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Real-World Outcomes of Biologic Therapy in Patients with Nasal Polyps: Clinical Profiles and the Impact of N-ERD

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ABSTRACT

Objective: Nasal polyps (NP) are chronic inflammatory lesions commonly associated with asthma and non-steroidal anti-inflammatory drug exacerbated respiratory disease (N-ERD). This study aimed to evaluate the clinical characteristics and real-world outcomes of biologic therapy in patients with NP and asthma, with particular focus on biologic agent subgroups and clinically defined N-ERD status.

Materials and Methods: In this single-center, retrospective, small cohort study conducted between May 2024 and August 2025, we reviewed patients with asthma and NP who received biologic therapy for at least six months in our Department of Allergy and Clinical Immunology. Patients were stratified according to the presence or absence of N-ERD. Demographic characteristics, laboratory findings, and clinical outcomes, including Asthma Control Test (ACT) and Sinonasal Outcome Test (SNOT-22) scores, were collected at baseline and after six months of treatment.

Results: A total of 28 patients with NP and asthma were included in the study. Of these, 22 patients were initiated on biologic therapy for severe asthma (SA), while 6 patients with mild persistent asthma received off-label biologic treatment for NP. Overall, 15 patients (53.6%) were classified as having clinically defined N-ERD. Eleven patients were treated with mepolizumab, 10 with benralizumab, and 7 with omalizumab. Biologic therapy was associated with significant improvements in patient-reported sinonasal symptoms, as reflected by reductions in SNOT-22 scores, when analyzed separately for each biologic agent. Significant clinical improvements were observed in both the N-ERD-positive and N-ERD-negative groups, including reductions in SNOT-22 scores and increases in ACT scores and FEV_1 values ($p<0.05$ for all outcomes).

Conclusion: With appropriate patient selection, biologic therapies were associated with improvements in both patient-reported sinonasal symptoms and asthma-related outcomes in patients with NP and concomitant asthma, irrespective of clinically defined N-ERD status. These findings support the potential real-world utility of type 2-targeted biologics in patients with NP and concomitant asthma.

Keywords: Nasal polyps, asthma, non-steroidal anti-inflammatory drug-exacerbated respiratory disease, biologics, real-world outcomes, SNOT-22

INTRODUCTION

Nasal polyps (NP) are benign, inflamed, and edematous mucosal protrusions resulting from persistent mucosal inflammation, epithelial barrier dysfunction, and tissue remodeling of the paranasal sinus and nasal cavity epithelium (1,2). Epidemiological studies estimate the prevalence of NP in the general adult population to be approximately 1-2% (3). NP is associated with 40% of patients with severe asthma, and this has been linked to a significant decrease in health-related quality of life (HRQoL) and an increase in asthma severity. This association also leads to increased asthma exacerbations, creating challenges in disease management. This has become a key focus for the development of new targeted therapeutic agents (4-6). Although most commonly associated with chronic rhinosinusitis, individuals with NP may also have concomitant non-steroidal anti-inflammatory drug-exacerbated respiratory disease (N-ERD), cystic fibrosis, systemic vasculitic disorders, and other inflammatory conditions (2).

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N-ERD is a chronic inflammatory syndrome affecting the upper and lower respiratory tracts. Clinically, it is characterized by the classic triad of NP, concomitant moderate-to-severe asthma (SA), and non-allergic hypersensitivity reactions to NSAIDs that inhibit cyclooxygenase-1 (COX-1). The prevalence of N-ERD is estimated at 0.6-2.5% in the general population but increases to approximately 7% in patients with asthma, 15% in those with SA, and 10-16% in individuals with NP (7-9).

Sinonasal involvement in N-ERD is generally more severe, frequently presenting with rapid NP growth and significant olfactory loss. Moreover, patients with N-ERD experience higher rates of postoperative polyp recurrence following sinus surgery and often require additional surgical interventions compared with those with NSAID-tolerant NP (10).

Biologic therapy may be considered for patients with NP who meet the required eligibility criteria. The EPOS/EUFOREA 2023 update refined the indications for biologic therapy in NP by clearly defining patient selection and treatment response criteria. According to these updated guidelines, biologic therapy may be offered to patients with severe, uncontrolled NP who have received appropriate medical and surgical management and who fulfill at least three of the following five criteria: evidence of type 2 inflammation, a regular need for systemic corticosteroids (or contraindications to their use), markedly reduced quality of life, significant olfactory impairment, and comorbid asthma (1).

The first biologic therapy approved by the FDA specifically for adults with inadequately controlled NP was dupilumab, which targets IL-4/IL-13 signaling and received approval in 2019. This was followed by the approval of omalizumab, an anti-IgE monoclonal antibody, in 2020, and subsequently mepolizumab, an anti-IL-5 agent, in 2021 for the same indication. Benralizumab, which targets the IL-5 receptor, has been approved for the treatment of severe eosinophilic asthma but is not currently authorized for NP. Together, these agents target key type 2 inflammatory pathways involved in NP pathobiology, including IgE-mediated and IL-5/IL-5 receptor-mediated eosinophilic inflammation. Their approval has expanded add-on maintenance treatment options for patients with persistent disease despite standard therapy (11). In addition, numerous studies have investigated the efficacy of biologic agents in the management of N-ERD, demonstrating their potential to improve both asthma control and sinonasal outcomes in patients with coexisting NP (10,12).

