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ORIGINAL PAPER

Treatment effectiveness in paediatric patients with eosinophilic oesophagitis

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ABSTRACT

Introduction: An increase in the incidence of eosinophilic oesophagitis (EoE) in children is being observed worldwide. The diagnosis is confirmed by the morphological examination of the mucosa biopsies. The aim of our study was to evaluate the clinical course of EoE in the first year of diagnosis, and the effectiveness of the first-line treatment of EoE in children.

Material and methods: This single-centre retrospective study included children with EoE newly diagnosed between January 2015 and December 2020. Patients were monitored after initial treatment and 12 months after diagnosis. The study assessed clinical, endoscopic, and histological responses to various therapeutic strategies.

Results: Of the 27 children diagnosed with EoE, 19 were enrolled in the study. The median age of children with EoE was 9 years (range 2–17 years) and the majority were male (84.2%). The most frequent initial treatments were proton pump inhibitors (PPIs) (47.4%), also in combination with an elimination diet (36.8%). Clinical improvement was noted in 73.7% of cases after initial therapy and in 84.2% of patients after 12-month follow-up. However, endoscopic and histological improvement was observed less frequently, in 52.6% and 47.4% of patients, respectively. Forty-two per cent of children with EoE obtained clinical, endoscopic, and histological improvement, and the majority of them received PPIs in mono- or combination therapy with an elimination diet.

Conclusions: Choosing an effective treatment that provides clinical, endoscopic, and histological improvement in patients with EoE is a challenge for clinicians. According to our observations, clinical improvement should not be a single indicator of treatment success; therefore, it is necessary to repeat upper endoscopy and oesophageal biopsy.

KEY WORDS:

children, proton pump inhibitors, elimination diet, eosinophilic oesophagitis.

INTRODUCTION

Eosinophilic oesophagitis (EoE) is a chronic, localized, immune-mediated disease of the upper gastrointestinal track with abnormal oesophageal function and infiltration of inflammatory cells, mainly eosinophils. The pathogenesis of EoE involves the presence of pathogenic aspects such as dysregulated immune response, and genetic and environmental factors [1, 2]. The diagnosis is confirmed by morphological examination of the mucosa biopsies. The minimum number of eosinophils in the oesophageal mucosa necessary for the EoE diagnosis is 15 per high-power field (hpf). In addition, other causes of local eosinophilia should be excluded [3, 4]. According to the latest guidelines, each of the anti-inflammatory therapies (proton-pump inhibitors [PPIs], topical steroid, elimination diet) may be equally effective and constitute the first-line treatment; however, the ideal treatment strategy

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is still undefined [3, 4]. Treatment delay may lead to the development of complications such as fibrosis with narrowing of the oesophagus requiring oesophageal dilation as a treatment option [5, 6].

The prevalence and incidence of EoE in children have continued to rise, according to population-based studies, and vary significantly between studies [1, 7–9]. There are very limited data referring to the natural history of paediatric EoE [10–14]. Monitoring paediatric patients diagnosed with EoE is extremely important and requires not only clinical evaluation, but also repeated endoscopies and oesophageal biopsies based on recent recommendations. However, some deviations from the guidelines have been observed, such as patient or parent refusal, random events, the patient's reluctance to perform multiple endoscopies and general anaesthesia [15]. Despite the growing understanding of the pathogenesis of EoE, there are still few data that can predict individual patient response to treatment in the paediatric population. Moreover, given the chronic nature of the disease, the need for the long-term treatment of EoE may have a significant impact on quality of life. However, there are no current guidelines for the duration of therapy in children. The aim of our study was to evaluate the clinical course of EoE in the first year of diagnosis and the effectiveness of the first-line treatment of EoE in children from north-eastern Poland.

