 3, 10 to 2, 6 to 1, respectively (P < 0.001). Patients experienced no adverse reaction with omalizumab treatment.

Conclusion: Omalizumab was an effective treatment in patients with recalcitrant CRSwNP with or without asthma.

Keywords: Chronic rhinosinusitis with nasal polyposis, Nasal polyps, Asthma, Omalizumab, Biologic agents in nasal polyps, Real-life study

INTRODUCTION

Nasal polyps are a subgroup of chronic rhinosinusitis (CRS) and benign inflammatory masses, developing from the mucosa of the nose and paranasal sinuses mainly in the osteomeatal complex. It is characterized by 2 or more symptoms, 1 of which should be either nasal blockage/
obstruction/congestion or nasal discharge (anterior/posterior nasal drip), with or without facial pain or pressure, and with or without reduction or loss of smell for ≥12 weeks. For diagnosis, endoscopic signs of nasal polyps or evidence of nasal polyps on computed tomography (CT) are needed so diagnostic confirmation is necessary with nasal endoscopy or CT.  

Nasal blockage/congestion, altered taste/smell, and the need to blow the nose are the major symptoms of nasal polyps.  

The prevalence of chronic rhinosinusitis with nasal polyposis (CRSwNP) is 1–2.6% and is higher in men and asthma, allergy, and allergic rhinitis were the most common comorbidities. Promsop et al found that 48.3% of patients with CRSwNP had asthma confirmed by pulmonary function testing. Fokkens et al reported that nasal polyposis decreased quality of life. When CRS was compared with diseases such as angina pectoris, congestive heart failure, chronic back pain, and chronic obstructive pulmonary disease as symptom severity, CRS had a higher impact on quality of life, according to Gicklich and Metson.  

Intranasal glucocorticoids and saline irrigation are recommended as treatments for patients with mild symptoms, and short-term use of systemic glucocorticoids and antibiotics may improve symptoms in patients with severe symptoms. Endoscopic sinus surgery to remove polyps can be performed in patients whose symptoms are not controlled with medical treatment, but rates of relapse and repeated interventions are higher.  

Effective treatment of nasal polyps becomes even more important because of its impact on quality of life. If it is resistant to standard medical treatment, surgery is performed, but recurrence is frequent so that additional treatments are needed in those patients. Most of them are idiopathic but the majority of patients with CRSwNP have a type 2 inflammation pattern in pathogenesis. There are many studies in the literature showing that biologic agents given to patients with type 2 phenotype asthma based on the pathogenesis of inflammation are also effective in the treatment of nasal polyps.  

Efficacy of omalizumab, an anti-Ig E antibody, which is a treatment option in severe allergic asthma, was shown in nasal polyps in randomized, clinical, phase 3 trials but data on real-life efficacy are limited, especially in CRSwNP patients without asthma. So, in this study, we aimed to report our real-life experience with omalizumab in CRSwNP patients with or without omalizumab.

**METHOD**

**Patients and study design**

A total of 70 adult patients (>18 years) who were treated with omalizumab for respiratory tract disease were evaluated retrospectively. Eighteen of them had CRSwNP and 17 of them were treated with omalizumab for more than 16 weeks. All patients with CRSwNP were evaluated by the ear, nose, and throat (ENT) department, and the diagnosis of CRSwNP was based on clinical criteria with nasal endoscopy or CT, as recommended by the European position paper on rhinosinusitis and nasal polyp. Ten patients with CRSwNP had asthma and their asthma diagnoses and therapies were appropriate according to the recent Global Initiative for Asthma (GINA) guideline, 9 patients of them were given omalizumab to treat their CRSwNP, primarily. Only 1 patient received omalizumab prescription primarily for severe asthma. Omalizumab was prescribed to patients with CRSwNP who had at least 1 surgery for polyps before, but had still severe symptoms although appropriate medical treatments according to the guideline. Dosages for omalizumab therapy were every 2 or 4 wks based on patients’ baseline total IgE level and weight according to the dosage guide for omalizumab. Although one patient’s total Ig E level was 18 IU/mL, omalizumab was given as 300 mg/4 weeks. Omalizumab was administered by subcutaneous injection as recommended.

