

The Effect of Antileukotrienes on the Results of Postoperative Treatment of Paranasal Sinuses in Patients with Non-Steroidal Anti-Inflammatory Drug-Exacerbated Respiratory Disease

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Keywords

Sinusitis · Endoscopic sinus surgery · Non-steroidal anti-inflammatory drug-exacerbated respiratory disease · Asthma · Antileukotrienes · Nasal glucocorticosteroids

Abstract

Background: Based on endoscopic examination, chronic rhinosinusitis (CRS) is divided into chronic inflammation with (CRSwNP) or without nasal polyps (CRSsNP). On the basis of the pathomechanism of inflammation, CRS is divided into endotypes. Eosinophilic CRSwNP with coexisting bronchial asthma and hypersensitivity to non-steroidal anti-inflammatory drugs (NSAIDs) is a real therapeutic challenge. **Aim:** Comparative analysis of the results of treatment of patients with CRSwNP, bronchial asthma, or hypersensitivity to NSAIDs (NSAID-exacerbated respiratory disease, NERD), using antileukotrienes (leukotriene receptor antagonists, LTRAs) or intranasal glucocorticoids or both drugs together after endoscopic sinus surgery (ESS). **Material and Methods:** 33 patients (11 male, 33%) with NERD divided into three groups treated with LTRAs or intranasal glucocorticoids or both drugs together were assessed in terms of general well-being, state of pathological changes, and olfactory disorders

using the following tools: Sino-Nasal Outcome Test, Visual Analogue Scale, Brief Identification Smell Test, and Lund-Kennedy score before and at 12 months after surgery. CT assessments were made prior to surgery using the Lund-Mackay scale. **Results:** Comparable efficacy of treatment with nasal steroids and antileukotrienes was found after 12 months of observation of patients. **Conclusions:** The results suggest comparable efficacy of treatment with nasal steroids and antileukotrienes in patients with NERD after ESS. Treatment with montelukast and mometasone has not been shown to be superior to both drugs administered separately.

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Introduction

According to the European Position Paper on Rhinosinusitis and Nasal Polyps 2012 (EPOS 2012) [1], chronic rhinosinusitis (CRS) is recognized when, despite maximal medical therapy, the symptoms such as nasal congestion, nasal secretions, facial pain or olfactory disturbance

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last longer than 12 weeks. Based on an endoscopic examination, two main phenotypes of chronic sinusitis are identified: with (CRSsNP) or without nasal polyps (CRSwNP). Clinical phenotypes do not provide full insight into all underlying cellular and molecular pathophysiologic mechanisms of CRS. This heterogeneity supports the concept that CRS consists of multiple biological endotypes, which might be defined by corresponding biomarkers [2]. Among Caucasians, inflammation with a predominance of Th2 cytokines (IL-4, IL-5, IL-13) and greater numbers of eosinophils, mastocytes, B lymphocytes, and neutrophils in tissues are observed in CRSwNP. Epithelial cytokines such as thymic stromal lymphopoietin, IL-25, and IL-33 support Th2-type inflammation by directly activating innate lymphoid cells-2, which are the source of IL-4, IL-5, IL-9, and IL-13 [3, 4]. Inflammation with a predominance of IL-5 and eosinophilic infiltrates is associated with a severer clinical course, and CRS is often accompanied by bronchial asthma. In the CRSsNP phenotype, the incidence of asthma is approximately 18%, whereas in CRSwNP it is 45–65% [3]. Eosinophilic CRSwNP with coexisting bronchial asthma and hypersensitivity to non-steroidal anti-inflammatory drugs (NSAIDs) is characterized by a higher CT sinus score, multiple sinus reoperations and more frequent use of systemic steroids, constituting a real therapeutic challenge [3, 5–7]. The etiology of the disease has not been explained. It is often associated with disruption of the arachidonic acid metabolic pathway and overproduction of leukotrienes [8, 9]. Feng et al. [10] have found that in patients with NSAID-exacerbated respiratory disease (NERD) eosinophils have a greater capacity to produce and secrete prostaglandins D₂ after aspirin stimulation compared to healthy subjects. The increased production of prostaglandins D₂ activates eosinophils, basophils, and T helper cells. There are studies on the identification of single nucleotide polymorphisms associated with the inflammatory process in patients with hypersensitivity to NSAIDs and the impact of environmental factors on the disease development [11, 12]. Aspirin-exacerbated respiratory disease is “a complex syndrome typified by underlying airway inflammation in which patients experience adult-onset asthma, nasal polyposis/chronic rhinosinusitis, and aspirin/nonsteroidal anti-inflammatory drug (NSAID) sensitivity” [13]. The authors have adopted the term “hypersensitivity to NSAIDs,” which is defined by the European Academy of Allergology and Clinical Immunology as objectively reproducible symptoms that are caused by exposure to a specific stimulus at a dose tolerated by other people. Clinical symptoms are related to the

