Alergologia Polska – Polish Journal of Allergology 2023; 10, 1: 52–56
DOI: https://doi.org/10.5114/pja.2023.125768
Received: 16.12.2022, Accepted: 10.01.2023.

Alergologia POLSKA
Polish Journal of Allergology

ORIGINAL PAPER/*PRACA ORYGINALNA*

Efficacy of mepolizumab treatment in patients with chronic rhinosinusitis with nasal polyps: a single-centre, real-life study

Skuteczność leczenia mepolizumabem u pacjentów z przewlekłym zapaleniem błony śluzowej nosa i zatok z polipami nosa: jednoośrodkowe badanie *real-life*

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ABSTRACT

Introduction: The anti-interleukin (IL)-5 antibody mepolizumab has been used in the treatment of patients with uncontrolled severe eosinophilic asthma.

Aim: In this real-life study, we aimed to evaluate the effect of mepolizumab on nasal symptoms in patients with chronic rhinosinusitis with nasal polyps (CRSwNP).

Material and methods: Adult patients (> 18 years old) with concomitant CRSwNP, who were treated with mepolizumab at a dose of 100 mg every 4 weeks for at least one year for severe eosinophilic asthma, between 2021 and 2022, were evaluated retrospectively. Asthma control testing (ACT), Sino-Nasal Outcome Test (SNOT-22), and a visual analogue scale (VAS) of 1 to 10 (from 1 to 10) for nasal symptoms were compared at baseline (pre-mepolizumab treatment), and at 6 and 12 months post-treatment. The need for endoscopic sinus surgery (ESS) and oral corticosteroid (OCS) was compared at 12 months pre-mepolizumab and post-mepolizumab treatment.

Results: The mean age of the 18 patients (9 (50%) males and 9 (50%) females) was 42.33 ±15.9 years. Mepolizumab significantly reduced the number of endoscopic sinus surgeries (ESSs) ($p = 0.002$). The need for short-course oral corticosteroid (OCS) decreased significantly after mepolizumab treatment ($p = 0.029$). Statistically significant improvements were found in the ACT, SNOT-22, and nasal symptom scores at 6 and 12 months post-treatment when compared to baseline. No side effects were observed post-treatment.

Conclusions: Mepolizumab improved nasal symptoms and reduced the need for OCS and ESS in patients with CRSwNP. However, the results obtained in the study should be confirmed with real-life studies involving larger numbers of patients.

KEY WORDS

mepolizumab, nasal polyp, sinusitis, asthma, eosinophils.

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INTRODUCTION

Anti-interleukin (IL)-5 antibody mepolizumab has been used in the treatment of patients with uncontrolled severe eosinophilic asthma since 2015 [1]. The efficacy of mepolizumab in eosinophilic asthma has been demonstrated, and it has been shown that mepolizumab reduces asthma exacerbations, improves quality of life, and reduces the need for oral corticosteroid (OCS) [2–4].

Adult-onset eosinophilic asthma is among the severe asthma phenotypes. The comorbidity of chronic rhinosinusitis with nasal polyps (CRSwNP) frequently accompanies adult-onset eosinophilic asthma. Hypersensitivity to aspirin and other nonsteroidal anti-inflammatory drugs is also frequently observed in these patients [5–7]. The prevalence of chronic rhinosinusitis in patients with severe asthma was reported to be 42.6% by the Italian Severe Asthma Network [8]. In severe asthma with the CRSwNP subphenotype, activated innate lymphoid cells (ILC2) often secrete IL-5, IL-13, and IL-4, and are referred to as the "T2 high" eosinophilic endotype. Cytokine release associated with activation of ILC2 has been demonstrated in nasal polyp tissue. IL-5 is the main cause of eosinophilic blood and tissue inflammation [9–11]. Symptoms of CRSwNP such as anterior or posterior nasal discharge, nasal congestion, sneezing, anosmia, facial pressure, and pain seriously affect the quality of life of patients [12].

Mepolizumab is an anti-IL-5 monoclonal antibody approved for patients with severe eosinophilic asthma according to the Global Initiative for Asthma (GINA) [13]. The drug is administered subcutaneously (sc) at a dose of 100 mg every 4 weeks. The therapeutic potential of the mepolizumab in patients with CRSwNP has been demonstrated [14–16]. There are limited real-life studies in the literature evaluating the effect of mepolizumab on nasal symptoms in patients with CRSwNP.