All patients were observed for adverse effects and they were also told of the possibility of delayed reactions and had the ability to recognize the signs and symptoms of anaphylaxis. Patients were evaluated monthly for adverse reactions and efficacy of omalizumab. For asthma, treatment efficacy was evaluated by the level of asthma symptom control as well controlled, partly controlled, and uncontrolled based on the assessment of asthma control of the GINA guideline. And also asthma severity was assessed into 3
groups as mild, moderate, and severe asthma according to GINA.\textsuperscript{11}

For CRSwNP, omalizumab efficacy was evaluated by validated questionnaires, scales, and scores. Symptoms and their impact on quality of life were evaluated by using the sino-nasal outcome test-22 (SNOT-22) questionnaire, visual analog scale (VAS), and nasal obstruction symptom evaluation (NOSE) score. The Turkish validated forms of SNOT-22 and NOSE scores were used.\textsuperscript{12,13} Patients were asked to fill the questionnaires of SNOT-22, NOSE score, and the VAS scales which were related to the severity of their symptoms before omalizumab therapy commenced and 16 weeks after starting omalizumab therapy and at the date of last visits. If the response was good at the sixteenth week of treatment, omalizumab treatment was continued.

For the VAS score, the patients were asked to indicate the point on the scale (0–10) that best corresponds to their status for severity of general nasal symptoms, nasal obstruction, rhinorrhea, postnasal drip, sneeze, and smell. These symptoms were evaluated separately.

The NOSE score consists of 5 items related to nasal obstruction, which can easily determine the severity of the patient’s complaints over the last month. In this scale, firstly, points are given between 0 and 4, and the points are added together then multiplied by the coefficient of 5. The total score was between 0 and 100 and higher scores indicate higher nasal airway obstruction.\textsuperscript{13}

Symptoms and their impact on quality of life were evaluated by the SNOT-22 test, which also measures symptoms that are not specific for CRSwNP, such as sneezing and otologic symptoms. In this test, scores from 0 to 5 were assigned for each item. The total score ranges from 0 to 110 and a higher score is associated with worse results.\textsuperscript{12}

Patients’ age, gender, total IgE value, weights, omalizumab dosage, treatment duration, nasal polypectomy number, their comorbidities, and other medications were noted from their medical records.

Before starting this study, permission from the director of the hospital and ethics committee approval from the ethics committee of Mustafa Kemal University were received.

**Statistical analysis**

Descriptive statistics are presented as numbers and percentages for categorical variables, and mean ± standard deviation, median (min-max) for continuous variables. Normal distribution for continuous variables was assessed with visual (histograms and probability graphics) and analytic methods (Kolmogorov-Smirnov test). All the data did not fit the normal distribution. Wilcoxon Signed Rank test was used to compare the parameters before and after omalizumab treatment. P < 0.05 was considered statistically significant.

**RESULTS**

Baseline demographic and clinical characteristics of the patients with CRSwNP are given in Table 1. There were 18 patients with CRSwNP in whom we started omalizumab therapy in our outpatient clinic. 17 patients with omalizumab therapy over 16 weeks were included in the study. The mean (SD) age of these patients was 41.9 (9.4) years (range, 26–67 years), and most patients were women (n: 9 [52.9%]). The mean (SD) total IgE levels, weights and polypectomy numbers were 198.8 (169.2) IU/mL, 78.6, (15) and 2.9 (1.5), respectively. The polypectomy numbers were 1 in 3 (17.6%) patients, 2 in 5 (29.4%) patients, 3 in 4 (23.5%) patients, 4 in 1 (5.9%) patient, 5 in 4 (23.5%) patients, respectively. Three (17.6%) patients with CRSwNP had mild, 6 (35.3%) had moderate, and only 1 (5.9%) patient had severe asthma. Seven (41.2%) patients had CRSwNP without asthma. Six (35.3%) had non-steroidal anti-inflammatory sensitivity. Only 4 (23.5%) patients had inhalant allergen sensitivity; 1 (5.9%) had grass pollen; 3 (17.6%) had dust-mite sensitivity. The mean (SD) duration of omalizumab therapy was 9.2 (13.3) months (range, 4–60 months). Omalizumab dosage was 150 mg/mo in 2 patients, 300 mg/mo in 6 patients, 450 mg/mo in 6 patients, 375 mg every 15 days in 1 patient, 450 mg every 15 days in 1 patient, and 600 mg every 15 days in 1 patient.

