Original paper

Quality of life in asthmatic children and their caregivers after two-year treatment with omalizumab, a real-life study

Anna Sztafińska[1], Joanna Jerzyńska[1], Włodzimierz Stelmach[2], Katarzyna Woicka-Kolejwa[1], Iwona Stelmach[1]

[1]Department of Pediatrics and Allergy, Medical University of Lodz, Copernicus Memorial Hospital, Lodz, Poland
[2]Department of Social and Preventive Medicine, Medical University of Lodz, Lodz, Poland

Adv Dermatol Allergol 2017; XXXIV (5): 439–447
DOI: https://doi.org/10.5114/ada.2017.71109

Abstract

Introduction: Omalizumab, a monoclonal anti-immunoglobulin E antibody, has been successfully used as a supplementary therapy to improve asthma control in children aged ≥ 6 years with severe persistent allergic asthma.
Aim: To demonstrate the quality of life in children with severe asthma and their caregivers, and changes from baseline in forced expiratory volume in 1 s (FEV_1) and daily inhaled corticosteroids (ICS) dose after 2-year treatment with omalizumab.
Material and methods: Participants were seen in the clinic at enrollment (visit 1), after 16 weeks (visit 2), after 52 weeks (visit 3) and after 104 weeks (visit 4) of treatment with omalizumab. We evaluated lung function, ICS use and the quality of life with the Pediatric Asthma Quality of Life Questionnaire (PAQLQ) and the Pediatric Asthma Caregiver's Quality of Life Questionnaire (PACQLQ).
Results: Nineteen children and caregivers were enrolled. Significant improvement was observed in PAQLQ and PACQLQ scores, both in all domains and in total scores. Significant differences were found between the first and the other visits. A positive correlation between PAQLQ and PACQLQ at the first and at the second visit was found, 63.3% of patients achieved reduction in ICS doses. We did not notice any significant improvement in FEV_1.
Conclusions: The improvement in quality of life in asthmatic children and adolescents observed after omalizumab correlates with the improvement of quality of life in caregivers, reduction in ICS use but not with FEV_1.

Key words: asthma, omalizumab, quality of life, children.

Introduction

Asthma has a strong emotional impact which may be expressed in social constraints, depression, insomnia, stress or even affective disorders for all members of the family [1, 2]. There are questionnaires referring to this area assessing the quality of life in children with severe asthma [3–6]; the Pediatric Asthma Quality of Life Questionnaire – PAQLQ (designed by Juniper) focuses on typical childhood issues [7]. The Pediatric Asthma Caregiver's Quality of Life Questionnaire (PACQLQ) assesses quality of life in caregivers of asthmatic children [8]. In our center, PAQLQ and PACQLQ were previously validated [9, 10].

Omalizumab (OMB), a monoclonal anti-immunoglobulin E antibody, has been successfully used as a supplementary therapy to improve asthma control in adults and children aged ≥ 6 years with severe persistent allergic asthma [11–13].

Our primary end point was assessment of the quality of life in severe asthmatic children and adolescents and their caregivers after 16, 52 and 104 weeks of treatment with OMB. The secondary end points were the correlations between changes in the quality of life and changes from baseline in forced expiratory volume in 1 s (FEV_1) and inhaled corticosteroids (ICS) use in studied children.

Aim

Moreover, we analyzed any correlation between age, sex, total IgE level, specific sensitization, number of eosinophils in blood, body mass index (BMI) and response to OMB therapy.

Address for correspondence: Prof. Iwona Stelmach MD, PhD, Department of Pediatrics and Allergy, Medical University of Lodz, Copernicus Memorial Hospital, 62 Pabianicka St, 93-513 Lodz, Poland, phone: +48 42 689 59 72, fax: +48 42 689 59 73, e-mail: alergol@kopernik.lodz.pl
Received: 24.02.2016, **accepted:** 24.06.2016.

Material and methods

Patients

This was a prospective, open, uncontrolled, observational study. We identified patients, aged 7–18 years (not randomly selected), with severe uncontrolled allergic asthma who attended our Allergic Outpatient Clinic from January 2011 to March 2015. The diagnosis of asthma was universally established, according to the standard definitions in the latest Global Initiative for Asthma (GINA) guidelines [11].

All patients fulfilled the criteria for anti-IgE therapy [11]. At least 6 months before treatment, patients underwent long-term therapy with high-dose inhaled corticosteroids (daily dose of ICS > 1000 μg of beclomethasone dipropionate or equivalent for adolescents and > 400 μg for children aged 6–11 years [11]) in combination with a long-acting β2-agonist and a leukotriene receptor antagonist. Omalizumab was administered according to a dosage table that considers the patient's body weight (kg) and total IgE levels (IU/ml).

Written consent was obtained from all participants and their parents.