mucous membranes of the respiratory and digestive tract as well as the skin and can be induced not only by aspirin, but also by one or more NSAIDs [14].

Clinically, 5 types of NSAID hypersensitivity are distinguished:

- NERD
- NSAID-exacerbated cutaneous disease
- NSAID-induced urticaria/angioedema
- single-NSAID-induced urticaria/angioedema or anaphylaxis
- single-NSAID-induced delayed hypersensitivity reactions (SNIDR or NIDHR) [9, 14]

NERD and NSAID-exacerbated cutaneous disease belong to nonallergic hypersensitivity to NSAIDs associated with blocking cyclooxygenase (COX-1), an enzyme that participates in the metabolism of arachidonic acid. Single-NSAID-induced urticaria/angioedema or anaphylaxis manifests itself as urticaria, angioneurotic edema, pruritus and rhinitis, bronchospasm, and even anaphylactic shock. The pathomechanism of this reaction is most likely strongly associated with the immunoglobulin E-dependent immunological mechanism. SNIDR/NIDHR is based on the participation of immunological mechanisms belonging to type IV reactions, in which cytotoxic T lymphocytes play the main role [15]. In the literature, the prevalence of hypersensitivity to NSAIDs is within 0.3–0.9% of the population, increasing to 40% among asthmatics with CRSwNP [16]. Meta-analysis of the literature performed by Rajan et al. [13] in 2014 suggests that the prevalence of NERD in patients with asthma is 14.89%, of those with CRSwNP 9.69%, and of those with CRSsNP 8.7%.

According to Stevens et al. [17], among patients with CRSwNP and coexisting asthma, 16% showed hypersensitivity to NSAIDs. Endoscopic sinus surgery (ESS) in patients with NERD is often extensive and performed repeatedly [9, 17], hence the need to develop the most beneficial postoperative treatment that would allow to avoid reoperation as long as possible. In addition to surgical treatment of patients with hypersensitivity to NSAIDs, it is recommended to use a low-acetylsalicylic acid diet [8, 18], drugs inhibiting cysteinyl leukotriene (CysLT) synthesis (Zileuton) or CysLT receptor blockers (montelukast, zafirlukast), and topical and systemic steroids [8, 19]. Aspirin desensitization is another option [8, 9, 20]. According to the EPOS 2012 guidelines, in addition to ESS, the treatment of patients with CRSwNP and hypersensitivity to NSAIDs is based on local or systemic steroids. Despite the significant importance of disturbances in the metabolism of arachidonic acid leading to the overproduction of proinflammatory CysLTs, drugs blocking

Table 1. Characteristics of treated patients with NERD

	Patients treated with nasal mometasone (group P)	Patients treated with montelukast (group S)	Patients treated with nasal mometasone and oral montelukast (group P + S)
<i>n</i> (%)	11 (33)	14 (42)	8 (24)
Male/female	4/7	5/9	2/6
Age, years			
Male	26–57	26–58	42–56
Female	35–67	36–71	35–68
Duration of bronchial asthma, years	2–40	1–40	2–30
Duration of NSAID hypersensitivity, years	5–23	1–40	2–22
Polyp surgery in the past, <i>n</i> (%)	8 (72)	10 (71)	5 (20)

receptor or leukotriene C4 synthase (LTC4S) are not recommended [1]. This is in contradiction with reports from the literature [6, 8, 12].

The aim of the authors was subjective and objective assessment of the results of treatment of patients with CRSwNP and NERD after ESS with antileukotrienes compared to the treatment using nasal steroids and both drugs together.