After treatment with omalizumab, the SNOT-22 score significantly improved from 96.9 ± 6.4 (median: 98, range: 79–105) to 23 ± 21.6 (median: 19,
When compared to the baseline measurement of 94.1 ± 9.9 (median: 100, range: 75–100), the NOSE score significantly decreased to 22.4 ± 2.2 (median: 20, range: 0–75), P < 0.001. After the treatment, the general VAS score improved from 9.8 ± 0.6 (median: 10, range: 8–10) to 2.4 ± 2.3 (median: 2, range: 0–7) (P < 0.001). And VAS scores of postnasal drip, rhinorrhea, nasal stuffiness, smell and sneeze were improved from 8.1 ± 0.8 (median: 8, range: 7–10) to 2 ± 1.9 (median: 2, range: 0–6), P < 0.001, 8 ± 1 (median: 8, range: 6–10) to 2.1 ± 1.9 (median: 2, range: 0–6), P < 0.001, 9.6 ± 0.7 (median: 10, range: 8–10) to 2.5 ± 2.4 (median: 3, range: 0–8), P < 0.001, respectively. These findings are shown in Table 2.

One patient discontinued the omalizumab treatment due to its ineffectiveness and 1 discontinued because of the higher cost. Two patients had used mepolizumab therapy for 1 year before omalizumab therapy was started for their nasal polyps. Their mepolizumab treatments were changed to omalizumab because of ineffectiveness of mepolizumab. They had good results after omalizumab.

There was no significant difference in the efficacy of omalizumab treatment between the asthmatic and non-asthmatic groups. It is shown in Table 3.

Any adverse event was not reported during omalizumab treatment.

### DISCUSSION

This study showed that omalizumab is an effective and safe therapy for CRSwNP patients with or without allergic asthma. In the literature the effectiveness of omalizumab in CRSwNP patients with severe allergic asthma was shown in some studies but only in a few studies patients had only CRSwNP without asthma. The effectiveness of omalizumab in CRSwNP patients may be variable according to environmental and genetic factors. To our knowledge, this is the first study from Turkey. In our patients, only 1 patient had severe asthma. Our primary aim was to treat the CRSwNP in other 16 patients. And in POLYP 1 and POLYP 2 studies, the effectiveness and safety of omalizumab in nasal polyps without asthma were shown and these studies were randomized placebo-controlled trials, but our study is a real life study. So that, we think, will contribute to the literature with this study.

The effectiveness of omalizumab in CRSwNP patients was evaluated by SNOT-22 questionnaire, VAS scale, and NOSE scores. All these tests do not have any costs or harm to patients and the health system. We did not use paranasal CT for evaluation of the omalizumab effectiveness because of the higher cost and side effects such as radiation. In
addition, ear, nose, and throat extra evaluations were not needed by a specialist after the omalizumab treatment, because in this study we firstly aimed at clinical effectiveness, not physical examination. But before the omalizumab therapy started, all patients were evaluated by ear, nose, and throat specialists.

One patient had no benefit from omalizumab therapy and consulted with the ear, nose, and throat specialist, and polypectomy was applied. This patient’s dosage of omalizumab is 150 mg/4 weeks according to the patient’s weight and total IgE level. Would the benefit be greater if the dose of omalizumab was higher? Now we do not know this answer, actually. New studies are necessary for this answer.

