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Assessment of Quality of Life in Asthmatic Children and their Caregivers after Treatment with Omalizumab

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

[1]*Department of Pediatrics and Allergy, Medical University of Lodz, Poland*

[2]*Department of Social and Preventive Medicine, Medical University of Lodz, Poland*

[*]**Corresponding author:** Iwona Stelmach, Department of Pediatrics and Allergy, Copernicus Memorial Hospital, 62 Pabianicka Street, 93-513 Lodz, Poland, Tel: 48426895972; Fax: 48426895973; E-mail: alergol@kopernik.lodz.pl

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Abstract

Background: 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. The aim of the study was to demonstrate the quality of life in children with severe asthma and their caregivers, changes from baseline in FEV1 and daily inhaled corticosteroids (ICS) dose after treatment with omalizumab.

Methods: Participants were seen in the clinic at enrollment (visit 1), after 16 weeks (visit 2) and after 52 weeks (visit 3) 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: 19 children and caregivers were enrolled. Significant improvement in PAQLQ and PACQLQ scores were achieved by 47.4% of children and 52.6% of caregivers after 16-week and by 63.6% of children and all caregivers after 52-week of treatment. Significant positive correlation between PAQLQ and PACQLQ at first and at second visit was found, 63.3% of patients achieved reduction in ICS doses. We did not notice significant improvement in FEV1.

Conclusions: The improvement in quality of life in asthmatic children and adolescents observed after Omalizumab correlates with reduction in ICS use but not with FEV1. Parents' information was different from children observation, therefore both questionnaires for children and their caregivers should be used to evaluate quality of life in children.

Keywords: Asthma; Omalizumab; Quality of life; Children

Abbreviations

FEV1: Forced Expiratory Volume in one Second; GINA: The Global Initiative for Asthma; ICS: Inhaled Corticosteroids; OMB: Omalizumab; PACQLQ: The Pediatric Asthma Caregiver's Quality of Life Questionnaire; PAQLQ: The Pediatric Asthma Quality of Life Questionnaire

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 centre 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 children aged ≥ 6 years with severe persistent allergic asthma [11].

Our primary end point was assessment of the quality of life in severe asthmatic children and adolescents and their caregivers after 16- and 52-weeks of treatment with omalizumab. The secondary end point were: the correlation between changes in the quality of life, the use of inhaled glicocorticosteroids (ICS) and changes from baseline in forced expiratory volume in one second (FEV1) in studied children.

Methods and Materials

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 2014. The diagnosis of asthma was universally established, according to the standard definitions in the latest GINA (The Global Initiative for Asthma) guidelines [11].