In our country, biologic therapies for NP are not reimbursed by the national health insurance system. Consequently, these agents can be administered either to patients who are initiated on biologic therapy for SA and who concurrently have NP, or to individuals with asthma in whom off-label approval is specifically requested for the treatment of NP. In our setting, three biologic agents consisting of omalizumab, mepolizumab, and benralizumab are currently authorized for the treatment of SA, while omalizumab and mepolizumab are also reimbursed off-label for the treatment of NP.

Although biologic therapies have been widely studied in terms of asthma-related outcomes, evidence focusing specifically on NP-related clinical outcomes remains more limited, particularly in real-world cohorts. Data regarding the patient-reported sinonasal symptom burden, biologic agent-specific responses, and treatment outcomes in patients with N-ERD are still needed. This gap is clinically relevant because NP substantially contributes to disease burden, quality-of-life impairment, and treatment complexity in patients with concomitant asthma.

Therefore, this study aimed to characterize the clinical profiles of patients with NP and concomitant asthma receiving biologic therapy, to evaluate changes in patient-reported sinonasal and asthma-related outcomes, and to explore whether clinically defined N-ERD status influenced baseline phenotype and treatment response in this real-world cohort.

MATERIAL and METHODS

This single-center, retrospective, small cohort study analyzed patients with SA and concomitant NP who received omalizumab, mepolizumab, or benralizumab, as well as patients with mild persistent asthma who were initiated on biologic therapy off-label for NP, all of whom were treated for at least six months at our Allergy and Immunology Clinic.

In accordance with national regulatory requirements in Türkiye, documented off-label approval from the Turkish Medicines and Medical Devices Agency (TITCK) was obtained before treatment initiation for all patients who received biologic therapy for NP outside the approved indication and without concomitant SA. In total, six patients in the cohort were treated under this regulatory framework.

SA was defined as persistent poor disease control despite optimized high-dose inhaled corticosteroid-long-acting β_2-agonist (ICS-LABA) therapy, or the need for such treatment to maintain disease stability. It was clearly distinguished from difficult-to-treat asthma attributable to inadequate therapy, poor adherence, or insufficient management of comorbid conditions (13).

The diagnosis of NP was based on an integrated assessment that included clinical findings, endoscopic examination, and radiological imaging.

N-ERD was defined according to the EAACI position paper as a cross-reactive NSAID hypersensitivity phenotype characterized by respiratory reactions triggered by COX-1-inhibiting NSAIDs in patients with asthma and/or chronic rhinosinusitis with NP (14). In the present study, N-ERD classification was based on a reliable clinical history of respiratory hypersensitivity reactions to at least two different cross-reactive NSAIDs, when this information was available in the medical records. Aspirin/NSAID provocation testing was not performed because of the retrospective design of the study and safety concerns, as most patients had severe asthma and were considered at increased risk for bronchospasm or severe respiratory reactions during aspirin/NSAID provocation or desensitization.

Patients received omalizumab, mepolizumab, or benralizumab according to their respective approved dosing regimens. Omalizumab was administered at doses and intervals determined by total serum IgE levels (IU/mL) and body weight (kg), in line with guideline recommendations, typically every 2-4 weeks. Mepolizumab was given subcutaneously at a fixed dose of 100 mg every 4 weeks, while benralizumab was administered subcutaneously at a dose of 30 mg monthly for the first three doses, followed by dosing every 8 weeks thereafter.

The duration of biologic therapy was recorded for each patient. However, treatment response was evaluated using standardized baseline and sixth-month follow-up data in all patients. Therefore, the primary pre-post analyses were based on the same follow-up time point, regardless of total biologic treatment duration.

Blood eosinophil counts and total IgE levels, pulmonary function parameters, Asthma Control Test (ACT) scores, and Sinonasal Outcome Test (SNOT-22) scores were recorded at baseline and after six months of treatment with omalizumab, mepolizumab, or benralizumab. Patients were further classified into two subgroups according to the presence or absence of N-ERD. The validated Turkish version of the SNOT-22 was used to evaluate physical, functional, emotional, and social domains in patients with chronic rhinosinusitis (15).

Pulmonary function parameters, including FEV_1 and FEF25-75, were recorded at baseline and at the sixth month of biologic treatment. FEF25-75 was included as an exploratory parameter reflecting small airway function, particularly in patients with N-ERD.

Changes in inflammatory biomarkers, including peripheral blood eosinophil count and total IgE levels, were evaluated before and after biologic therapy. These changes were also analyzed descriptively according to the biologic agent received.

Data on NSAID tolerance, NSAID consumption, or changes in NSAID-related respiratory reactions after biologic therapy were not systematically available in the retrospective medical records; therefore, these parameters were not included as treatment outcomes.

Because of the retrospective nature of the study, comprehensive and standardized data on pre- and post-biologic agent systemic corticosteroid use were not available for all patients, precluding a reliable analysis of steroid dependence and reduction as outcome parameters.

Statistical Analysis

All statistical analyses were performed using IBM SPSS Statistics. Continuous variables are presented as mean ± standard deviation or median with the observed range, whereas categorical variables are expressed as counts and percentages. The Shapiro-Wilk test was applied to assess the normality of continuous data.