Study design

This was a 104-week cohort study. Children or adolescents and their parents/caregivers were seen in the clinic at enrollment (visit 1), after 16 weeks (visit 2), after 52 weeks (visit 3) and after 104 weeks of treatment with OMB (visit 4). At each visit, the Polish version of PAQLQ by Juniper was assessed for each child. Each caregiver received PACQLQ in every clinic visit and completed it alone. Parents were absent when the interviews with their children were performed. The study was approved by the Ethics Committee of the Medical University of Lodz, Poland.

At each visit, the efficacy assessment included physician's overall assessments of treatment and lung function (FEV_1) and the ICS dose were evaluated. The doses of ICS were modified according to GINA recommendations which advise to step down the controller treatment due to improvement of asthma control. Pulmonary function testing was performed using a Master Screen unit (Erich Jaeger GmbH-Hochberg, Germany). Flow-volume curves were performed according to the American Thoracic Society standards. Relative changes from baseline in FEV_1 and daily ICS doses were assessed after 16, 52 weeks and 104 weeks. Adherence to anti-asthma therapy was systematically assessed at each visit. The design of the study is shown in Figure 1.

Pediatric Asthma Quality of Life Questionnaire (PAQLQ)

PAQLQ is a disease-specific quality of life questionnaire which contains 23 questions, grouped into 3 domains: Symptoms, Emotional function, Activity limitations.

Responses to each item in the PAQLQ are given on a 7-point scale where 1 represents severe impairment and 7 represents no impairment. Individual items within the PAQLQ score were equally weighted and results expressed as the mean score per item for each of the domains as well as for overall quality of life. Differences in the PAQLQ score ≥ 1.5 were considered significant [7].

Pediatric Asthma Caregiver's Quality of Life Questionnaire (PACQLQ)

Quality of life of the parents was assessed using PACQLQ by Juniper *et al*. [8] validated in our center [9]. It is a self-administered instrument, which includes 13 items (4 concern Activity limitations and 9 concern Emotional function). Responses to each item of the PACQLQ are given on a seven-point scale, ranging from 1 to 7, with the higher scores indicating less impairment. The result was expressed as a mean score per item for each of the domains, as well as for the overall quality of life.

Statistical analysis

To assess the changes in PAQLQ / PACQLQ over time (baseline, after 16 and after 52 weeks of treatment), an

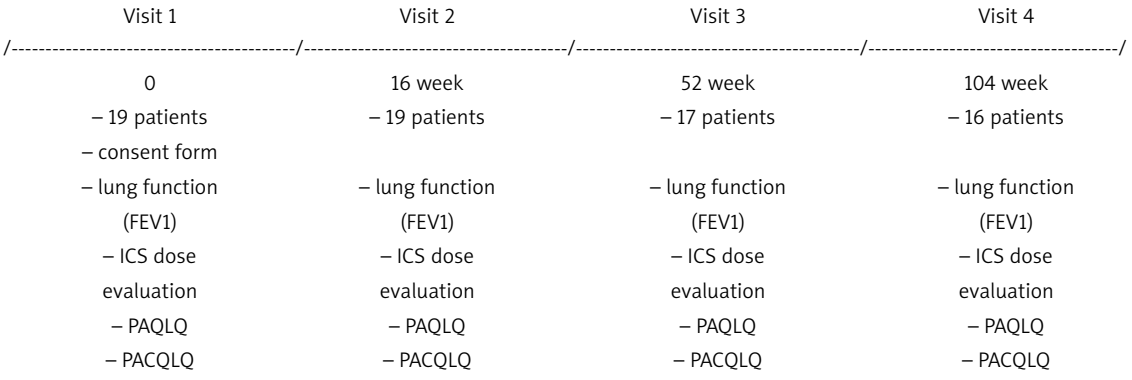

Figure 1. Design of the study

analysis of variance (ANOVA) was implemented. Linear correlation analysis was used to assess the relationship between changes in PAQLQ/PACQLQ and ICS dose reduction after 52 weeks of treatment. All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) 11.5. $P < 0.05$ was used as a definition of statistical significance.

Results

Demographics and baseline characteristics

Nineteen children and adolescents treated with OMB and their nineteen primary caregivers were enrolled.

Seventeen patients and caregivers completed the study. One patient and his caregiver completed the study after 16 weeks of treatment because of poor asthma control during OMB therapy and one patient and his caregiver have not completed 104 weeks of treatment yet. Moreover 1 patient underwent 52-week therapy because of unsatisfactory asthma control, however he was assessed after 104 weeks after the start of OMB treatment (it was after 1 year of discontinuation of OMB therapy). One patient was also treated for 52 weeks but he ended the therapy because of some personal problems, not related to asthma control. He also agreed to be assessed after 104 weeks. Detailed characteristics of the participants are shown in Table 1. Baseline results of PAQLQ and PACQLQ are given in Table 2.