MATERIAL AND METHODS

A retrospective study included children with EoE newly diagnosed in 2015–2020 at a tertiary paediatric teaching hospital in the north-eastern part of Poland. The study protocol was approved by the local Ethics Committee and conformed to the tenets of the Declaration of Helsinki. We obtained data from follow-up visits at the gastroenterology outpatient clinic or hospitalizations at the gastroenterology department carried out 3 and 12 months after the diagnosis. The chart review of all paediatric patients diagnosed with EoE during the study period is presented in Figure 1.

The EoE diagnosis was based on the recent guidelines and required oesophageal symptoms and oesophageal eosinophilia defined as at least 15 eosinophils per hpf [3]. Patients who had other causes of oesophageal eosinophilia (hypereosinophilic syndrome, drug hypersensitivity, connective tissue disorders) or presented a prominent eosinophilic infiltrate in gastric or duodenal biopsies or were treated with systemic steroids due to other disease were excluded from the analysis. Patients diagnosed with EoE in a medical facility other than our department or without follow-up visits were also not enrolled in the study.

Demographic data, presenting symptoms, biopsy results, and endoscopic findings were collected at baseline and at least 2 follow-up visits. During the diagnosis and follow-up visits patients/guardians filled in a standard symptom questionnaire, and then the information was completed by physicians and included in the patients' medical records. Patients/guardians were asked to rate the severity of symptoms after treatment as "clinical improvement" or "no clinical improvement". Clinical improvement was defined as a remission of clinical symptoms. Patients with persistent clinical symptoms of the same or increased severity compared to the time of diagnosis were included in the "no clinical improvement" group. Laboratory results routinely performed at each visit were also reported. Initial upper gastrointestinal endoscopy with oesophageal biopsy was performed in each enrolled patient. According to our general clinical practice, all patients were instructed to undergo control upper gastrointestinal endoscopy with oesophageal biopsy after a 6- to 12-week initial course of therapy, as recommended in the guidelines [3]. Among patients who underwent control endoscopy, it was assessed whether there was "endoscopic improvement", defined as the resolution or reduction in severity of lesions compared to the previous examination, as noted in the patient's medical records, or "no endoscopic improvement", defined as the persistence of previously identified abnormalities.

Oesophageal biopsies at 2 or more levels were taken during diagnostic endoscopy. All samples were analysed by the same pathologist. Among patients who underwent