For within-group comparisons of pre- and post-treatment measurements, the paired samples t-test was used for normally distributed variables, whereas the Wilcoxon signed-rank test was applied for variables that did not meet normality assumptions. Baseline demographic, clinical, laboratory, and pulmonary function characteristics were compared between patients with and without N-ERD. Categorical variables were compared using Fisher's exact test because of the small sample size. Continuous variables were compared using the independent samples t-test or the Mann-Whitney U test, according to data distribution.

Because of the limited number of patients in each biologic treatment subgroup, formal between-agent comparative analyses were not performed. Treatment responses across biologic subgroups were interpreted descriptively. All between-group comparisons were considered exploratory. A two-sided p-value of<0.05 was considered statistically significant.

RESULTS

A total of 28 patients with NP were included in the study; 22 were initiated on biologic therapy for SA, while 6 had mild persistent asthma and received off-label biologic therapy for NP. Overall, 15 patients (53.6%) were clinically defined N-ERD (+), while 13 (46.4%) were N-ERD (−). Eighteen patients (64.3%) were female and 10 (35.7%) were male. The proportion of female patients was higher in the N-ERD (+) group compared to the N-ERD (−) group (80% vs. 46.2%).

The mean age of the total cohort was 49.25 ± 13.86 years (range: 21-76), and the mean age was similar between the N-ERD (+) and N-ERD (−) groups (47.33 vs. 51.46 years).

The mean number of previous NP surgeries was 2.25 ± 2.28 (range: 0-9) in the overall population. This number was higher in the N-ERD (+) group (2.8 ± 2.04; range: 0-7) compared with the N-ERD (−) group (1.61 ± 2.46; range: 0-9).

Regarding biologic therapies, 7 patients (25%) received omalizumab, 11 patients (39.3%) received mepolizumab, and 10 patients (35.7%) received benralizumab. The median duration of biologic therapy in the overall cohort was 8 months (range: 6-15). According to biologic agent, the median treatment duration was 7 months (range: 6-13) for omalizumab, 10 months (range: 6-15) for mepolizumab, and 8 months (range: 6-11) for benralizumab. All clinical outcome analyses were performed using baseline and sixth-month follow-up data. The distribution of biologic treatments was similar between the N-ERD (+) and N-ERD (−) groups.

Atopy was present in 21 patients (75.0%) overall, with a numerically higher prevalence in the N-ERD (−) group than in the N-ERD (+) group, although this difference was not statistically significant (84.6% vs. 66.7%, p=0.396). The most common atopic sensitization was pollens (42.9%), followed by mold (39.3%), house dust mite (32.1%), pet dander (28.6%), and cockroach (21.4%). The distribution of atopic sensitizations was comparable between the N-ERD (+) and N-ERD (−) groups, with no statistically significant differences observed for house dust mite, pollens, mold, pet dander, or cockroach sensitization.

The demographic and clinical characteristics of patients with NP according to the presence of N-ERD are summarized in Table I.

Blood eosinophil percentage and counts, total IgE levels, pulmonary function parameters, ACT scores, and SNOT-22 scores were comparable between the N-ERD (+) and N-ERD (−) groups, with no statistically significant differences observed at baseline. FEF25-75 was also evaluated as an exploratory small airway parameter. In the overall cohort, FEF25-75 increased from 1.53 L/s (0.51-5.37) to 2.17 L/s (0.71-4.64) after six months of biologic therapy (p=0.019). In patients with N-ERD, FEF25-75 increased from 1.43 L/s (0.51-3.67) to 1.76 L/s (0.71-4.64) (p=0.078), whereas in patients without N-ERD it increased from 1.63 L/s (0.79-5.37) to 2.48 L/s (0.72-4.58) (p=0.074). Given the limited sample size and the known variability of this parameter, these findings should be interpreted cautiously.

Laboratory characteristics and clinical scores of patients with NP according to N-ERD status are presented in Table II.

Baseline demographic, clinical, laboratory, and pulmonary function characteristics were compared between patients with and without N-ERD, and p values were added to Tables I and II. Except for the number of previous NP surgeries, which was higher in the N-ERD (+) group, no statistically significant differences were observed between the groups for baseline variables.

Changes in inflammatory markers were also evaluated according to the biologic agent received. In the benralizumab group, eosinophil percentage decreased from 7.64% (2.30-19.31) to 0.00% (0.00-6.60) after treatment (p=0.007), whereas total IgE changed from 483.00 IU/mL (85.40-910.00) to 460.00 IU/mL (68.00-1000.00) without statistical significance (p=0.139). In the mepolizumab group, eosinophil percentage decreased from 5.31% (1.33-24.30) to 1.70% (0.26-3.79) after treatment (p=0.008), whereas total IgE changed from 107.65 IU/mL (15.20-476.00) to 136.15 IU/mL (13.80-474.00) without statistical significance (p=0.401). In the omalizumab group, eosinophil percentage decreased from 4.54% (4.09-8.89) to 3.50% (2.09-6.66) after treatment (p=0.018), whereas total IgE

Table I: Demographic and clinical characteristics of patients with nasal polyps according to N-ERD presence