Material and Methods

Study Population

333 patients over 18 years of age were admitted and qualified for ESS in accordance with the EPOS 2012 guidelines at the Department of Laryngology and Laryngological Oncology in Katowice-Ochojec in the period from July 1, 2016 to June 1, 2017. Observation involved 37 operated patients reporting CRSwNP, bronchial asthma or hypersensitivity to NSAIDs in the medical interview. 4 out of 37 patients did not complete the study (3 people discontinued observation after the first visit, and 1 patient was administered a systemic steroid on an outpatient basis for 6 weeks after ESS). Clinical characteristics of the patients are shown in Table 1, and the flowchart of the study selection process is shown in Figure 1.

Inclusion Criteria

Patients reporting nasal congestion and/or nasal disturbances combined with facial pain and/or olfactory disorder lasting over 12 weeks, despite applying the maximum treatment according to the EPOS 2012 guidelines, were qualified for ESS. The group of patients with NERD was selected based on the data from the medical interview.

Bronchial asthma was diagnosed in the outpatient setting according to GINA (Global Initiative for Asthma) [21]. Chronic treatment was recommended by a specialist in allergology or pulmonology in outpatient care. Patients with coexisting asthma, depending on its control, took SABA (short-acting beta2 agonists), inhaled corticosteroids combined or not with LABA (long-acting beta2 agonists).

Hypersensitivity to NSAIDs was diagnosed based on the medical history. Patients who reported symptoms such as dyspnea, watery nasal discharge/nasal mucosa edema, acute urticaria or angioedema after taking at least two different chemically nonrelated groups of NSAIDs were described as patients with NSAID hypersensitivity. Aspirin provocations were not performed in patients with evident anamnesis data. Information about unexpected symptoms after taking NSAIDs was provided during the medical interview, not in a questionnaire form.

Exclusion Criteria

Exclusion criteria were as follows: patients under 18 years of age, rhinosinusitis exacerbation, and the use of antileukotrienes or systemic steroids less than 4 weeks prior to the admission to hospital, partially or uncontrolled bronchial asthma, or symptomatic intermittent allergic rhinitis with documented allergy to grass, tree or weed pollen during pollen season. Moreover, patients with SNIRD and those with tumors identified in the histopathological examination of the material collected from the sinuses were excluded from the study.

The actual (the last 4 weeks before the surgical treatment) level of asthma control (good, partial or lack) was assessed. Asthma was considered well controlled when the patient did not report any nocturnal symptoms, daily symptoms were less frequent than twice a week, drugs (SABA) were used less than twice a week, and if the disease had no effect on daily activities.

Methods

Patients were randomly divided into three groups depending on the pharmacological treatment applied after the surgery and continued in outpatient care for the observation period, which was 12 months. Group 1 received 200 µg mometasone nasal spray bid (group S), group 2 used 1 × 10 mg of montelukast qd (group P), and group 3 used both medicines (group S + P). The patients underwent nasal endoscopy aimed at assessing the extent of polyps according to the Lund-Kennedy score. The tomographic examination of the sinuses was performed in each patient, and the inflammatory changes were assessed according to the Lund-MacKay staging system (the degree of opacification in the maxillary, anterior and posterior ethmoid, frontal, and sphenoid sinuses as well as the obstruction of the ostiomeatal complexes were evaluated on both sides on a scale from 0 to 2 – a maximum of 24 points), and then the extent of ESS was planned. The surgery was performed under general anesthesia and