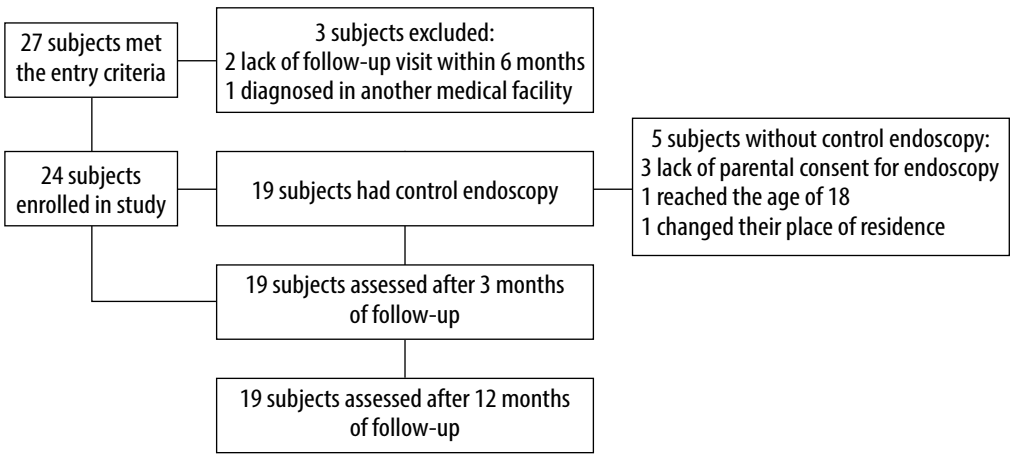

FIGURE 1. Flow diagram of patients' enrollment

TABLE 1. Demographic data and comorbidities in EoE patients

Factor	Baseline ($n = 19$)	Follow-up after 12 months ($n = 19$)
Age (years), median (range)	9 (2–17)	NA
Male, *n* (%)	16 (84.2)	NA
BMI < 10th percentile, *n* (%)	3 (15.8)	1 (5.3)
BMI >90th percentile, *n* (%)	2 (10.5)	0 (0.0)
Allergy, *n* (%)	16 (84.2)	17 (89.5)
Food allergy, *n* (%)	10 (52.6)	10 (52.6)
Inhaled allergy, *n* (%)	10 (52.6)	11 (57.9)
Atopic dermatitis, *n* (%)	2 (10.5)	2 (10.5)
Diabetes mellitus type 1, *n* (%)	0 (0.0)	0 (0.0)
Celiac disease, *n* (%)	5 (26.3)	5 (26.3)
IBD, *n* (%)	4 (21.1)	4 (21.1)
GERD, *n* (%)	3 (15.8)	NA

BMI – body mass index, IBD – inflammatory bowel disease, GERD – gastroesophageal reflux disease, NA – not applicable

a control oesophageal biopsy, it was assessed whether there was a histological remission. "Histological remission" was defined as up to 14 eosinophils/hpf in all oesophageal biopsy specimens, and "no histological remission" was defined as ≥ 15 eosinophils/hpf in any oesophageal biopsy sample, similarly to other studies [16–18].

To assess the effectiveness of the first-line therapy, patients were assigned to the 4 groups depending on the treatment used: 1) PPIs, 2) elimination diet, 3) PPIs and elimination diet, 4) other therapy. PPI therapy was based on omeprazole (1–2 mg/kg daily). An elimination diet was based on an empiric 6-food (milk, egg, soy, wheat, fish, nuts) elimination (SFED) or allergy testing-based food elimination (ATBD). The time frame between the beginning of each change in therapeutic intervention and analysis of its impact on the course of EoE was at least 8 weeks.

Due to the small size of individual groups, the statistical analysis was abandoned.

RESULTS

From January 2015 to December 2020, 27 children with EoE were diagnosed in our department. On the basis of the inclusion and exclusion criteria, initially 24 children were enrolled in the study. All patients had a follow-up visit within 3 months and 12 months. Clinical follow-up was achieved in 100% of EoE patients, while endoscopic follow-up was achieved only in 79.2% of EoE patients (Figure 1). The reasons for the failure to perform the control endoscopy to assess therapeutic success were the lack of parental consent for endoscopy ($n = 3$), the patient's transfer to a gastroenterological care for adult patients due to reaching the age of 18 years ($n = 1$), and the change of the patient's place of residence ($n = 1$). Only patients undergoing follow-up endoscopy ($n = 19$) were included in the subsequent stages of the study due to the need to simultaneously assess the clinical, endoscopic, and histological response.

CLINICAL OUTCOME

Demographic data and coexisting diseases at the time of diagnosis and after 12-month follow-up are presented in Table 1.

At the time of EoE diagnosis, the median age of children was 9 years (range 2–17 years) and the majority were male (84.2%). Allergic diseases occurred in 84.2% of patients, among them the most common were food and inhalation allergies (noted in 52.6% of cases). Among inhaled allergies, rhinoconjunctivitis was predominant, observed in 47.4% of children with EoE. In 3 patients (15.8%), on the basis of the diagnostic tests performed, no allergic disease was diagnosed. During the 12-month follow-up, one more patient was diagnosed with rhinoconjunctivitis. Abnormal gastroesophageal reflux in 24-h oesophageal pH-monitoring was observed in 15.8% of patients with EoE at the time of EoE diagnosis. After 12 months of follow-up, pH monitoring was not repeated.

The most frequently used initial treatment was PPIs (47.4%), followed by combination therapy with PPIs plus an elimination diet (36.8%) and only an elimination diet (10.5%) (Table 2).