Variables	Total (n=28)	N-ERD (+) (n=15)	N-ERD (-) (n=13)	p value
Sex, n (%)				
Female	18 (64.3)	12 (80)	6 (46.2)	0.114
Male	10 (35.7)	3 (20)	7 (53.8)	
Age, years, mean ± SD (minimum-maximum)	49.25±13.86 (21-76)	47.33±11.36 (21-64)	51.46±16.49 (26-76)	0.442
Number of previous NP surgeries, mean ± SD (minimum-maximum)	2.25±2.28 (0-9)	2.8±2.04 (0-7)	1.61±2.46 (0-9)	0.040
Biologic agent, n (%)				0.955
Omalizumab	7 (25)	4 (26.7)	3 (23.1)	
Mepolizumab	11 (39.3)	6 (40)	5 (38.5)	
Benralizumab	10 (35.7)	5 (33.3)	5 (38.5)	
Atopy, n (%)	21 (75)	10 (66.7)	11 (84.6)	0.396
House dust mite sensitization, n (%)	9 (32.1)	4 (26.7)	5 (38.5)	0.689
Pollen sensitization, n (%)	12 (42.9)	7 (46.7)	5 (38.5)	0.718
Mold sensitization, n (%)	11 (39.3)	7 (46.7)	4 (30.8)	0.460
Pet dander sensitization, n (%)	8 (28.6)	4 (26.7)	4 (30.8)	0.569
Cockroach sensitization, n (%)	6 (21.4)	2 (13.3)	4 (30.8)	0.372

Data are presented as mean ± standard deviation (minimum-maximum) or n (%). Percentages are column percentages unless otherwise indicated.

Table II: Laboratory characteristics and clinical scores of patients with nasal polyps according to N-ERD presence

Variables	Total (n=28)	N-ERD (+) (n=15)	N-ERD (-) (n=13)	p value
Blood eosinophil, %	8.53±5.95 (1.3-24.3)	8.39±6.58 (1.3-24.3)	8.38±4.94 (2-16)	0.872
Blood eosinophil count, cells/μL	731±539.56 (180-2250)	764±624.05 (180-2250)	680±405.44 (200-1430)	0.963
Total IgE, IU/mL	338±261.34 (15-910)	308±268.79 (39-910)	373.23±258.69 (15-811)	0.433
FEV1, % predicted	80.78±21.82 (36-113)	82.6±22.44 (39-113)	78.6±21.79 (36-104)	0.645
FEV1, mL	2353±829.27 (900-4410)	2288±871.01 (900-4410)	2430±806.53 (1400-3890)	0.660
FEF25-75, L/s	1.53 (0.51-5.37)	1.43 (0.51-3.67)	1.63 (0.79-5.37)	0.661
ACT score	12.68±4.84 (5-21)	13±4.29 (5-21)	12.2±5.78 (5-21)	0.695
SNOT-22 score	62±16.6 (34-88)	62.13±18.54 (34-84)	61.80±14.38 (44-88)	0.846

Data are presented as mean ± standard deviation (minimum-maximum) or median (minimum-maximum), as appropriate. FEF25-75 is presented as median (minimum-maximum).

increased from 346.00 IU/mL (103.00-582.00) to 838.00 IU/mL (322.00-1666.00) (p=0.043). Because of the small number of patients in each biologic subgroup, these biomarker changes were interpreted descriptively.

Following biologic therapy, both N-ERD (+) and N-ERD (-) patients demonstrated significant improvements. In the N-ERD (+) group, mean SNOT-22 scores decreased from 62.13 to 28.20 (p<0.001), ACT scores increased from 13 to 19.2 (p<0.001), and predicted FEV_1 % improved from 82.6% to 93% (p=0.024) (Figure 1). Similarly, in the N-ERD (-) group, SNOT-22 scores decreased from 61.80 to 30.62 (p=0.001), ACT scores rose from 12.2 to 19.37 (p=0.003), and predicted FEV_1 % increased from 78.6% to 99.8% (p=0.039) (Figure 2).

When treatment-related changes were evaluated according to biologic agent subgroups, omalizumab, mepolizumab, and benralizumab were each associated with reductions in SNOT-22 scores from baseline to six months, indicating improvement in patient-reported sinonasal symptom burden. In the omalizumab group, SNOT-22 scores decreased from 71 to 21.8 (p=0.005); in the mepolizumab group, from 61.75 to 26.87 (p<0.001); and in the benralizumab group, from 57.7 to 35.7 (p=0.001) (Figure 3). However, because of the small number of patients in