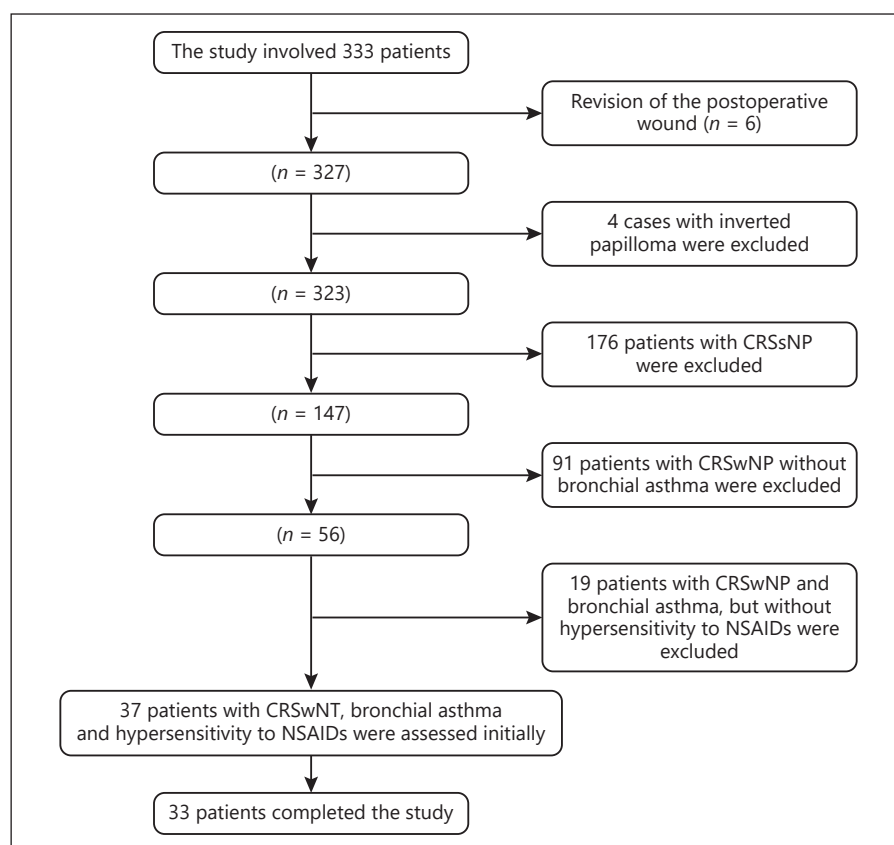


Fig. 1. Flowchart of the study selection process.

controlled hypotension. The examination of the general well-being using the visual analogue scale (VAS) and the scale of subjective assessment of symptoms (well-being) and their impact on the health-related quality of life (SNOT-22, Sino-Nasal Outcome test) as well as an olfactory examination were performed in each patient. Using the VAS, the patients indicated how much the disease hindered their life, on a scale from 1 to 10, where 10 points meant unbearable discomfort and 1 lack of discomfort. A similar assessment of 22 symptoms was made on the basis of the SNOT-22 questionnaire, where points from 1 to 5 were used to assess each discomfort related to the disease (1 meant lack of discomfort). The sense of smell was examined using three scent markers; the patients assessed whether they sensed the smell and whether they could recognize it. For this purpose, the BIST (Brief Identification Smell Test) scale was applied, evaluating 3 scents on a scale from 0 to 5 (0 point – can smell and recognize 3 scents, 1 point – can smell and recognize 2 scents or only recognize 3 scents, 2 points – can recognize 1 scent or smell 2 scents, 3–4 points – can smell 1–3 scents poorly, 5 points – cannot smell and recognize the scents). During nasal endoscopy, the presence of polyps (on a scale from 0 to 3), secretions or mucus edema (0–2 points for each symptom on the right and left side of the nasal cavity) was assessed. Allergies were confirmed by skin prick tests or the presence of specific immunoglobulin E antibodies in the patient's serum. The examinations were performed on an outpatient basis and correlated with clinical symptoms occurring in the patients. The patients were under constant care of an allergist who applied maximum medical therapy; some patients were also subjected to specific allergen immunotherapy. Skin prick or in vitro tests were not per-

formed in every patient admitted to the ward. It was assumed that a positive test without clinical symptoms did not qualify patients to the group with allergies. The patients with clinical symptoms and positive pollen allergy tests were operated outside the pollen season for specific allergens. During the endoscopic surgery, each polyp was collected for histopathological examination to determine the type of inflowing inflammatory cells. Observation of the patients lasted 12 months. Every 10–12 weeks, nasal endoscopy was performed, VAS and SNOT-22 scores were evaluated using the appropriate questionnaire, and the degree of asthma control was checked based on the medical history and inhalation medications used. BIST score was assessed immediately before the surgery and at the fourth (last) visit.

Statistical Methods

Results were expressed as median values with interquartile ranges. Nonparametric tests were used (Kruskal-Wallis ANOVA test and Wilcoxon test). All analyses were performed with a software package (The STATISTICA 12.5). *p* values less than 0.05 were considered significant.