The first reports of omalizumab on nasal polyps came from a few small studies in which patients received omalizumab for their asthma and also had nasal polyp as comorbid. These patients had a significant benefit from omalizumab for their nasal polyps. In a randomized, double-blind, placebo-controlled trial (n = 24) that investigated the efficacy of omalizumab in patients with nasal polyps and comorbid asthma over 16 weeks, a significant decrease was observed in total nasal endoscopic polyp scores after 16 weeks in the omalizumab-treated group (Δ/C0 2.67, P = 0.001), which was confirmed by computed tomographic scanning (Lund-Mackay score). And also beneficial effects of omalizumab on nasal congestion, anterior rhinorrhea, loss of smell, wheezing, dyspnea, and quality-of-life scores were shown. In a real-life study, omalizumab efficacy was shown in 24 patients with severe allergic asthma and CRSNP. In this study, omalizumab improved the sino-nasal clinical outcomes, and the sinus computed tomographic images without an important effect on the nasal endoscopy polyps score.

The omalizumab’s double-blind, placebo-controlled phase III trials for CRSwNP are POLYP 1

| Parameters | Pretreatment | Posttreatment | P value |
|------------|-------------|--------------|---------|
| SNOT-22    |             |              |         |
| Median (range) | 98 (79-105) | 19 (0-70) | <0.001a |
| Mean (SD)  | 96.9 (6.4)  | 23 (21.6)   |         |
| VAS scale (SD) |      |              |         |
| Postnasal drip | 8 (7-10)    | 2 (0-6)     | <0.001a |
| Mean (SD)  | 8.1 (0.8)   | 2 (1.9)     |         |
| Rhinorrhea |             |              |         |
| Median (range) | 8 (6-10)    | 2 (0-6)     | <0.001a |
| Mean (SD)  | 8 (1)       | 2.1 (1.9)   |         |
| Nasal stuffiness |       |              |         |
| Median (range) | 10 (8-10)   | 3 (0-8)     | <0.001a |
| Mean (SD)  | 9.6 (0.7)   | 2.5 (2.4)   |         |
| Smell      |             |              |         |
| Median (range) | 10 (6-10)   | 2 (0-7)     | <0.001a |
| Mean (SD)  | 9.4 (1.1)   | 2.3 (2.1)   |         |
| Sneeze     |             |              |         |
| Median (range) | 6 (3-10)    | 1 (0-3)     | <0.001a |
| Mean (SD)  | 6.1 (1.7)   | 1.2 (1.2)   |         |
| General    |             |              |         |
| Median (range) | 10 (8-10)   | 2 (0-7)     | <0.001a |
| Mean (SD)  | 9.8 (0.6)   | 2.4 (2.3)   |         |
| NOSE score |             |              |         |
| Median (range) | 100 (75-100)| 20 (0-75)   | <0.001a |
| Mean (SD)  | 94.1 (9.9)  | 22.4 (22.5) |         |

Table 2. Clinical characteristics of the patients with CRSwNP before and after the omalizumab treatment. Abbreviations: SNOT-22, sinonasal outcome test-22; VAS, visual analog scale; NOSE, nose obstruction symptom evaluation score. *Wilcoxon Signed Rank Test
and POLYP 2 which are evaluating 265 adults with treatment-resistant nasal polyposis, measuring 2 co-primary endpoints of nasal congestion symptoms and an intranasal polyp score over 24 weeks of treatment. Secondary endpoints of this study were to detect the changes from baseline to week 24 in SNOT-22 score, University of Pennsylvania Smell Identification Test, sense of smell, postnasal drip, runny nose, and adverse events. Across the studies, there were 48.5%-61.3% of patients with comorbid asthma; most had mild (35.1%) or moderate (58.3%). The mean changes from baseline at week 24 for omalizumab versus placebo were as follows in POLYP 1 and POLYP 2 studies: Nasal polyp score (NPS), $-1.08$ versus $-0.06$ ($P < 0.0001$) and $-0.90$ versus $-0.31$ ($P 0.0140$); SNOT-22 score, $-24.7$ versus $-8.6$ ($P < 0.0001$) and $-21.6$ versus $-6.6$ ($P < 0.0001$) and nasal congestion score, $-0.89$ versus $-0.35$ ($P 0.0004$) and $-0.70$ versus $-0.20$ ($P 0.0017$).