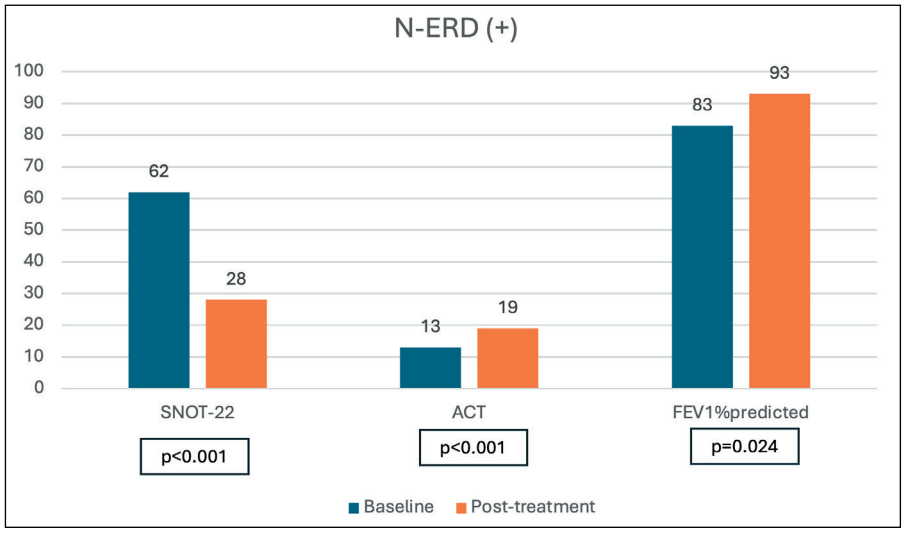

Figure 1: Clinical outcomes before and after biologic therapy in N-ERD (+) patients

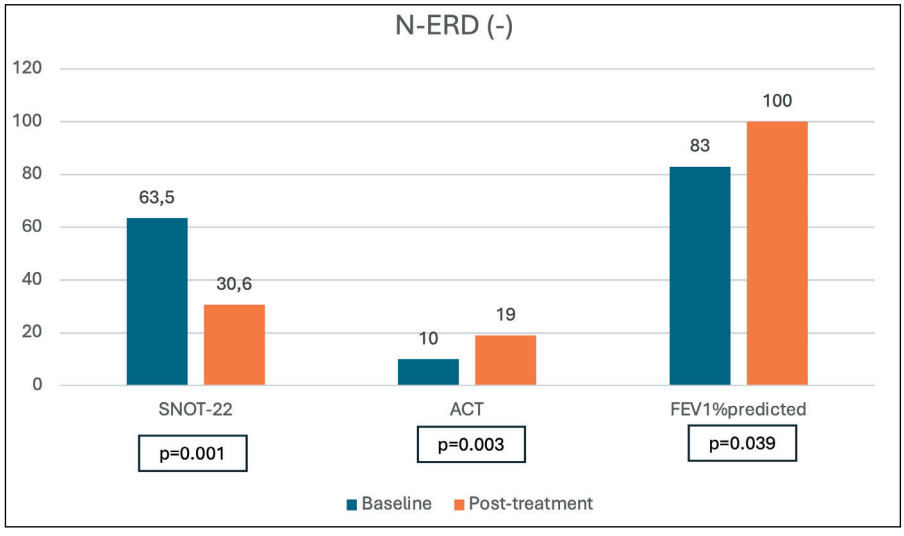

Figure 2: Clinical outcomes before and after biologic therapy in N-ERD (-) patients

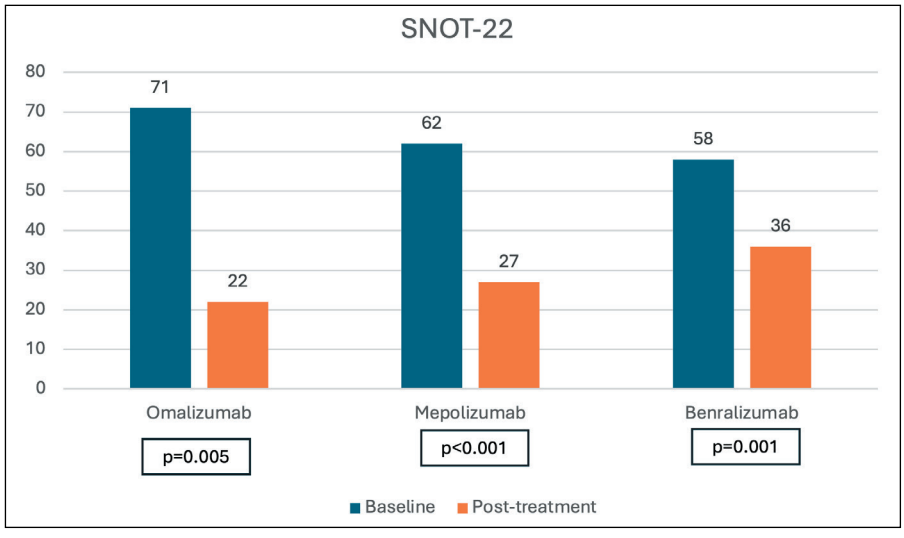

Figure 3: Effect of different biologic agents on sinonasal symptoms (SNOT-22)

each biologic subgroup, these findings should be interpreted as exploratory and descriptive rather than confirmatory. No formal inter-agent comparative efficacy analysis was performed.

DISCUSSION

This study assessed the clinical characteristics and treatment outcomes of patients with NP and asthma receiving biologic therapy, with a particular focus on the impact of N-ERD on disease phenotype and treatment response. Biologic therapy was associated with significant improvements in both upper and lower airway outcomes, regardless of N-ERD status. Although N-ERD (+) patients are generally considered to exhibit a more severe disease phenotype, baseline demographic, laboratory, and clinical characteristics were largely similar between the N-ERD (+) and N-ERD (−) groups in this cohort.