Results

Patients had asthma lasting from 1 to 40 years, hypersensitivity to NSAIDs lasting from 1 to 39 years. Dyspnea after taking NSAIDs was reported by 31 patients, includ-

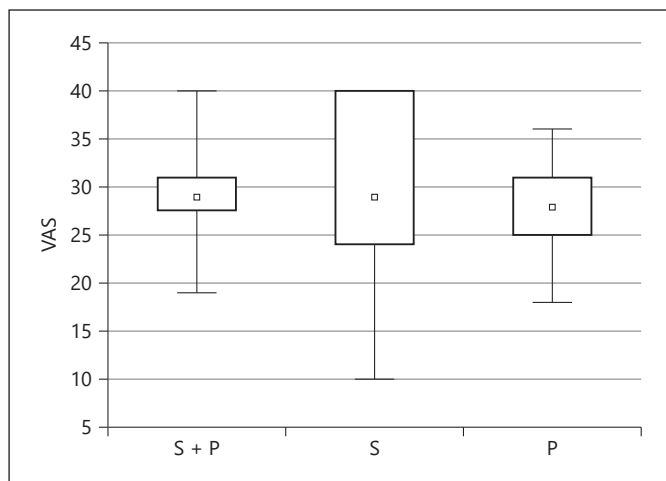


Fig. 2. VAS values at the “zero” visit in all groups. In all comparisons, the *p* value was nonsignificant. Data are shown as median, interquartile and total ranges. “S + P” means the group treated with montelukast and mometasone, “S” indicates the group treated with montelukast, and “P” indicates the group treated with mometasone.

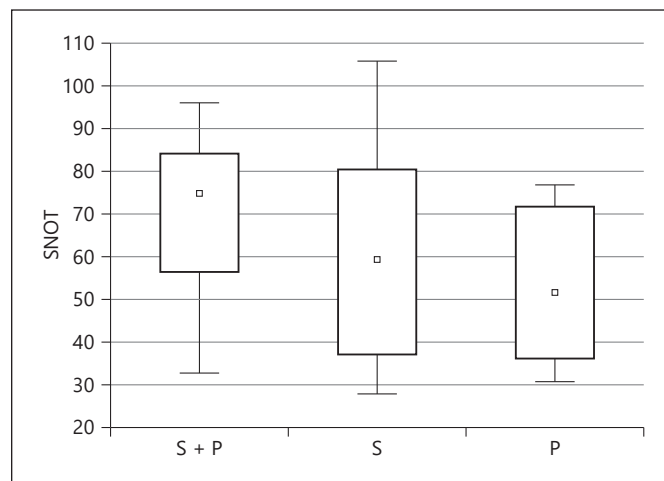


Fig. 3. SNOT-22 values at the “zero” visit in all groups. In all comparisons, the *p* value was nonsignificant. Data are shown as median, interquartile and total ranges. “S + P” means the group treated with montelukast and mometasone, “S” indicates the group treated with montelukast, and “P” indicates the group treated with mometasone.

Table 2. Cell infiltrates in nasal polyps

Group	Cell infiltrates in polyps	
	eosinophilic	mixed eosinophilic-neutrophilic
P	38–74.9% (<i>n</i> = 8)	4.2–19.7% (<i>n</i> = 3)
S	23.7–71.6% (<i>n</i> = 10)	5–12.6% (<i>n</i> = 4)
S + P	34.5–56.1% (<i>n</i> = 8)	–

ing 1 person reporting also rhinorrhea, 1 reporting acute urticaria, and 1 patient reporting lost consciousness. Three patients did not experience dyspnea after taking NSAIDs, in 1 patient acute urticaria was observed, 1 patient had facial edema and rhinorrhea, and another patient lost consciousness. Symptoms occurred after taking aspirin in 8 patients, aspirin and other NSAIDs in 16 patients, and in 10 patients after taking NSAIDs other than aspirin (for more details, see Table 1).

In group P, there were 8 patients previously operated on due to polyps (endoscopically or not), in group S, there were 10, and in group S + P, there were 5 patients. Patients underwent 1–10 operations on polyps and sinuses. The other patients had ESS for the first time.

In 26 cases, eosinophilic and in 7 cases, mixed eosinophilic-neutrophilic (noneosinophilic) infiltrates were found in polyps. In group P, there were 8 cases of eosino-

philia, 3 with mixed infiltrates, in group S, there were 10 cases of eosinophilia, 4 with mixed infiltrates, and in group S + P, there were 8 eosinophilic infiltrates (Table 2).