Assessment of the quality of life of children treated with omalizumab

We observed that children after 16-week (visit 2), 52-week (visit 3) and 104-week (visit 4) treatment with OMB (at visit 2, 3 and 4) had higher PAQLQ scores in all three domains compared to the baseline assessment (Figure 2). Improvement was stable during the entire observation period (at all visits). Dunn's multicomparison test showed significant differences between the first and other visits. Differences between visits 2, 3 and 4 did not reach the level of significance. Significant improvement in total PAQLQ scores > 1.5 points [7] was achieved after 52 weeks of treatment by 41.5% of children and by 39.6% after 104 weeks of treatment (Table 2). The greatest improvement was observed in the symptoms domain (38.1% of children after 16 weeks, 47.6% of children after 52 weeks and 44.4% of children after 104 weeks of treatment). The improvement in both emotions and activity domains was the highest after 52 weeks (visit 3).

Table 1. Baseline characteristics

Patient no.	Age	Gender	BMI [kg/m^2]	FEV_1 %	Total IgE [IU/ml]	Number of eosinophils (%)	Sensitization profile*
1	10	M	23.7	98.1	389.8	10	1, 2, 3, 4, 6
2	12	M	18.4	89.6	1388	1	1, 2, 4, 6, 9, 10
3	14	F	24.8	85	913.5	4	1, 2, 3, 4, 5, 6, 8, 11
4	10	F	19.4	102.6	1396	8	1, 2, 3, 4, 6, 8
5	12	M	23.2	109.1	200.6	7	1, 2, 10
6	9	M	20.5	108.1	1118	5	1, 2
7	13	M	22.6	94.6	368.4	10	4, 5, 9, 10
8	12	M	19.6	69.1	1034	14	1, 2, 4, 5
9	13	M	30.4	94.2	1130	5	1, 2, 3, 4, 5
10	6	M	20.3	136	276.8	6	3, 4, 6, 10, 11
11	9	M	22.5	92.5	1232	12	1, 2, 3, 4, 6, 7, 8, 11
12	13	F	27.4	109.8	1139	2	1, 2, 3, 4, 5
13	11	M	23.5	101.4	689.4	4	1, 2
14	13	F	20.4	112.7	522	5	1, 2, 3, 4, 5, 10
15	15	M	28.6	72.2	309.2	6	1, 2
16	10	M	30.1	96.7	270.8	5	1, 2
17	14	M	24.1	99.7	439.7	1	1, 2
18	7	M	19.8	98	1360	21	5, 6, 7, 10
19	13	M	23.1	116.9	453	2	1, 2, 3, 4

*Calculated on beclomethasone dipropionate, *1 – D. pteronyssinus, 2 – D. farinae, 3 – rye, 4 – timothy, 5 – cocksfoot, 6 – birch-tree, 7 – alder, 8 – hazel, 9 – dog fur, 10 – cat fur, 11 – Alternaria.*

Table 2. Baseline results of PAQLQ and PACQLQ (at visit 1 – start of the treatment)

Patient no.	PAQLQ symptoms	PAQLQ emotions	PAQLQ activity	PAQLQ total	PACQLQ emotions	PACQLQ activity	PACQLQ total
1	3.0	6.13	5.8	4.7	3.56	4.25	3.77
2	4.2	5.25	5.0	4.74	2.78	3.0	2.85
3	6.0	6.13	5.4	5.91	3.78	3.5	3.69
4	3.3	1.88	2.6	2.65	3.44	3.75	3.54
5	6.5	6.63	5.6	6.35	3.78	4.5	4.0
6	4.5	5.0	4.6	4.7	1.78	3.0	2.15
7	5.7	6.25	5.0	5.74	5.78	6.25	5.92
8	2.6	2.75	2.2	2.57	2.78	3.25	2.92
9	2.7	3.25	4.4	3.26	2.78	2.5	2.69
10	3.6	4.25	3.6	3.83	2.33	2.25	2.3
11	3.0	4.63	3.2	3.61	2.67	3.5	2.92
12	5.2	4.88	5.0	5.04	3.22	3.75	3.38
13	4.9	6.63	5.6	5.65	3.22	4.0	3.46
14	2.7	3.63	2.2	2.91	2.56	2.75	2.62
15	4.7	6.0	4.4	5.09	3.89	4.0	3.92
16	4.6	4.13	4.4	4.39	3.0	3.5	3.15
17	3.3	3.63	3.2	3.39	2.11	2.75	2.31
18	3.8	4.0	4.2	3.96	2.67	4.0	3.08
19	5.3	4.88	5.8	5.26	3.89	4.75	4.15