In a previous meta-analysis, the prevalence of N-ERD among patients with NP was reported as 9.69% (16). Subsequent studies conducted in later years found that N-ERD prevalence in this population ranged from 10% to 16% (7-9). A study from our country on patients with asthma reported an N-ERD prevalence of 13.6% (17). In the present study, however, the prevalence of N-ERD among patients with both NP and asthma was 53.5% (n=15), notably higher than previously reported. This elevated rate may reflect the inclusion of patients with more SA who had already initiated biologic therapy. Differences in referral patterns, disease severity, and patient selection may have contributed to the higher observed prevalence. Additionally, because aspirin challenge testing was not performed, some degree of misclassification cannot be excluded, and the true prevalence of N-ERD in this cohort remains uncertain.

Among the 15 patients (53.5%) who met the clinical diagnostic criteria for N-ERD, the majority (80%) were women. This finding is consistent with previous reports (18,19) and suggests that factors beyond sex hormones may contribute to the higher prevalence of N-ERD in women.

Although serum total IgE levels may be elevated in patients with N-ERD, there is no consistent association between N-ERD and a predisposition to atopy (20). A recent study reported an overall atopy prevalence of 47% among asthma patients, with no significant difference between those with and without N-ERD (17). In the present study, consistent with the literature, atopy was observed in 75.0% of patients overall, with a numerically higher prevalence in the N-ERD (−) group compared with the N-ERD (+) group (84.6% vs. 66.7%); however, this difference was not statistically significant.

In the study by Stevens et al., patients with N-ERD underwent approximately twice as many sinus surgeries as non-N-ERD patients ($p<0.001$) (8). Similarly, Bavbek et al. reported a significant association between aspirin hypersensitivity and the frequency of polypectomy procedures ($p=0.016$) (17). In the present study, patients with N-ERD also had a significantly higher number of NP surgeries than those without N-ERD (2.8 vs. 1.6, $p=0.040$), supporting the known refractory nature of N-ERD-associated sinonasal disease.

Previous studies have shown that biological agents may reduce polyp burden and improve quality of life in patients with recurrent NP who do not respond adequately to standard treatments, regardless of the presence of asthma (1, 21). In a multicenter study from our country evaluating the effectiveness of omalizumab and mepolizumab in patients with NP, both biologics led to significant improvements in patient-reported sinonasal outcomes, including visual analog scale (VAS), SNOT-22, and nasal congestion score (NCS) (22). In the present study, all biologic subgroups, including omalizumab, mepolizumab, and benralizumab, showed significant reductions in SNOT-22 scores, suggesting improvement in patient-reported sinonasal symptom burden. Because of the small number of patients in each biologic subgroup, these findings should be interpreted as exploratory and hypothesis-generating rather than as evidence of comparative efficacy.

This improvement may be explained by the distinct but overlapping effects of these agents on type 2 inflammatory pathways involved in NP pathobiology. Omalizumab targets IgE-mediated inflammation, whereas mepolizumab and benralizumab suppress eosinophilic inflammation through the IL-5/IL-5 receptor pathway. These mechanisms may contribute to the improvement in sinonasal symptoms observed across biologic subgroups (1,11).

Changes in inflammatory markers were generally consistent with the expected mechanisms of the biologic agents used. Eosinophil percentages decreased across all biologic subgroups, with marked reductions in the benralizumab and mepolizumab groups, in line with inhibition of the IL-5/IL-5 receptor pathway. Total IgE levels

remained statistically unchanged in the benralizumab and mepolizumab groups but increased in the omalizumab group, consistent with the known effect of omalizumab on measured total IgE levels. Given the small subgroup sizes, these biomarker findings should be interpreted cautiously.

Because objective endoscopic and radiological assessments were not available, the improvement in SNOT-22 scores should not be interpreted as direct evidence of NP regression. Rather, these findings indicate improvement in patient-reported sinonasal symptom burden. Future prospective studies incorporating standardized endoscopic NP scoring, Lund-Mackay CT scoring, and olfactory testing are needed to better characterize objective sinonasal responses to biologic therapy in this population.

Aspirin desensitization represents a well-established and effective therapeutic strategy in patients with N-ERD, with demonstrated benefits on NP recurrence, asthma control, and corticosteroid-sparing effects. Previous studies have shown that aspirin desensitization can lead to sustained clinical improvement, reduced sinonasal disease burden, and decreased need for surgical interventions in appropriately selected patients (7,8,14). In recent years, biologic therapies have emerged as targeted treatment options for severe type 2 inflammation in N-ERD, offering an alternative or complementary strategy to aspirin desensitization. Within this evolving therapeutic landscape, aspirin desensitization and biologic therapies should be considered as part of an individualized, patient-centered treatment approach, taking into account disease severity, comorbidities, safety considerations, and patient preference.

Studies investigating the use of biologic agents in patients with N-ERD have demonstrated improvements in both asthma control and sinus outcomes in individuals with concomitant NP (10,12). Consistent with these reports, our study found significant improvements in sinonasal symptoms, as well as in respiratory symptoms and lung function, in both N-ERD (+) and N-ERD (−) patients following biologic therapy.