All three groups were comparable before surgical treatment in terms of endoscopic examination (Lund-Kennedy scale), CT scale (Lund-MacKay scale), BIST, VAS and SNOT-22 scales (Kruskall-Wallis test, *p* > 0.05) (Fig. 2, 3). Patients in all groups, irrespective of the treatment mode, had significantly lower VAS, and SNOT-22 scores 12 months after surgery and the improvement was comparable among all three groups (Kruskall-Wallis ANOVA test, in all comparisons *p* was nonsignificant) (Fig. 4, 5). Patients in all groups, irrespective of the treatment mode, had significantly lower Lund-Kennedy scores 12 months after surgery. However, the improvement was statistically lower in the group treated with both nasal mometasone and oral montelukast than in the groups treated with a single medicine (Fig. 6). The improvement of the Lund-Kennedy score was comparable in groups treated either with montelukast (S) or mometasone (P) (Table 3).

Discussion

According to the EPOS 2012 guidelines, the treatment of patients with CRSwNP and hypersensitivity to NSAIDs, besides ESS, is based on local or systemic steroids. Despite

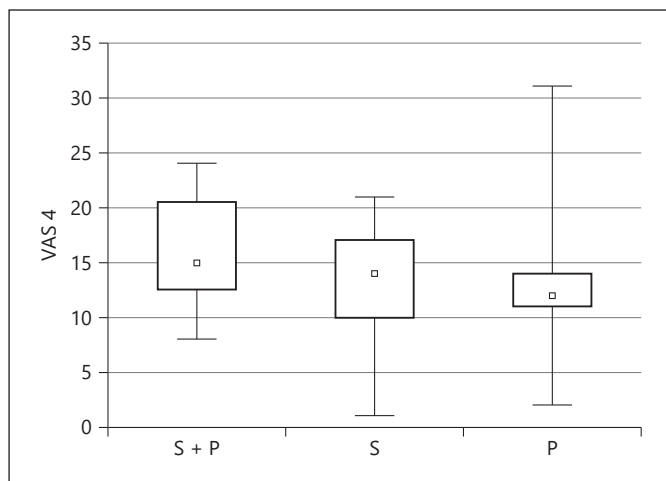


Fig. 4. VAS values at the fourth visit in all groups. In all comparisons, the p value was nonsignificant. Data are shown as median, interquartile and total ranges. “S + P” means the group treated with montelukast and mometasone, “S” indicates the group treated with montelukast, and “P” indicates the group treated with mometasone.

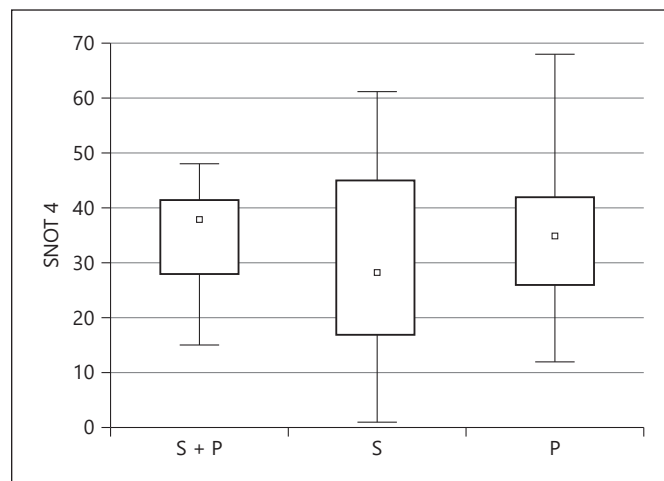


Fig. 5. SNOT-22 values at the fourth visit in all groups. In all comparisons, the p value was nonsignificant. Data are shown as median, interquartile and total ranges. “S + P” means the group treated with montelukast and mometasone, “S” indicates the group treated with montelukast, and “P” indicates the group treated with mometasone.