In our study, the SNOT-22 score decrease is significantly important and patients had 58.8% asthma, like as Polyp 1 and 2. And we used the nose scale which was more exhaustive instead of

|                                      | Without Asthma (n = 7) | With Asthma (n = 10) |
|--------------------------------------|------------------------|----------------------|
|                                      | Pretreatment           | Posttreatment        | Pretreatment           | Posttreatment |
| Snot-22 score                        |                        |                      |                        |               |
| Median (range)                       | 100 (96-101)           | 3 (1-56)             | 98 (79-105)            | 19.5 (0-70)   |
| Mean (SD)                            | 99.3 (1.9)             | 20 (24.3)            | 95.2 (7.9)             | 25.1 (20.6)   |
| P value                              | 0.018                  | 0.005                |                        |               |
| VAS                                   |                        |                      |                        |               |
| Postnasal drip                       |                        |                      |                        |               |
| Median (range)                       | 8 (8-9)                | 0 (0-4)              | 8 (7-10)               | 2.5 (0-6)     |
| Mean (SD)                            | 8.1 (0.4)              | 1.3 (1.7)            | 8.1 (0.9)              | 2.5 (1.9)     |
| P value                              | 0.017                  |                       | 0.005                  |               |
| Rhinorrhea                           |                        |                      |                        |               |
| Median (range)                       | 8 (6-9)                | 0 (0-4)              | 8 (7-10)               | 2.5 (0-6)     |
| Mean (SD)                            | 7.7 (0.9)              | 1.3 (1.7)            | 8.2 (1.1)              | 2.7 (1.9)     |
| P value                              | 0.017                  |                       | 0.005                  |               |
| Nasal stuffiness                     |                        |                      |                        |               |
| Median (range)                       | 10 (8-10)              | 0 (0-6)              | 10 (8-10)              | 3 (0-8)       |
| Mean (SD)                            | 9.6 (0.8)              | 1.9 (2.5)            | 9.6 (0.7)              | 3 (2.4)       |
| P value                              | 0.017                  |                       | 0.005                  |               |
| Smell                                |                        |                      |                        |               |
| Median (range)                       | 10 (8-10)              | 0 (0-6)              | 10 (6-10)              | 2.5 (0-7)     |
| Mean (SD)                            | 9.7 (0.8)              | 1.9 (2.5)            | 9.2 (1.3)              | 2.6 (2.1)     |
| P value                              | 0.016                  |                       | 0.005                  |               |
| Sneeze                               |                        |                      |                        |               |
| Median (range)                       | 5 (3-6)                | 0 (0-2)              | 6 (4-10)               | 1.5 (0-3)     |
| Mean (SD)                            | 5.1 (1.1)              | 0.6 (0.9)            | 6.7 (1.8)              | 1.6 (1.2)     |
| P value                              | 0.017                  |                       | 0.005                  |               |
| General                              |                        |                      |                        |               |
| Median (range)                       | 10 (10-10)             | 0 (0-6)              | 10 (8-10)              | 2.5 (0-7)     |
| Mean (SD)                            | 10 (0)                 | 2 (2.6)              | 9.6 (0.7)              | 2.7 (2.1)     |
| P value                              | 0.016                  |                       | 0.005                  |               |
| NOSE skoru                           |                        |                      |                        |               |
| Median (range)                       | 100 (100-100)          | 0 (0-50)             | 95 (75-100)            | 20 (0-75)     |
| Mean (SD)                            | 100 (0)                | 18.6 (24)            | 90 (11.3)              | 25 (22.2)     |
| P value                              | 0.018                  |                       | 0.005                  |               |

Table 3. Effects of omalizumab treatment on parameters in asthmatic and non-asthmatic patients with CRSwNP. Abbreviations: SNOT-22, sinonasal outcome test-22; VAS, visual analog scale; NOSE, nose obstruction symptom evaluation score. *Wilcoxon Signed Rank Test
the nasal congestion score, but the results were similar.

Gevaert et al also reported on an open-label extension study evaluating the efficacy, safety, and durability of responses to omalizumab in adults with CRSwNP who had completed the POLYP 1 and POLYP 2 trials. Patients who continued omalizumab experienced more improvements in endpoints through 52 weeks and also patients who switched from placebo to omalizumab experienced better responses across endpoints through week 52 that were similar to POLYP 1 and 2 at week 24. After omalizumab discontinuation, scores gradually worsened over the 24-week follow-up but remained still improved from pretreatment levels for both groups.\(^{18}\) And in both these studies, adverse events were similar between groups.\(^{8,18}\) And also in our study, we did not observe any adverse reactions.