Small airway involvement may contribute to respiratory morbidity in patients with N-ERD. Therefore, FEF25-75 was evaluated as an exploratory marker of small airway function in the present study. Although changes in FEF25-75 may provide additional information beyond FEV_1, this parameter should be interpreted cautiously because of its variability and the limited sample size of our cohort.

Real-world data evaluating biologic therapies specifically in N-ERD subphenotypes remain limited. In a study from Türkiye, Tepetam et al. evaluated omalizumab and mepolizumab in patients with severe asthma and N-ERD and reported improvement in both pulmonary and nasal outcomes, with more pronounced improvement in nasal parameters among patients receiving omalizumab (23). This observation may be mechanistically relevant, as omalizumab reduces IgE-mediated activation and downregulates FcεRI expression on mast cells and basophils, which may subsequently decrease mediator release, including leukotriene-related inflammatory activity in the upper airway. In our cohort, improvements in sinonasal outcomes were observed across biologic subgroups; however, because of the small sample size and the absence of formal inter-agent comparison, our findings should be interpreted as exploratory. Together with previous national data, our results support the need for larger prospective studies to better define biologic selection in patients with NP, asthma, and N-ERD.

Overall, these findings support the effectiveness of biologic agents in managing NP and asthma symptoms regardless of N-ERD status. Larger, long-term studies are warranted to better assess sustained outcomes and identify factors associated with optimal treatment response in this patient population.

Strengths and Limitations

This study has several limitations. First, because of the retrospective design, N-ERD diagnosis was based on clinical history rather than aspirin provocation testing, which may have introduced diagnostic uncertainty. In addition, the exact interval between the most recent nasal polypectomy and initiation of biologic therapy could not be reliably determined.

Second, sinonasal response was assessed using total SNOT-22 scores as a patient-reported outcome measure. Individual item-level SNOT-22 data and objective sinonasal assessments, including endoscopic NP scores, Lund-Mackay computed tomography scores, and formal olfactory testing, were not available. Therefore, improvement in SNOT-22 scores should be interpreted as improvement in patient-reported sinonasal symptom burden rather than direct evidence of NP regression.

Third, data on systemic corticosteroid use, NSAID tolerance, and NSAID consumption were not systematically

documented. Therefore, the steroid-sparing effect of biologic therapy and its impact on NSAID tolerance could not be evaluated. Finally, the small sample size, particularly within biologic agent subgroups, limited statistical power and precluded reliable inter-agent efficacy comparisons; thus, subgroup analyses should be considered exploratory.

CONCLUSION

In patients with NP and concomitant asthma, biologic therapy was associated with improvements in patient-reported sinonasal symptoms, asthma control, and pulmonary function, regardless of N-ERD status. These findings suggest that biologic agents may represent a valuable therapeutic option in this clinically complex population. However, given the retrospective design, small sample size, and lack of objective sinonasal outcome measures, the results should be interpreted with caution. Future large-scale, prospective studies with longer follow-up and standardized endoscopic, radiological, and olfactory assessments are needed to confirm these findings and to identify factors associated with optimal treatment response.

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Ethical Approval

The study was carried out following the principles of the Declaration of Helsinki and received approval from the Medical Research Ethics Committee, Elazığ Fethi Sekin City Hospital (May 8, 2025: 2025/9-23).

Conflict of Interest

The author declares no conflicts of interest.

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Author Contributions

The author **(HSA)** confirm responsibility for the following: study conception and design, data collection or processing, analysis and interpretation of results, and manuscript preparation.