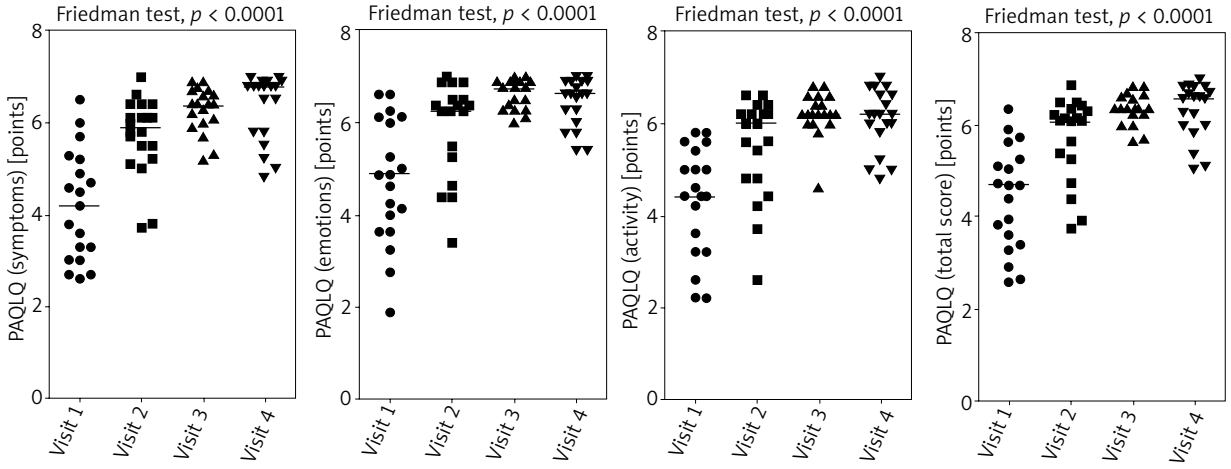

Figure 2. PAQLQ scores in all three domains and in total score at baseline, after 16-, 52- and 104-week treatment with omalizumab. *P* < 0.05 was used as a definition of statistical significance

Next, we calculated the differences in PAQLQ between baseline and follow-up visits for each participant (Figure 3). Children who experienced improvement in PAQLQ lower than 0.5 points were defined as non-responders. According above criteria, 5% of our patients did not respond to OMB therapy. A higher non-responding rate was observed in emotions (16%) and activity (10%) domains. Importantly improvement was stable during treatment.

Assessment of the quality of life of caregivers whose children were treated with omalizumab

Caregivers after 16-week, after 52-week and after 104-week treatment of their children with OMB had higher