In a multicenter retrospective study, 23 patients with recalcitrant nasal polyposis and mild asthma were detected and in all patients, a significant and sustained reduction in total nasal endoscopic polyp score and lower SNOT-22 scores were observed over time.\(^{19}\) In our study, we evaluated our patients monthly but here we did not determine statistics for each month.

In a recent study, patients in subgroups from POLYP 1 and POLYP 2 were examined and these subgroups were included blood eosinophil count at baseline (>300 or ≤300 cells/µL), previous sinonasal surgery (yes or no), asthma status (yes or no), and aspirin sensitivity status (yes or no). This study showed the extensive efficacy of omalizumab across clinical and patient-reported outcomes in patients with CRSwNP, independent of patient factors, including those with high eosinophil counts and those who have previous surgery, which are associated with high recurrence.\(^{20}\) Since the number of our patients was small, we could not perform subgroup analysis except for the presence of asthma; however, we demonstrated that omalizumab was effective in our heterogeneous patient group.

Our study has a few limitations. One is the small cohort size and our study was conducted in a single-center as a pilot study. The duration of follow-up is not too long (mean [SD], mo; 9.2 [13.3]) which might be another limitation. On the other hand, retrospective analyses are important because they reflect real-life conditions and patients are clinically heterogeneous. It was one of the strengths of this work.

**CONCLUSION**

To our knowledge, this is the first real-life efficiency and safety study from Turkey, that specifically addresses CRSwNP patients without allergic asthma, and also in the literature, there were only a few studies about this topic. Our data indicates that omalizumab is effective and safe in CRSwNP patients with or without asthma under real-life conditions. However, it is clear that further studies of larger cohorts are needed.

**Abbreviations**

CRSwNP, Chronic rhinosinusitis with nasal polyposis; SNOT-22, Sinonasal outcome test-22; NOSE, Nose obstruction symptom evaluation; CRS, Chronic rhinosinusitis; CRSwNP, Chronic rhinosinusitis with nasal polyposis; CT, Computed tomography; ENT, Ear, nose, and throat; GINA, Global Initiative for Asthma; Ig E, Immunoglobulin E; SNOT-22, Sino-nasal outcome test questionnaire; VAS, Visual analog scale; NOSE, Nasal obstruction symptom evaluation score; NPS, Nasal polyp score; NSAID, Non-steroidal anti-inflammatory drugs.

**Funding sources**

There was no financial source for this study.

**Statement of Ethics**

Before starting this study, permission from the director of the hospital and ethics committee approval from the ethics committee of Mustafa Kemal University was received on 29.11.2021 as meeting number 13, decision number 16. The informed consent form was not obtained from the patients because this study was conducted as a retrospective file scan and the information was extracted from the patients’ files. According to the regulation of our country-Turkey, there is no need for a patient constant form in such retrospective studies.

**Declaration of competing interest**

The author declares no conflict of interest in relation to this research, authorship, and/or publication of this article. However, unrelated to the submitted work, it is reported that TST was a speaker and/or advisor for Novartis.

**Acknowledgments**

The author thanks Dilek Yapar for the statistical analysis of the study.
REFERENCES

1. Fokkens WJ, Lund VJ, Mullol J, et al. EPOS 2012: European position paper on rhinosinusitis and nasal polyps 2012. A summary for otorhinolaryngologists. *Rhinology*. 2012;50(1):1-12.

2. Abdalla S, Alreefy H, Hopkins C. Prevalence of sinonasal outcome test (SNOT-22) symptoms in patients undergoing surgery for chronic rhinosinusitis in the England and Wales National prospective audit. *Clin Otolaryngol*. 2012;37(4):276-282.

3. Chen S, Zhou A, Emmanuel B, Thomas K, Guiang H. Systematic literature review of the epidemiology and clinical burden of chronic rhinosinusitis with nasal polyposis. *Curr Med Res Opin*. 2020;36(11):1897-1911.