AIM

In this study, we aimed to evaluate the effect of mepolizumab on nasal symptoms in patients with CRSwNP.

MATERIAL AND METHODS

STUDY DESIGN, SETTING, AND DATA COLLECTION

In this study, adult patients (> 18 years old) with concomitant CRSwNP, who were treated with mepolizumab at a dose of 100 mg every 4 weeks for at least 1 year for severe eosinophilic asthma, between 2021 and 2022, were evaluated retrospectively. The indication for treatment with mepolizumab in patients with severe eosinophilic asthma was approved based on the Turkish Social Security Institution Health Application Communique. All the asthmatic patients were receiving step 5 treatment according to the GINA guidelines [13], and no treatment changes were made in the drugs they used for asthma or the drugs they used for nasal complaints (intranasal corticosteroid (INS), intranasal antihistamine (INAH), leukotriene receptor antagonist (LTRA), and oral antihistamine (OAH)) during mepolizumab treatment. Mepolizumab was administered at a dose of 100 mg sc every 4 weeks.

Demographic data, comorbidities, nasal surgeries, and laboratory data (eosinophil count, total IgE level and forced expiratory volume in 1 s (FEV_1)) of the patients were recorded from the patient files. The skin prick test or specific IgE measurement was performed for atopy. Asthma was diagnosed according to the GINA guidelines [13]. The diagnosis of CRSwNP was based on the presence of nasal symptoms (nasal congestion, rhinorrhoea, facial pressure, and hyposmia) for more than 12 weeks in addition to evidence of chronic inflammatory disease on paranasal sinus computed tomography (CT) imaging or nasal endoscopy. Sinonasal involvement was evaluated with paranasal sinus CT and nasal endoscopy [17]. Mepolizumab side effects were recorded in patient files. Asthma control testing (ACT) [18] was routinely performed when the patients came for each injection. Patients with CRSwNP were routinely administered the Sino-Nasal Outcome Test (SNOT-22) [19] and a visual analogue scale (VAS) of 1 to 10 (from 1 to 10) for nasal symptoms when they came for each injection. Their ACT, SNOT-22, and VAS scores were compared at baseline (pre-mepolizumab treatment), and at 6 and 12 months post-treatment. The need for endoscopic sinus surgery (ESS) and OCS was compared at 12 months pre-mepolizumab and post-mepolizumab treatment.

Patients who were < 18 years old, pregnant, had malignancies, immuno-deficiencies, or received monoclonal antibody therapy in the previous 6 months due to severe asthma, as well as patients who did not have CRSwNP were excluded from the study.

ETHICS STATEMENT

The study protocol was approved by the Ethics Committee (No. 2021.196). The study was conducted in accordance with the principles of the Declaration of Helsinki. All participants were informed about the nature of the study, and written informed consent was obtained.

STATISTICAL ANALYSIS

The data were analysed with IBM SPSS Statistics for Windows 20.0 (IBM Corp., Armonk, NY, USA). The Kolmogorov-Smirnov test was used to test the normal distribution

TABLE 1. Demographic data and general characteristics of the patients ($n = 18$)

Parameter	Value
Age [years] (mean ± SD)	44.33 ±15.90
Sex male, *n* (%)	9 (50%)
BMI (mean ± SD)	26.60 ±4.46
Total IgE [kU/l] (mean ± SD) (pre-mepolizumab treatment)	886 ±1058.12
Eosinophil [cells/µl] (mean ± SD) (pre-mepolizumab treatment)	616.67 ±323.72
Atopy (skin prick/sIgE +), *n* (%)	9 (50%)
FEV_1 (%) (mean ± SD)	72.22 ±13.78
Regular medications for CRSwNP, *n* (%):	
INAH	5 (27.8%)
OAH	14 (77.8%)
INS	16 (88.9%)
LTRA	17 (94.4%)
GINA:	
Step 5 treatment, *n* (%)	18 (100%)
Smoking story, *n* (%):	
Never smoked	11 (61.1%)
Ex-smoker	6 (33.3%)
Current smoker	1 (5.6%)

of the data. Descriptive statistics were expressed as the mean ± standard deviation for the numerical data and as the frequency (*n*) and percentage (%) for the categorical variables. Student's *t* test was used to compare the means of 2 dependent groups. The marginal homogeneity test was applied in the comparison of the proportions of 2 dependent groups. $P < 0.05$ was accepted as statistically significant.