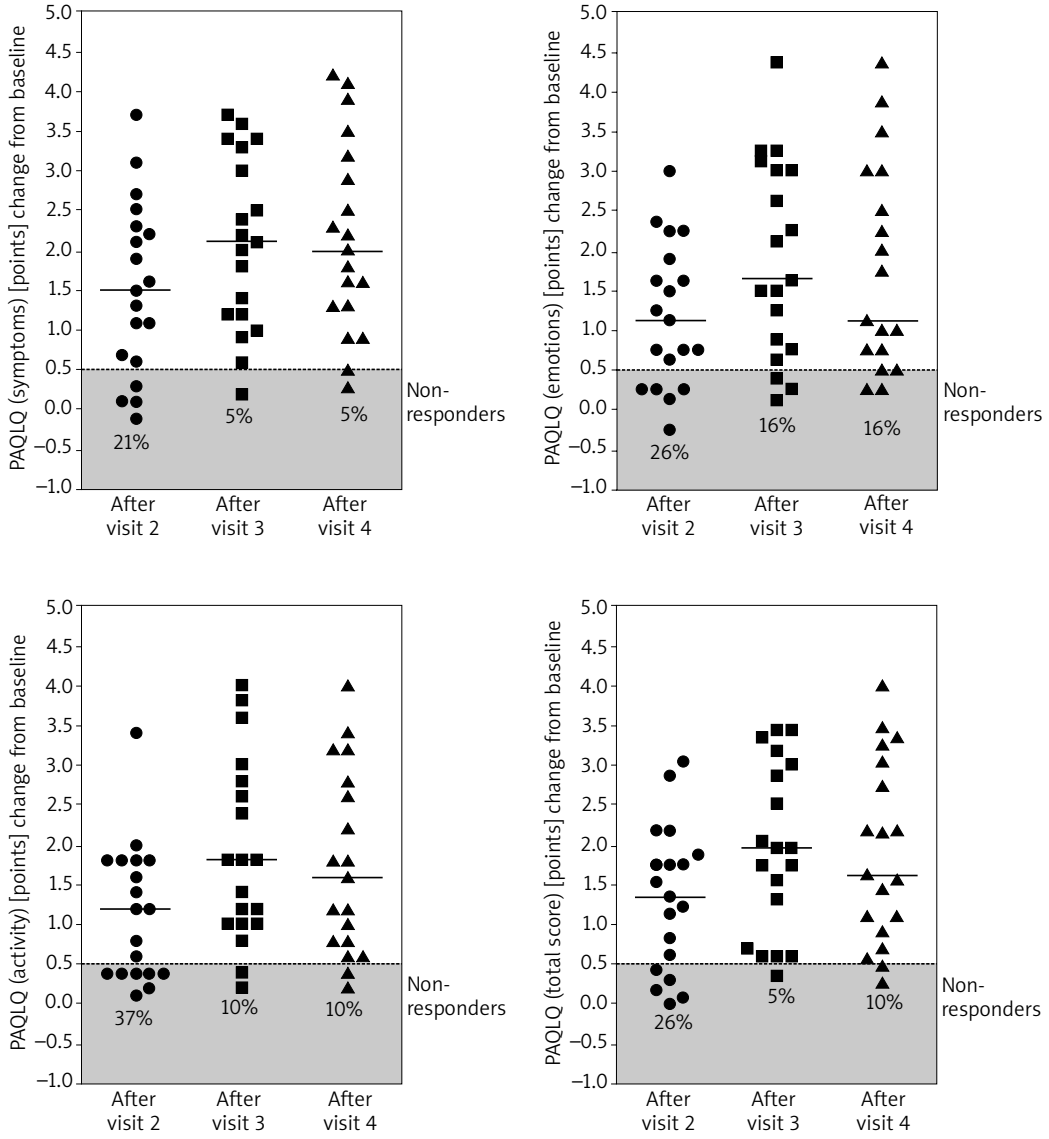

Figure 3. PAQLQ scores in all three domains and in total score change from baseline, after 16-, 52- and 104-week treatment with omalizumab. $P < 0.05$ was used as a definition of statistical significance

PACQLQ scores in both domains, as well as in total PACQLQ (Figure 4). Significant improvement in total PACQLQ scores > 1.5 points [8] was achieved by 40.4% of caregivers after 16-week treatment, 69.5% of caregivers after 52 weeks of treatment and by 79.6% of caregivers after 104 weeks. There was no significant difference between single domains after 16 weeks (visit 2). The greatest improvement was noticed in the emotions domain after 52 weeks (80.8% of caregivers), also the improvement in the activity domain was the highest after 52 weeks (75% of caregivers). Patients were stable during all visits. Dunn's multicomparison test showed, similar to PAQLQ, significant differences between the first and other visits, since the differences between the other visits did not reach the level of significance.

Inhaled glucocorticosteroids dose reduction

After 52-week therapy, 63.3% of patients achieved reduction in inhaled glucocorticosteroids doses; median ICS dose reduction was 300 μg/day and we did not notice differences between total daily ICS use after 52 and after 104 weeks of treatment. There was also no relation between PAQLQ nor PACQLQ and steroid sparing effect.

Lung function

We did not notice any significant improvement of FEV_1 after 16, 52 or after 104 weeks of treatment with OMB in children.