In one case, the child's parents did not consent to the standard form of EoE treatment (8-year-old female diagnosed with ulcerative colitis, treated with mesalazine). None of the children with EoE were treated with steroids or an elemental formula as initial therapy.

TABLE 2. Treatment strategy for patients prescribed during the diagnosis and at the control visits in the 3rd and 12th month

Treatment	Baseline ($n = 19$)	Follow-up after 3 months ($n = 19$)	Follow-up after 12 months ($n = 19$)
Proton pump inhibitors (PPIs), *n* (%)	9 (47.4%)	8 (42.1%)	7 (36.8%)
Elimination diet, *n* (%)	2 (10.5%)	1 (5.3%)	0 (0.0%)
Proton pump inhibitors (PPIs) and elimination diet, *n* (%)	7 (36.8%)	8 (42.1%)	7 (36.8%)
Proton pump inhibitors (PPIs) and elimination diet and topical steroids, *n* (%)	0 (0.0%)	1 (5.32%)	3 (15.8%)
Elimination diet and topical steroid, *n* (%)	0 (0.0%)	0 (0.0%)	1 (5.3%)
Other treatment, *n* (%)	1 (5.3%)	1 (5.3%)	1 (5.31%)

TABLE 3. Clinical manifestations at baseline, at diagnosis, and at the control visits in the 3rd and 12th month

Symptoms	Baseline ($n = 19$)	Follow-up after 3 months ($n = 19$)	Follow-up after 12 months ($n = 19$)
Abdominal pain, *n* (%)	10 (52.6)	6 (31.6)	1 (5.3)
Failure to thrive, *n* (%)	4 (21.1)	0 (4.2)	0 (0.0)
Dysphagia, *n* (%)	6 (31.6)	3 (15.8)	2 (10.5)
Halitosis, *n* (%)	1 (5.3)	0 (0.0)	1 (5.3)
Vomiting, *n* (%)	1 (53.0)	1 (5.3)	1 (5.3)
Lack of appetite, *n* (%)	2 (10.5)	0 (4.2)	0 (0.0)
Heartburn, *n* (%)	2 (10.5)	1 (5.3)	1 (5.3)
Nausea, *n* (%)	1 (5.3)	0 (4.2)	1 (5.3)
Weight loss, *n* (%)	1 (5.3)	0 (0.0)	0 (0.0)
Eructation, *n* (%)	0 (0.0)	0 (0.0)	0 (0.0)
Regurgitation, *n* (%)	2 (10.5)	0 (0.0)	0 (4.2)
Chest pain, *n* (%)	0 (0.0)	0 (0.0)	0 (0.0)
Clinical improvement, *n* (%)	–	14 (73.7)	16 (84.2)
No clinical improvement, *n* (%)	–	5 (26.3)	3 (15.8)

Treatment was intensified in patients who showed no improvement. Three months after diagnosis, 2 children required intensification of treatment, and in the subsequent 9 months the treatment was changed in 3 other children. At first follow-up visit, those patients who achieved clinical remission after first-line therapy with PPI alone or in combination with an elimination diet were advised to continue their current treatment. Patients without clinical improvement (26.3%) required intensification of treatment as a combination of elimination diet, PPIs, and topical steroids (oral viscous budesonide) or received a combination of elimination diet and PPIs. At the follow-up visit 12 months after diagnosis of EoE, almost half of the patients (36.8%) still required a combination therapy consisting of PPIs and elimination diet to maintain remission. Due to no improvement 12 months after diagnosis, 3 patients (15.8%) required triple therapy consisting of PPIs, an elimination diet, and topical steroids, and one patient (5.3%) was treated with an elimination diet and topical steroids. Further evaluation of the treatment used at 12 months of follow-up was not the purpose of this study due to the time-limited analysis. In the group with clinical, endoscopic, and histological improvement, the treatment continuation was associated with the maintenance of the therapeutic effect.