RESULTS

The mean age of the 18 patients (9 (50%) males and 9 (50%) females) who were evaluated in this study was 42.33 ±15.9 years. Nine (50%) patients were atopic. All 18 (100%) patients were undergoing step 5 asthma treatment according to GINA. The demographic data and general characteristics of the patients are shown in Table 1.

The total number of ESSs among the 18 patients prior to mepolizumab treatment was 14 (0.83 ±0.98). None of the patients required ESS in the 12-month period after the mepolizumab treatment. Mepolizumab significantly reduced the number of ESSs ($p = 0.002$). None of the patients received regular systemic steroid or OCS treatment in the one-year period before the mepolizumab treatment. The patients received short-course OCS (< 10 days) treatment during periods of asthma attacks or during periods of increased nasal complaints. The need for short-course OCS decreased significantly after mepolizumab treatment ($p = 0.029$). A comparison of the number patients who underwent ESS and those who received short-course OCS pre-mepolizumab and post-mepolizumab treatment is shown in Table 2.

The ACT, SNOT-22, and nasal symptom scores (VAS) were compared at baseline and at 6 and 12 months. Statistically significant improvements were found in the ACT, SNOT-22, and nasal symptom scores at 6 and 12 months post-treatment when compared to baseline (Table 3). No side effects were observed post-treatment.

DISCUSSION

This was a real-life study evaluating the efficacy of mepolizumab over a 1-year period in patients with CRSwNP who were receiving mepolizumab. In the current study, improvements were observed in the nasal symptom scores and a decrease in the need for OCS treatment. None of the patients needed ESS during the 1-year period under mepolizumab treatment. No side effects related to mepolizumab treatment were observed.

Nasal symptoms such as rhinorrhoea, nasal congestion, and loss of smell affect both quality of life and asthma control in patients with CRSwNP [20]. Significant clinical improvement in patients with CRSwNP was demonstrated by measuring the patient-reported symptoms. In the current study, significant improvements were observed in the nasal symptom scores at 6 and

TABLE 2. Comparison of patients' number of ESS and receiving short-course (< 10 days) OCS pre-mepolizumab and post-mepolizumab treatment

Total ESS number of the patients pre-mepolizumab treatment, *n* (mean ± SD)	14 (0.83 ±0.98)	$p = 0.002$
Total ESS number of the patients during the 12 months post-mepolizumab treatment	0	
Total short-course OCS number of the patients during the 12 months pre-mepolizumab treatment, *n* (mean ± SD)	83 (4.61 ±3.14)	$p = 0.029$
Total short-course OCS number of the patients during the 12 months post-mepolizumab treatment, *n* (mean ± SD)	6 (0.33 ±0.59)	

TABLE 3. Comparison of the ACT, SNOT-22, and nasal symptom scores (VAS) at baseline, and 6 and 12 months post-treatment ($n = 18$)

Parameter	Baseline	6 months	*P*-value	12 months	*P*-value
ACT (mean ± SD)	10 ±4.13	15.78 ±5.14	< 0.001*	20.22 ±3.79	< 0.001*
SNOT-22 (mean ± SD)	59.33 ±15.83	37.28 ±15.35	< 0.001*	25.83 ±10.41	0.001*
Nasal symptom scores (mean ± SD):					
Rhinitis	6.44 ±2.47	4.50 ±1.94	0.002#	2.83 ±1.72	0.001#
Nasal itching	5.67 ±2.56	3.67 ±1.68	0.003#	2.94 ±1.62	0.003#
Sneezing	6.11 ±2.42	3.61 ±1.53	0.001#	2.39 ±1.14	0.001#
Nasal congestion	8.17 ±1.68	6.17 ±1.94	0.001#	5.06 ±1.86	< 0.001#
Loss of sense of smell	8.67 ±1.57	7.89 ±1.87	0.06#	7.39 ±1.94	0.08#
Facial pressure or pain	7.39 ±1.68	5.78 ±1.86	0.002#	4.72 ±1.90	< 0.001#

Symptom scores (VAS score) were scored from 1 to 10 (1 – none, 10 – very severe). *Student's t test, #marginal homogeneity test.