4. Promsopa C, Kansara S, Citardi MJ, Fakhri S, Porter P, Luong A. Prevalence of confirmed asthma varies in chronic rhinosinusitis subtypes. *Int Forum Allergy Rhinol*. 2016;6(4):373-377. https://doi.org/10.1002/air.21674.

5. Fokkens WJ, Lund VJ, Hopkins C, et al. Executive summary of EPOS 2020 including integrated care pathways. *Rhinology*. 2020;58(2):82-111.

6. Gliklich RE, Metson R. The health impact of chronic sinusitis in patients seeking otorhinolaryngologic care. *Otolaryngol Head Neck Surg*. 1995;113(1):104-109.

7. Hopkins C. Chronic rhinosinusitis with nasal polyps. *N Engl J Med*. 2019;381(1):55-63.

8. Gevaert P, Omachi TA, Corren J, et al. Efficacy and safety of omalizumab in nasal polyposis: 2 randomized phase 3 trials. *J Allergy Clin Immunol*. 2020;146(3):595-605.

9. Agarwal A, Spath D, Sherris DA, Kita H, Ju Ponikau. Therapeutic antibodies for nasal polypsis treatment: where are we headed? *Clin Rev Allergy Immunol*. 2020;59(2):141-149.

10. Bachert C, Zhang N, Cavailler C, Weiping W, Gevaert E, Krysko O. Biologics for chronic rhinosinusitis with nasal polyps. *J Allergy Clin Immunol*. 2020;145(3):725-739.

11. Global Strategy for Asthma Management and Prevention. *GINA Report 2021*. https://ginasthma.org/wp-content/uploads/2021/05/GINA-Main-Report-2021-V2-WMS.pdf/ Accessed 02 Jan, 2022.

12. Hanci D, Altun H, Şahin E, Altıntoprak N, Cingi C. Turkish translation, cross-cultural adaptation and validation of the SinoNasal Outcome Test (SNOT)-22. *ENT Updates*. 2015;5(2):51-57.

13. Karahatay S, Taşlı H, Karaköç Ö, Aydın Ü, Türker T. Reliability and validity of the Turkish nose obstruction symptom evaluation (NOSE) scale. *Turk J Med Sci.* 2018;48(2):212-216.

14. Penn R, Mikula S. The role of anti-IgE immunoglobulin therapy in nasal polyposis: a pilot study. *Am J Rhinol*. 2007;21(4):428-432.

15. Vennera Mdel C, Picado C, Mullol J, Alobid I, Bernal-Sprekelsen M. Efficacy of omalizumab in the treatment of nasal polyps. *Thorax*. 2011;66(9):824-825.

16. Gevaert P, Calus L, Van Zele T, et al. Omalizumab is effective in allergic and nonallergic patients with nasal polyps and asthma. *J Allergy Clin Immunol*. 2013;131(1):110-116.e1.

17. Tiotiu A, Oster JP, Roux PR, et al. Effectiveness of omalizumab in severe allergic asthma and nasal polyposis: a real-life study. *J Investig Allergol Clin Immunol*. 2020;30(1):49-57. https://doi.org/10.18176/jiaci.0391.

18. Gevaert P, Saenz R, Corren J, et al. Long-term efficacy and safety of omalizumab for nasal polyposis in an open-label extension study. *J Allergy Clin Immunol*. 2022;149(3):957-965. https://doi.org/10.1016/j.jaci.2021.07.045. e3.

19. Armengot-Carceller M, Gómez-Gómez MJ, Garcia-Navalón C, et al. Effects of omalizumab treatment in patients with recalcitrant nasal polyposis and mild asthma: a multicenter retrospective study. *Am J Rhinol Allergy*. 2021;35(4):516-524.

20. Damask C, Chen M, Holweg CTJ, Yoo B, Millette LA, Franzese C. Defining the efficacy of omalizumab in nasal polyposis: a POLYP 1 and POLYP 2 subgroup Analysis. *Am J Rhinol Allergy*. 2022;36(1):135-141. https://doi.org/10.1177/19458924211030486. Epub 2021 Aug 12.