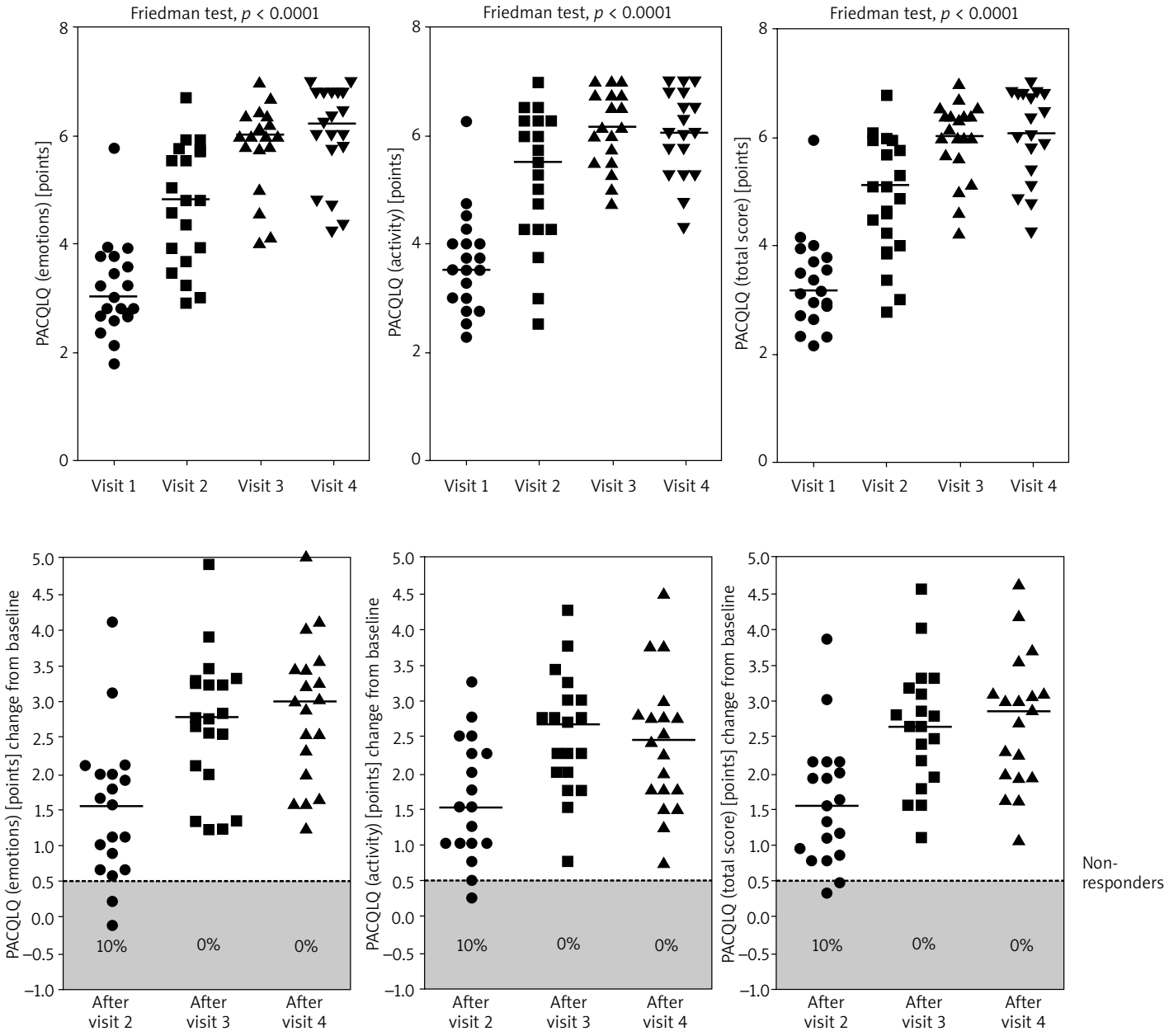

Figure 4. PACQLQ scores in two domains and in total score at baseline, after 16-, 52- and 104-week treatment with omalizumab. *P* < 0.05 was used as a definition of statistical significance

Non-responders

Additional risk factors were analyzed with the reference to OMB responding. We observed an association between baseline PAQLQ and the prevalence of non-responding to initial OMB therapy. Although it did not reach the level of significance, it suggested that children with higher baseline PAQLQ tend to obtain less response to OMB. There were no other risk factors in such logistic regression approach (Table 3).

Discussion

Although randomized controlled trials evidence has demonstrated the efficacy of OMB on quality of life in children [14–16], the real-life studies are necessary to verify the results. Clinical trial results do not analyze specific domains in both children and caregivers quality-of-life questionnaires. The main merit of this study was to assess the quality of life in severe asthmatic children and their parents with specific pediatric tools for the first time

Table 3. Risk factors of non-responding after initial omalizumab therapy

Parameter	OR[a]	95% CI		*P*-value
Age [years] (continuous variable)	1.06	0.68	1.65	0.7992
Male vs. female	1.09	0.09	13.78	0.9464
BMI [kg/m^2] (continuous variable)	1.09	0.82	1.44	0.5601
PAQLQ [points] (continuous variable)	4.52	0.94	21.64	0.0590
ICS dose [µg/day] (continuous variable)	1.00	1.00	1.00	0.5735
IgE [IU/l] (continuous variable)	1.00	0.99	1.00	0.1056
Eo [%] (continuous variable)	0.91	0.70	1.18	0.4823
Allergy profile:				
Molds vs. other	8.67	0.58	130.11	0.1182
Cat vs. others	1.67	0.20	14.05	0.6386
HDM vs. other	0.67	0.05	9.47	0.7646
Number of sensitizing allergen:				
2 vs. 1	0.30	0.02	4.91	0.3985
≥ 3 vs. 1	1.50	0.11	21.31	0.7646

[a]*Dependent variable: non-responders vs responders (non-responders were defined as children with less than 0.5 point increase from baseline in total PAQLQ after visit 2).*

in a real life situation. No questionnaire other than the Pediatric Asthma Quality of Life Questionnaire (PAQLQ) by Juniper *et al.*, specifically developed and validated to measure asthma control, refers to typical childhood issues [17]. Our study shows significant improvements in quality of life both in children with severe asthma and their caregivers. This is in contradiction to our previous study, which showed that parents' quality of life is different than children's quality of life [9].

We noticed a positive correlation between asthma quality of life in parents and children treated with OMB, but the improvement with a significance level was seen only between the first and other visits.

Most patients in our study experienced the great reduction in ICS use. The systematic review and meta-analysis by Normansell *et al.* [18] identified 25 double-blind randomized clinical trials comparing OMB to placebo in adults and children with chronic asthma. The review revealed that patients with moderate to severe asthma treated with omalizumab were statistically significantly more likely to be able to withdraw from their ICS completely than those treated with placebo.

In our previous study we observed that children with better control of asthma had higher PAQLQ scores in all three domains [10]. However, weak correlations were found between clinical parameters such as asthma diary, FEV_1 and PEF, and the activities domain of PAQLQ, between FEV_1 and the symptoms domain and between asthma diary and the emotions domain of PAQLQ. In the evaluation of the effectiveness of treatment in children with asthma, it is very important to assess each separate domain of the quality-of-life questionnaire.