The two most frequently reported symptoms at the time of EoE diagnosis were abdominal pain (52.6%) and dysphagia (31.6%) (Table 3).

Abdominal pain was still the most frequent symptom at 3 months of follow-up, and it was reported by only one patient after 12 months. Although dysphagia resolved in 15.8% of patients 3 months after diagnosis of EoE, it was the most common persistent symptom after 12 months of follow-up (10.5%). Clinical improvement was reported in 73.7% of patients after 3 months and in 84.2% after 12 months (Table 3). Three patients, who showed no clinical improvement after 12 months of follow-up, were initially treated with various treatment regimens (elimination diet, PPIs, and combination therapy with PPIs and elimination diet) (Suppl Table 1).

ENDOSCOPIC, HISTOLOGICAL, AND BIOCHEMICAL RESULTS

The endoscopy and histology findings at baseline and follow-up are shown in Table 4.

At the time of diagnosis, the most common endoscopic findings were longitudinal furrowing (84.2%), decrease vascular pattern (42.1%), and whitish exudates (26.3%). The median number of eosinophils/hpf at diagnosis was 30. *Helicobacter pylori* gastric infection was diagnosed in 26.3% of patients with EoE. Despite the recommendation that every patient with EoE should have a follow-up endoscopy after 6 to 12 weeks of initial treatment, the mean time frame between the beginning of therapeutic intervention and the endoscopic/histology control was 18 weeks. The main reason for endoscopy delay was failure to attend follow-up visits (it was also affected by the COVID-19 pandemic). Eight patients (42.1%) did not comply with the timing of a control endoscopy. Among them, clinical improvement was observed in 6 children.

Persisting endoscopic EoE symptoms, despite treatment, included longitudinal furrowing, decrease vascular pattern, whitish exudates, and trachealization. On the other hand, the oesophageal erosion, mucosal oesophageal erythema, papules, and oesophageal polyps completely resolved. None of the patients had oesophageal stricture at baseline and in the control endoscopy. Endo-

scopic improvement was observed in 52.6% of patients, who were treated with PPIs in the majority of cases. On the other hand, lack of endoscopic improvement was observed in 47.4% of patients, also after PPI therapy in 80% of children (Suppl Table 2).

Taking into account the histological assessment, as many as 52.6% of patients did not achieve remission despite PPI treatment in most cases (Table 4, Suppl Table 3). Moreover, none of the children on an elimination diet developed histological response. In 4 patients, oesophageal eosinophilia (≥ 15 eosinophils/hpf) persisted despite combination therapy with PPIs and an elimination diet; however, 3 of them became asymptomatic. Looking for the relationship of any factors with histological results, we found no differences in demographics, comorbidities, and laboratory tests between children with and without histological improvement (Suppl Table 4). Interestingly, most of the children without histological remission attained clinical improvement (80.0%), and 10% of them showed also endoscopic improvement (Figure 2).

Forty-two per cent of patients who obtained clinical, endoscopic, and histological improvement were treated with PPIs, in mono- or combination therapy in the majority of cases (Figure 2). However, almost the same percentage of patients (37%) with similar treatment achieved only clinical improvement, without endoscopic and histological remission. On the other hand, one patient after PPI therapy still reported symptoms despite endoscopic and histological remission. No improvement of any 3 assessed aspects was noted in 10.5% of children receiving the elimination diet alone or in combination with PPIs (Figure 2). Looking for a possible link between the clinical symptoms at the time of diagnosis and lack of histological improvement, we noted that only abdominal pain was more frequently reported in a group without histological improvement (70.0% vs. 33.3%). Due to persistent dysphagia in 3 children after the initial therapy with an elimination diet alone or in combination with PPIs, and lack of endoscopic and histologic remission, the treatment was intensified (in one case an elimination diet was added, in other 2 cases, triple treatment was applied, i.e. PPIs, elimination diet, and local steroid; Table 2). However, dysphagia was still reported after 12 months of follow-up by 2 children. In one case without conventional EoE treatment, clinical, endoscopic, and histological improvement was observed (8-year-old girl with ulcerative colitis treated with mesalazine). The remaining IBD patients received mesalazine for treatment. Due to EoE, they also received PPIs in monotherapy or in combination with an elimination diet. In our department, none of the patients diagnosed with IBD and EoE was treated with systemic steroids.