the significant importance of disturbances in the metabolism of arachidonic acid leading to the overproduction of proinflammatory CysLTs, drugs blocking receptor or leukotriene C4 synthase (LTC4S) are not recommended [1]. This is in contradiction with reports from the literature [3, 6, 8, 12, 16]. The last update of the ARIA document (Allergic Rhinitis and its Impact on Asthma) from 2016 allows to use antileukotrienes (LTRAs) as a supplement to therapy, especially in patients with asthma, in the case of seasonal allergic rhinitis [22]. Contradictory opinions present in the literature prompted the authors of this paper to conduct 12-month observations of patients with CRSwNP and hypersensitivity to NSAIDs, in whom LTRA was included in the treatment after ESS. Statistical analysis of the assessment of the extent of inflammatory changes in the sinuses and subjective values of SNOT-22, VAS and BIST scales showed no differences among the observed groups of patients during the qualification for ESS. The VAS, SNOT-22, BIST and Lund-Kennedy scores were compared between the first and last (fourth) visit, concluding that patients in all groups, irrespective of the treatment mode, had significantly lower VAS and SNOT-22 scores at 12 months after surgery and the improvement was comparable among all three groups (Kruskal-Wallis ANOVA test, in all comparisons p was nonsignificant). There was no improvement in the sense of smell in all the studied groups of patients. Similarly, Gudziol et al. [23], based on their own research, suggest that patients

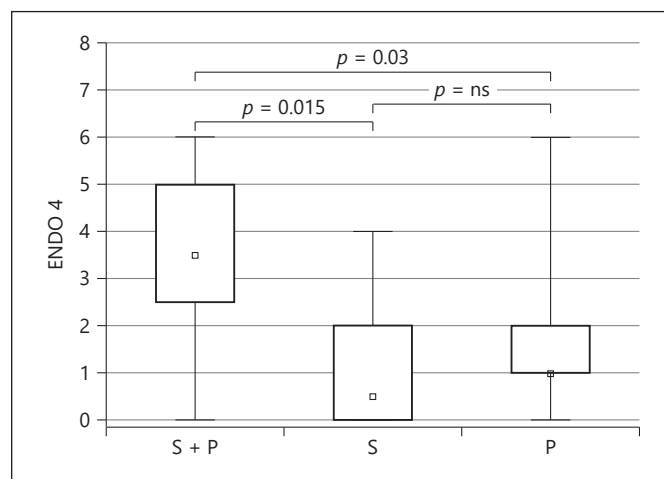


Fig. 6. Endoscopic evaluation at the fourth visit in all groups. Data are shown as median, interquartile and total ranges. “S + P” means the group treated with montelukast and mometasone, “S” indicates the group treated with montelukast, and “P” indicates the group treated with mometasone.

with CRSwNP and hypersensitivity to NSAIDs have an impaired sense of smell significantly more often than patients with CRSwNP but without NSAID hypersensitivity. Several studies have shown that greater olfactory disturbances indicate greater sinonasal disease and correlate with the degree of inflammation in patients with CRSwNP [3]. Based on the literature review, Levy et al. [8] recom-

Table 3. Results of all assessments performed in the three groups

	Patients treated with nasal mometasone (group P-1)	Patients treated with montelukast (group S-2)	Patients treated with nasal mometasone and oral montelukast (group P + S-3)	Comparison between groups P, S and P + S (Kruskall-Wallis ANOVA test)
Lund-MacKay	16 (12–19)	16.5 (13–19)	17 (14–22)	ns
BIST – 0	5 (5–5)	5 (5–5)	5 (5–5)	ns
VAS – 0	29 (26–30.5)	29 (24–40)	28 (27–30)	ns
VAS – 4	12 (11–14)	14 (10–17)	15 (12.5–20.5)	ns
Comparison between visit 0 and 4	0.003	0.001	0.019	
SNOT 22–0	48.5 (35.5–71.5)	59.5 (37–81)	70 (56.5–84.5)	ns
SNOT 22–4	35 (26–42)	28.5 (17–45)	38 (28–41.5)	ns
Comparison between visit 0 and 4	0.005	0.008	0.012	
Endoscope (Lund-Kennedy) – 0	12	12	12	ns
Endoscope (Lund-Kennedy) – 4	1 (1–2)	0.5 (0–2)	3.5 (2.5–5)	0.026
				S + P versus S $p = 0.015$
				S + P versus P $p = 0.03$
				S versus P $p = ns$
Comparison between visit 0 and 4	0.003	0.0009	0.011	

BIST, Brief Identification Smell Test; VAS, Visual Analogue Scale; SNOT-22, Sino-Nasal Outcome test.