Most patients in our study had a significantly increased blood eosinophil count at the beginning of the study (Table 1). Improvement in asthma control after 16 weeks was noticed in almost all children. This observation is similar to Kupryś-Lipińska *et al.* results [19]. They observed that OMB is particularly effective in patients with peripheral blood eosinophilia and after 16 weeks of treatment the eosinophil blood count usually decreases to a nearly normal level. However, in our study, even children with a normal baseline eosinophil count, experienced improvement in asthma control. We analyzed also other risk factors in association to OMB responding, however none of this (baseline total IgE level, FEV_1, BMI, sensitization profile) correlated with effectiveness of OMB therapy.

The main limitation of our study in which preliminary data are presented is the small sample of patients and the lack of a control group. In our clinic all children who fulfill the criteria for IgE therapy are treated with omalizumab and therefore a similar sample of patients that are not treated with omalizumab could not be indicated.

We compared our results with other studies, however instruments applied to our sample were different. Barnes *et al.* evaluated the "real world" effects of omalizumab in patients above 12 years of age in the UK [20]. This retrospective analysis showed that quality of life improved significantly from baseline, both at 16 weeks and up to 12 months post-OMB initiation and the improvement in AQLQ scores was better than in the PERSIST study [21]. Vieira *et al.* [22] performed a prospective study assessing short- and long-term quality of life and asthma control with omalizumab in 15 Portuguese adults. Our study confirms the outcomes reached in Vieira's trial. Treatment

with omalizumab gives a global benefit in quality of life, both in short- and long-term observation, however we did not observe a significant improvement in the lung function test.

In our study the interesting point was the observation of these participants who discontinued OMB treatment, as to our knowledge, there are limited data referring to this area. In our study, there were three patients who were assessed after OMB cessation. None of them experienced the loss of asthma control. However, we are aware that it was a very small sample of patients and time of observation could be too short as shown in Molimard *et al.* [23] study. They collected data from 61 adult patients and demonstrated that a median interval between discontinuation and loss of asthma control was of 13.0 months. The longest study assessing OMB real-life efficacy was conducted by Nopp *et al.* [24]. Eighteen patients in this trial underwent 6-year OMB treatment (all of them were responders) and then they were assessed after the next 3 years. One third of the patients lost asthma control after OMB cessation during 3 years of the observation. Another study, conducted by Baena-Cagnani *et al.* [25], was a 4-year follow-up of a group of children with uncontrolled asthma after withdrawal of a 1-year OMB treatment. The interesting fact is that in this trial children during the first 3 years of follow-up, were completely free of asthma symptoms without any need of ICS or rescue medication. The Polish evaluation of asthma control after OMB cessation in adults showed that 9 of 11 patients experienced severe exacerbation after OMB withdrawal [26]. The optimal time of OMB therapy is still unknown.

Reducing ICS use is an important goal of therapy for children with severe asthma. The results presented in Annett *et al.* [27] study in children with asthma who participated in the Childhood Asthma Management Program (CAMP) provided findings on how medication treatment contributes to changes in the child or parent quality of life. In this study, the use of steroid therapy was the single determinant of moderate improvement in child-reported participation in the Physical Activities domain of quality of life. This observation encouraged us to conduct additional analysis to assess the effect of ICS use on quality of life in children. After 12 months of therapy, in 63% of our patients, we observed a reduction in the daily use of ICS with a median dose reduction of 300 µg/day. However, we did not observe a statistically significant reduction in ICS use after 104 weeks of treatment. The study also did not demonstrate any relation between PAQLQ nor PACQLQ and the steroid sparing effect, which could be related to the small sample of patients.

Conclusions

Our study showed that improvement in quality of life in asthmatic children and adolescents observed after omalizumab correlates well with quality of life in caregivers, reduction in ICS use but does not correlate with FEV_1. We observed good asthma control in these patients who discontinued the therapy. Our interesting finding needs further evaluation in a larger study.

Acknowledgments

This study was funded by grant 502-12-760 and 503-2056-1 from the Medical University of Lodz, Poland.

Conflict of interest

The authors declare no conflict of interest.