No case of adverse reaction related to the used treatment was reported. None of the children with EoE required endoscopic food removal. However, one patient needed an emergency room visit for upper gastrointestinal bleeding following an ambulatory endoscopy without oesophageal dilation. Twenty-five per cent of patients required more frequent visits to the gastroenterologist due to EoE.

TABLE 4. Oesophagogastroduodenoscopy findings and histology results at the time of initial and control endoscopies

Endoscopy and histology findings	Baseline ($n = 19$)	Follow-up ($n = 19$)
Longitudinal furrowing, *n* (%)	16 (84.2)	15 (78.9)
Decrease vascular pattern, *n* (%)	8 (42.1)	7 (36.8)
Whitish exudates, *n* (%)	5 (26.3)	4 (21.1)
Oesophageal erosion, *n* (%)	4 (21.1)	0 (0.0)
Mucosal oesophageal erythema, *n* (%)	3 (15.8)	0 (0.0)
Papules/plaques, *n* (%)	2 (10.5)	0 (0.0)
Trachealization/rings, *n* (%)	3 (15.8)	3 (15.8)
Oesophageal polyp, *n* (%)	1 (5.3)	0 (0.0)
Oesophageal hernia, *n* (%)	2 (10.5)	2 (10.5)
Oesophageal stricture, *n* (%)	0 (0.0)	0 (0.0)
Helicobacter pylori infection, *n* (%)	5 (26.3)	0 (0.0)
Endoscopic improvement, *n* (%)	NA	10 (52.6)
No endoscopic improvement, *n* (%)	NA	9 (47.4)
Peak eosinophil count/hpf median (range)	30 (15–45)	20 (0–50)
Histological remission, *n* (%)	NA	9 (47.3)
Lack of histological remission, *n* (%)	NA	10 (52.6)

hpf – high-power field

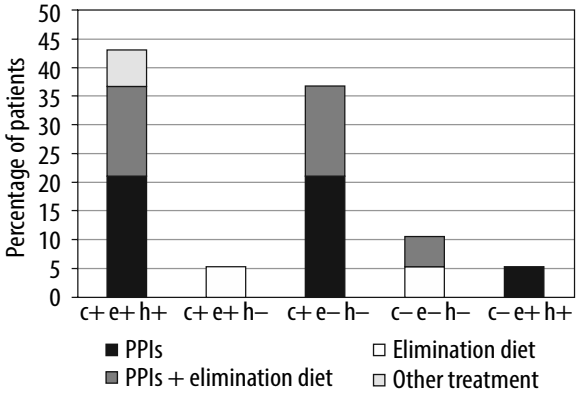

FIGURE 2. Clinical, endoscopic, and histological response of patients

c – clinical, e – endoscopic, h – histological, PPIs – proton pump inhibitors
The individual colours are assigned to the selected therapeutic options. Obtaining improvement is marked as "+" and no improvement as "–".

The results of laboratory tests during the study are presented in Suppl Table 5.

Most of the children had eosinophilia at the time of EoE diagnosis (70.8%), and its incidence decreased after treatment, but still it was found in 42% of patients after 12 months of follow-up (Suppl Table 5). Blood results such as C-reactive protein (CRP), haemoglobin (Hb), and platelets (PLT) were within normal limits at each stage of the patient's assessment (at diagnosis and at 3 and 12 months).

The clinical, endoscopic, and histological results of patients classified into age categories (2–9 years and 10–17 years) are shown in Suppl Table 6.