mend 6-week LTRA administration to patients with polyps and NERD. In the cited studies, an improvement in sinonasal symptoms, subjective recognition of smells and nasal patency were found. A similar review of literature data made by Adelman et al. [24] highlights the clear improvement in sinonasal symptom severity and frequency, endoscopy score, quality of life, and asthma severity. In postoperative treatment, aspirin desensitization or inclusion of LTRAs are suggested [25, 26]. In the literature cited, in contrast to our observations, an improvement in the sense of smell was found more often together with improved SNOT-22 values. The authors' observations showed a comparable improvement in terms of VAS, SNOT-22, and endoscopy in patients treated with LTRAs and nasal steroids. The results of nasal endoscopy at the fourth visit were worse in the group treated with both drugs than in the other groups, i.e., treated with only one of the drugs. This is surprising, but the therapeutic result in this group was also good. The aforementioned group was the least numerous and had the highest Lund-MacKay score in the beginning, and a decrease in the endoscopic score was from 12 to 6 points, which went hand in hand with the clinical improvement. In the endoscopic assessment of the nose in the Lund-Kennedy scoring system, not only the possible presence of polyps is taken into account, but also swelling of the mucosa, secretions,

which are variable in nature and depend on many factors such as infection, improper cleansing of the nose, harmful working conditions, contact with the allergen, the state of the ciliated epithelium or squamous metaplasia. Thus, a statistically worse endoscopic result in the group treated with mometasone and montelukast does not suggest earlier regrowth of polyps and a greater risk of reoperation, and the demonstration of statistical significance has no clinical significance in this case.

Anselmo-Lima et al. [27] presented studies in which a reduction in polyps and tomographic score after LTRA administration was achieved. These drugs added to nasal steroids improved the nasal symptoms in patients with CRS, with and without polyps. Postoperative montelukast and mometasone combination therapy contributed to a significant reduction in SNOT-22 values and the size of polyps, compared to patients receiving montelukast alone. In the meta-analysis of studies [6] in which LTRAs and nasal steroids were used, a good effect was obtained in patients with CRSwNP, but no statistically significant improvement was observed in patients with NERD. Nasal pruritus, discharge, facial pain, sneezing, and olfactory disorders were evaluated. In the presented work, a statistically significant subjective and objective improvement of the health of patients with CRSwNP and NERD was achieved, regardless of

whether they were treated with LTRAs, nasal steroids or both. This confirms the efficacy of LTRAs in postoperative treatment of patients with polyps and NERD. Another study comparing the effects of LTRAs in patients with eosinophilic hypertrophic sinusitis and patients with CRSwNP without tissue eosinophilia showed an improvement in their sinus disease, and in some cases, the sense of smell was restored [28]. The results of control tests of patients with NERD after ESS are affected by many factors. Patients after reoperations usually have a weakened sense of smell for many years, damaged ciliated epithelium of the mucous membrane and anatomical structures of the nasal cavity, which affects the subjective assessment of patency. Frequent, chronic bacterial colonization and viral infections deteriorate the quality of patients' lives, which is reflected in the results of VAS, SNOT-22, and BIST. Quite often, bad results in subjective studies were not reflected in the examination of the nasal cavity and vice versa, the well-being of the patient did not translate into the endoscopic image. The conducted observations showed no statistically significant advantage of the introduction of LTRA in relation to the steroid, but all patients after 12 months retained patency of the nasal cavity, were not eligible for reoperation and did not report any pain. The effects of treatment with LTRA were comparable to the ones obtained when using topical steroids. Patients in all groups most often complained of the presence of secretions and olfactory disorders. The weaknesses of the study are small groups of patients and many different factors affecting the degree of inflam-

mation of the nasal mucosa. Further observations and testing of this particular group of patients with CRSwNP and NERD are necessary.

Conclusions

Twelve-month pharmacological treatment of chronic sinusitis after ESS significantly improves general well-being and quality of life in patients with NERD irrespective of the treatment mode.

LTRAs and intranasal glucocorticoids have a comparable effect on endoscopic assessment of paranasal sinuses 12 months after ESS.

The concomitant treatment with montelukast and mometasone has not been shown to be superior to both drugs administered separately.

Statement of Ethics

The Ethics Committee was asked whether the treatment and research required special approval. In response, it was stated that the conducted observation and treatment did not require the consent of the Ethics Committee, because they did not differ from the applied standards of treatment of patients after ESS.

Disclosure Statement

The authors have no conflicts of interest to declare.

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