REFERENCES

1. Fokkens WJ, Viskens AS, Backer V, Conti D, De Corso E, Gevaert P, et al. EPOS/EUFOREA Update on Indication and Evaluation of Biologics in CRSwNP 2023. Rhinology 2023;61(3):194-202. doi: 10.4193/Rhin22.489.
2. del Toro E, Hardin FML, Portela J. Nasal Polyps. 2025 May 5. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan. PMID: 32809581.
3. Min HK, Lee S, Kim S, Son Y, Park J, Kim HJ, et al. Global Incidence and Prevalence of Chronic Rhinosinusitis: A Systematic Review. Clin Exp Allergy 2025;55(1):52-66. doi: 10.1111/cea.14592.
4. Canonica GW, Malvezzi L, Blasi F, Paggiaro P, Mantero M, Senna G, et al. Chronic rhinosinusitis with nasal polyps impact in severe asthma patients: evidences from the Severe Asthma Network Italy (SANI) registry. Respir Med 2020;166:105947. doi: 10.1016/j.rmed.2020.105947.
5. Seccia V, D'Amato M, Scioscia G, Bagnasco D, Di Marco F, Fadda G, et al. Management of patients with severe asthma and chronic rhinosinusitis with nasal polyps: a multidisciplinary shared approach. J Pers Med 2022;12(27):1096. doi: 10.3390/jpm12071096.
6. Chung KF, Wenzel SE, Brozek JL, Bush A, Castro M, Sterk PJ, et al. International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma. Eur Respir J 2014;43(2):343-73. https://doi.org/10.1183/09031936.00202013.
7. Thiagarajan K, Anderson L. Aspirin Desensitization in Treatment of Chronic Rhinosinusitis with Nasal Polyposis: Current Protocols and Evidence. Curr Treat Options Allergy 2024;11:123-35. https://doi.org/10.1007/s40521-024-00365-w.
8. Stevens WW, Jerschow E, Baptist AP, Borish L, Bosso JV, Buchheit KM, et al. The role of aspirin desensitization followed by oral aspirin therapy in managing patients with aspirin-exacerbated respiratory disease: A Work Group Report from the Rhinitis, Rhinosinusitis and Ocular Allergy Committee of the American Academy of Allergy, Asthma & Immunology. J Allergy Clin Immunol 2021;147(3):827-44. https://doi.org/10.1016/j.jaci.2020.10.043.
9. White AA, Woessner K, Simon R. Aspirin-exacerbated respiratory disease: Update on medical management. World J Otorhinolaryngol Head Neck Surg 2020;6(4):241-7. https://doi.org/10.1016/j.wjorl.2020.07.009.
10. Mullur J, Buchheit KM. Aspirin-exacerbated respiratory disease: Updates in the era of biologics. Ann Allergy Asthma Immunol 2023;131(3):317-324. doi: 10.1016/j.anai.2023.05.016. Epub 2023 May 22. Erratum in: Ann Allergy Asthma Immunol. 2024;133(1):118. doi: 10.1016/j.anai.2024.04.001.
11. Cergan R, Berghi ON, Dumitru M, Vrinceanu D, Manole F, Serboiu CS. Biologics for Chronic Rhinosinusitis-A Modern Option for Therapy. Life (Basel) 2023;13(11):2165. doi: 10.3390/life13112165.
12. Mullur J, Steger CM, Gakpo D, Bensko JC, Maurer R, Laidlaw TM, et al. Aspirin desensitization and biologics in aspirin-exacerbated respiratory disease: Efficacy, tolerability, and patient experience. Ann Allergy Asthma Immunol 2022;128(5):575-82. doi: 10.1016/j.anai.2022.01.043.
13. Global Strategy for Asthma Management and Prevention (2024 update) [homepage on the internet]. Available from: https://ginasthma.org/reports/.
14. Kowalski ML, Agache I, Bavbek S, Bakirtas A, Blanca M, Bochenek G, et al. Diagnosis and management of NSAID-Exacerbated Respiratory Disease (N-ERD)-a EAACI position paper. Allergy 2019;74(1):28-39. doi: 10.1111/all.13599.

15. Cakir Cetin A, Kumus O, Keskinoglu P, Sutay S, Ecevit MC. Turkish validation of the Sino-Nasal Outcome Test-22. Clin Otolaryngol 2019;44(4):557-64. doi: 10.1111/coa.13332.
16. Rajan JP, Wineinger NE, Stevenson DD, White AA. Prevalence of aspirin-exacerbated respiratory disease among asthmatic patients: A meta-analysis of the literature. J Allergy Clin Immunol 2015;135(3):676-81.e1. doi: 10.1016/j.jaci.2014.08.020.
17. Bavbek S, Yilmaz I, Celik G, Aydin O, Erkekol FÖ, Orman A, et al. Prevalence of aspirin-exacerbated respiratory disease in patients with asthma in Turkey: a cross-sectional survey. Allergol Immunopathol (Madr) 2012;40(4):225-30. doi: 10.1016/j.aller.2011.05.015
18. Szczeklik A, Nizankowska E, Duplaga M. Natural history of aspirin-induced asthma. AIANE Investigators. European Network on Aspirin-Induced Asthma. Eur Respir J 2000;16:432-6. doi: 10.1034/j.1399-3003.2000.016003432.x
19. Stevens WW, Peters AT, Hirsch AG, Nordberg CM, Schwartz BS, Mercer DG, et al. Clinical Characteristics of Patients with Chronic Rhinosinusitis with Nasal Polyps, Asthma, and Aspirin-Exacerbated Respiratory Disease. J Allergy Clin Immunol Pract 2017;5(4):1061-70.e3. doi: 10.1016/j.jaip.2016.12.027.
20. Cahill KN, Boyce JA. Aspirin-exacerbated respiratory disease: Mediators and mechanisms of a clinical disease. J Allergy Clin Immunol 2017;139(3):764-6.
21. Laidlaw TM, Mullol J, Woessner KM, Amin N, Mannent LP. Chronic Rhinosinusitis with Nasal Polyps and Asthma. J Allergy Clin Immunol Pract 2021;9(3):1133-41. doi: 10.1016/j.jaip.2020.09.063.
22. Demir M, Tunakan Dalgic C, Mete Gokmen EN, Savas R, Eroglu S, Ozden G, et al. The Effectiveness of Biological Agents on Chronic Rhinosinusitis with Nasal Polyposis in Patients with Comorbid Asthma: A Multicenter Real-Life Study from Türkiye. Medicina (Kaunas) 2024;60(3):448. doi: 10.3390/medicina60030448.
23. Tepetam FM, Özden Ş, Kılıç FK, Örçen C, Yakut T. Does NSAID exacerbated respiratory disease (N-ERD) accompanying severe asthma affect biological treatment response? Efficacy of omalizumab and mepolizumab in N-ERD. World Allergy Organ J 2023;16(9):100817. doi: 10.1016/j.waojou.2023.100817. Erratum in: World Allergy Organ J 2024;17(2):100861. doi: 10.1016/j.waojou.2023.100861.