DISCUSSION

Despite the worldwide increase in the incidence of EoE, knowledge of the natural history of the disease is still limited [3]. Our retrospective analysis presented the course of EoE in children during first year after initial EoE therapy. EoE has a progressive nature and requires chronic treatment in most patients, to improve not only clinical symptoms but also to induce endoscopic and histological remission [19]. Appropriate therapy protects against both disease recurrence and EoE complications related to tissue remodelling, such as fibrosis with thickened walls, abnormal fragility, and strictures [3, 4, 20]. Due to the lack of direct recommendations regarding the choice of a pharmacological or dietary approach, it is important to evaluate different therapeutic strategies in patients with EoE.

In our study, first-line therapy mainly included PPIs as monotherapy or in combination with a diet. According to the latest guidelines, the treatment effectiveness of PPIs may range from 30% to 70% [4, 21, 22]. Clinical improvement was observed in the majority of our patients, as in other reports [13, 23–25]. A very high percentage (95%) of clinical responses after administration of PPIs or H2 blockers was reported in Korean children with EoE. However, there is no post-treatment endoscopic and histological response data in this study [13]. The higher percentage of positive clinical responses among patients receiving acid-blocking drugs compared to our study may be related to the study population (Asian vs. Caucasian). However, in other studies PPIs were less effective in the induction of a clinical response than an elimination diet or topical steroids [10, 16].

The most frequently reported symptoms by our patients at the time of EoE diagnosis were abdominal pain and dysphagia. Abdominal pain is not a specific symptom of EoE, in contrast to dysphagia, which was reported mainly by adolescents in our study, who were already able to describe this symptom. The prevalence of various symptoms in different age groups (infants, children, adolescents) among paediatric patients with EoE is observed [26]. In our study, dysphagia was the most common persisting symptom after one year of follow-up, with an associated lack of endoscopic and histological improvement after initial therapy. The lack of clinical, endoscopic, and histological improvement was the reason for intensification of treatment. Due to the time frame of the study, we do not have data on endoscopic and histological improvement after treatment modifications. It seems that the presence of dysphagia at the time of EoE diagnosis may be a predictor of poor response to treatment, and therefore the patient may require more frequent monitoring in the event that the treatment needs to be intensified.

Taking into account the histological remission in our study, PPIs were effective in half of the children receiving this treatment, similarly to other reports in which PPIs were effective in 57.1–66.1% of paediatric patients [11, 23]. In a meta-analysis concerning both children and adults, the overall efficacy in inducing histological remission of EoE (< 15 eosinophils/hpf) for any PPIs at any dose was 50.5%, with no statistical significance between the age groups [22]. Data provided by a multi-centre retrospective cohort study showed that only 29.7% of patients did not respond to PPIs according to histological outcome [15]. Also in the study by Bora *et al*., the effectiveness of PPIs was higher than in our study (74–81%); however, the majority of included patients were treated with different regimens of combination therapy (PPIs and dietary elimination or swallowed topical corticosteroids) [24]. Other authors found that younger age and lower BMI values were risk factors for histological failure to respond to PPI treatment, but these observations were made in adult EoE patients [27]. We did not find such associations in our paediatric study. Moreover, we did not observe any association between comorbidities and treatment effectiveness. Another important factor that can influence the response to treatment is patient compliance. The assessment of medical adherence was not the aim of our study, but it was already reported that 82.3 ±22.4% of patients had documented self-reported adherence to the prescribed therapy [28]. However, in the group of children with sustained long-term clinical improvement, non-compliance was statistically less frequently observed than in the group of non-responders. Differences in the effectiveness of PPIs between studies may also be affected by the various ages of the included patients, the duration of treatment, or use of distinct types and doses of PPIs. It is worth mentioning that the long-term effect of PPI therapy in the form of improvement of clinical symptoms in the period of 3.0 ±2.4 years of follow-up was noted in children with EoE [25].