References

1. McQuaid EL, Kopel SJ, Assau JH. Behavioral adjustments in children with asthma: a metaanalysis. J Dev Behav Pediatr 2001; 22: 430-9.
2. Merikallio VJ, Mustalahti K, Remes ST, et al. Comparison of quality of life between asthmatic and healthy school children. Pediatr Allergy Immunol 2005; 16: 332-40.
3. Sthoeger ZM, Eliraz A, Asher I, et al. The beneficial effects of Xolair (omalizumab) as add-on therapy in patients with severe persistent asthma who are inadequately controlled despite best available treatment (GINA 2002 step IV) – the Israeli arm of the INNOVATE study. Isr Med Assoc J 2007; 9: 472-5.
4. Vignola AM, Humbert M, Bousquet J, et al. Efficacy and tolerability of anti-immunoglobulin E therapy with omalizumab in patients with concomitant allergic asthma and persistent allergic rhinitis: SOLAR. Allergy 2004; 59: 709-17.
5. Lemanske RF Jr, Nayak A, McAlary M, et al. Omalizumab improves asthma-related quality of life in children with allergic asthma. Pediatrics 2002; 110: e55.
6. Finn A, Gross G, van Bavel J, et al. Omalizumab improves asthma-related quality of life in patients with severe allergic asthma. J Allergy Clin Immunol 2003; 111: 278-84.
7. Juniper EF, Guyatt GH, Ferrie DH, et al. Measuring quality of life in children with asthma. Qual Life Res 1996; 5: 35-46.
8. Juniper EF, Guyatt GH, Feeny DH, et al. Measuring quality of life in the parents of children with asthma. Qual Life Res 1996; 5: 27-34.
9. Stelmach I, Podlecka D, Smejda K, et al. Pediatric asthma Caregiver's Quality of Life Questionnaire is a useful tool for monitoring asthma in children. Qual Life Res 2012; 21: 1639-42.
10. Stelmach I, Podlecka D, Majak P, et al. Validity of the Pediatric Asthma Quality of Life Questionnaire in Polish children. Pediatr Allergy Immunol 2011; 22: 660-6.
11. Global Initiative for Asthma (GINA). From the Global Strategy for Asthma Management and Prevention, Global Initiative for Asthma (GINA) 2014. Available at: http://www.ginasthma.org/local/uploads/files/GINA_Report_2014.
12. Bodzenta-Łukaszyk A, Fal AM, Jassem E, et al. The statement of the Polish Society of Allergology experts on the treatment of difficult-to-treat asthma. Pneumonol Alergol Pol 2015; 83: 324-34.
13. Kupczyk M, Kuna P. Omalizumab in an allergology clinic: real life experience and future developments. Post Dermatol Alergol 2014; 31: 32-5.

14. Humbert M, Beasley R, Ayres J, et al. Benefits of omalizumab as add-on therapy in patients with severe persistent asthma who are inadequately controlled despite best available therapy (GINA 2002 step 4 treatment): INNOVATE. Allergy 2005; 60: 309-16.
15. Bousquet J, Siergiejko Z, Swiebocka E, et al. Persistency of response to omalizumab therapy in severe allergic (IgE-mediated) asthma. Allergy 2011; 66: 671-8.
16. Korn S, Thielen A, Seyfried S, et al. Omalizumab in patients with severe persistent allergic asthma in a real-life setting in Germany. Respir Med 2009; 103: 1725-31.
17. Lang A, Mowinckel P, Sachs-Olsen C, et al. Asthma severity in childhood, untangling clinical phenotypes. Pediatr Allergy Immnunol 2010; 21: 945-53.
18. Normansell R, Walker S, Milan SJ, et al. Omalizumab for asthma in adults and children. Cochrane Database Syst Rev 2014; 1: CD003559.
19. Kupryś-Lipińska I, Kołacińska-Flont M, Marczak J, et al. Effectiveness of omalizumab in an asthmatic patient with severe airway and blood eosinophilia. Post Dermatol Alergol 2015; 32: 478-9.
20. Barnes N, Menzies-Gow A, Mansur AH, et al. Effectiveness of omalizumab in severe allergic asthma: a retrospective UK real-world study. J Asthma 2013; 50: 529-36.
21. Brusselle G, Michils A, Louis R, et al. "Real-life" effectiveness of omalizumab in patients with severe persistent allergic asthma: The PERSIST study. Respir Med 2009; 103: 1633-42.
22. Vieira T, de Oliveira JF, da Graça Castel-Branco M. Short and long-term quality of life and asthma control with omalizumab therapy in a real life setting in Portugal. Allergol Immunopathol (Madr) 2014; 42: 3-10.
23. Molimard M, Le Gros V, Bourdeix I. Observational study in severe asthmatic patients after discontinuation of omalizumab for good asthma control. Respir Med 2014; 108: 571-6.
24. Nopp A, Johansson SG, Adédoyin J, et al. After 6 years with Xolair: a 3-year withdrawal follow-up. Allergy 2010; 65: 56-60.
25. Baena-Cagnani CE, Teijeiro A, Canonica GW. Four-year follow-up in children with moderate/severe uncontrolled asthma after withdrawal of a 1-year omalizumab treatment. Curr Opin Allergy Clin Immunol 2015; 15: 267-71.
26. Kupryś-Lipińska I, Kuna P. Loss of asthma control after cessation of omalizumab treatment: real life data. Post Dermatol Alergol 2014; 31: 1-5.
27. Annett RD, Bender BG, Skipper B, Allen C. Predicting moderate improvement and decline in pediatric asthma quality of life over 24 months. Qual Life Res 2010; 19: 1517-27.