12 months post-treatment when compared to baseline. The only score that was not statistically significant was the improvement in the loss of sense of smell symptoms. In addition, the improvement in the SNOT-22 score was statistically significant. There are real-life studies of the efficacy of mepolizumab on nasal symptoms in patients with CRSwNP in the literature. In a real-life study conducted by Yılmaz *et al.* [21], a significant improvement in the nasal symptom scores after mepolizumab treatment for 24 weeks in patients with OCS-dependent severe eosinophilic asthma with CRSwNP was observed. Similarly, in a real-life study by Detoraki *et al.* [22], mepolizumab improved the nasal and asthma symptoms, and reduced polyp growth in patients with severe eosinophilic asthma and CRSwNP at 12 months post-treatment. In a retrospective series of 6 cases by Chan *et al.* [23], no significant improvement was found in the nasal polyp score with mepolizumab treatment. In a multicentre, randomized, placebo-controlled study, significant improvement in nasal obstruction VAS score was found at 52 weeks with mepolizumab treatment [24].

Severe eosinophilic asthma with CRSwNP patients often receive OCS when their asthma is uncontrolled or their nasal symptoms increase. One of the important findings in this study was that the need of short-course OCS under mepolizumab treatment was significantly reduced. The total number of short-course OCS received by 18 patients in the 12-month period pre-mepolizumab treatment was 83, while this number was 6 in the 12-month period post-mepolizumab. Before mepolizumab treatment, none of patients was receiving regular OCS, and none of patients required long-course OCS (> 10 days) in the 12-month period pre-mepolizumab treatment. In the 12-month period post-mepolizumab treatment, there was no need for long-course OCS. There are studies in the literature showing that mepolizumab reduces the need for OCS. In the study by Yılmaz *et al.* [21], in patients with OCS-dependent severe eosinophilic asthma with CRSwNP, mepolizumab reduced the daily dose of OCS, and OCS treatment was discontinued in 40% of the patients after 24 weeks. The efficacy of mepolizumab has been shown in some studies on patients with OCS-dependent asthma, CRSwNP, and severe eosinophilic asthma [2–4, 15, 25].

In the current study, none of the patients required ESS during the 12-month period post-mepolizumab treatment. Of these 18 patients, 14 required ESS pre-mepolizumab treatment. There are reports in the literature that different doses of mepolizumab reduce the nasal polyp size or the need for ESS. In 2 randomized controlled studies, 750 mg of mepolizumab administered every 4 weeks reduced nasal polyp size and the need for ESS. This dose was higher than the dose of 100 mg every 4 weeks used for severe eosinophilic asthma [14, 26]. In the SYNAPSE study, it was observed that the need for ESS was reduced with 100 mg of mepolizumab [24]. In a 12-month real-life study by Detoraki *et al.* [22], a decrease in the total endoscopic nasal polyp score (TENPS) with the administration of 100 mg mepolizumab every 4 weeks was observed.

The incidence of asthma in patients with CRSwNP is 66%, and the asthma phenotype in these patients is severe asthma [27]. Control of nasal symptoms in patients with CRSwNP also increases asthma control. In this study, significant improvements were observed in the nasal symptom scores and ACT scores over a 12-month period.

There were some limitations to this study. The first was that it was a retrospective study. The second was that a limited number of patients were included. A larger number of patients and control groups are needed to obtain more meaningful clinical results. Despite these limitations, the study was an original real-life study evaluating the effect of mepolizumab on nasal symptoms in patients with persistent CRSwNP, and it provided important data for the literature.

CONCLUSIONS

In the current study, it was observed that mepolizumab administered at a dose of 100 mg every 4 weeks improved nasal symptoms and reduced the need for OCS and ESS in patients with CRSwNP. However, it is necessary to confirm the results obtained in the study with real-life studies involving larger numbers of patients.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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