Many studies have observed a weak correlation between clinical and histological improvement in children and adults [17, 23, 29]. In our analysis, clinical remission was observed more often than endoscopic or histological remission, as in other studies. Histological improvement is more difficult to achieve and requires a longer period of monitoring and treatment. Therefore, resignation from control endoscopy with oesophageal biopsy in asymptomatic patients does not seem advisable and may lead to persistent inflammation, oesophageal remodelling, and progression to stricture. On the other hand, in one case we observed endoscopic and histological improvement during PPI treatment despite persistent clinical symptoms. Maintenance of clinical symptoms despite histological improvement (< 15 eos/hpf) was also observed in another study conducted in adult EoE patients [30]. In our study, only 57.9% of patients complied with the time of follow-up endoscopy. Loss of follow-up endoscopy has also been reported in other studies [17, 19, 29, 31].

In a retrospective, registry-based cohort study, control biopsy after 8 weeks of PPI treatment was performed in 67% of patients, with a higher rate in those treated with high-dose PPIs [17]. Shukla-Udawatta *et al.* noted that initially only one-third of paediatric patients with EoE had control endoscopy [31]. Medical adherence seems to be a serious problem among adolescents; therefore, in this age group the role of proactive education in the field of EoE and the need for treatment should be emphasized [11]. On the basis of publications, the lack of follow-up endoscopy is a significant clinical problem in patients with EoE, which also increases the risk of underestimating the scale of the problem in clinical trials. Less invasive methods of assessing EoE activity to reduce the need for repeat endoscopic biopsy may help to better monitor the patient. This is especially important in the paediatric population, where general anaesthesia is required for the procedure in many cases. As a non-invasive marker reported by some authors, a high absolute blood eosinophil count was associated with persistent post-treatment oesophageal eosinophilia, similarly to our observations [27, 32]. Therefore, combination therapy may be considered in patients with high blood eosinophil levels at the time of diagnosis of EoE. However, more research is needed to determine the exact blood eosinophil cut-off point that indicates a higher risk of treatment failure.

An elimination diet, as one of the treatment options, was used in 10.5% of children with EoE in our study. The reason for the low percentage of children with EoE receiving an elimination diet as monotherapy in the first-line therapy was probably the difficulty of strict adherence to medical recommendations by the patients (most of the school-age patients). In a prospective study, the effectiveness of an elimination diet was assessed at 36% [33]. On the other hand, in a retrospective study from Slovenia, almost 80% of children developed clinical remission during treatment with an elimination diet (SFED or ATBD). In addition, the intensification of treatment by adding a topical steroid led to an improvement in symptoms in another 15% of children, while in about 5% of cases the symptoms persisted despite the combination treatment [12]. Currently, new therapeutic options, such as budesonide effervescent tablets or monoclonal antibodies (including mepolizumab, reslizumab, dupilumab, omalizumab, and vedolizumab) are of great interest, but they are still not widely available [34].

The strength of our study is the analysis of paediatric patients with clearly defined demographic and clinical data. In addition, clinical symptoms were analysed not only at the time of diagnosis, but also after initial treatment. Additionally, we assessed the response to initial treatment – clinical, endoscopic, and histological. The main limitation of our study was the small number of enrolled patients, which was due to the low number of diagnosed children. This was the reason why a statistical analysis comparing the effects of different treatment strategies between groups was not performed.

CONCLUSIONS

Treatment options of EoE should be individually tailored to achieve lasting compliance. Despite a good clinical response, less than half of the children enrolled in the study achieved histological improvement. According to our observation, clinical improvement should not be a single indicator of treatment success; therefore, it is necessary to repeat upper endoscopy and oesophageal biopsies. Further studies including larger cohorts of patients with a longer follow-up period are needed to investigate the treatment effectiveness in paediatric patients with EoE.

DISCLOSURE

The authors declare no conflict of interest.

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