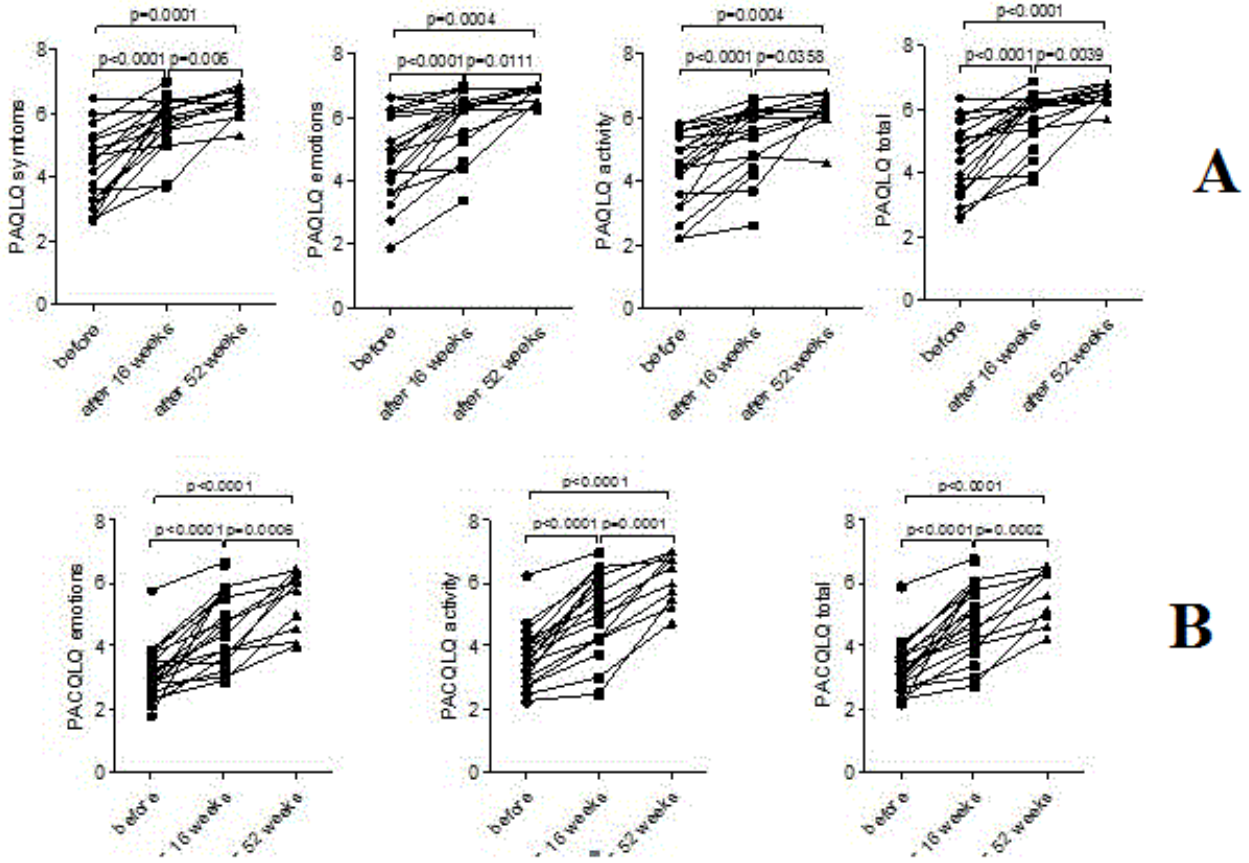

Figure 1: A. PAQLQ scores in all three domains and in total score at baseline, and after 16- and 52-week treatment with omalizumab. P<0.05 was used as a definition of statistical significance. **B.** PACQLQ scores in all two domains and in total score at baseline and after 16- and 52-week treatment of their children with omalizumab. P<0.05 was used as a definition of statistical significance.

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 beclometasone dipropionate or equivalent for adolescents and >400 μg for children 6-11 years [11]) in combination with a long-acting beta2-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 52-week period cohort study. Children or adolescents and their parents/caregivers were seen in the clinic at enrollment (visit 1), after 16 weeks (visit 2) and 52 weeks (visit 3) of treatment with omalizumab. At each visit, Polish version of PAQLQ by Juniper was assessed to each child and the ICS use doses were evaluated. 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, lung function (FEV1) 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 American Thoracic Society standards. Relative change from baseline in FEV1 and daily ICS dose were assessed after 16 and 52 weeks. Adherence to anti-asthma therapy was systematically assessed at each visit.

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 [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 analysis of variance (ANOVA) was implemented. Linear correlation analysis was used to assess relationship between changes in PAQLQ / PACQLQ and ICS dose reduction after 52 weeks of treatment. All statistical analyses were performed using 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 omalizumab and their nineteen primary caregivers were enrolled.

All patients and caregivers completed the study. Detailed characteristics of the participants are shown in Table 1. All patients remained controlled during the study.

Characteristics	
Age [years], mean ± SD	11.4 ± 2.4
Male gender	15
PAQLQ symptoms [points], mean ± SD	4.12 ± 1.20
PAQLQ emotions [points], mean ± SD	4.73 ± 1.36
PAQLQ activity [points], mean ± SD	4.33 ± 1.18
PAQLQ total [points], mean ± SD	4.41 ± 1.14
PACQLQ emotions [points], mean ± SD	3.16 ± 0.88
PACQLQ activity [points], mean ± SD	3.65 ± 0.93
PACQLQ total [points], mean ± SD	3.31 ± 0.87

Table 1: Baseline characteristics.

Assessment of the quality of life of children treated with omalizumab

We observed that children after 16-week and 52-week treatment with omalizumab (at visit 2 and 3) had higher PAQLQ scores in all three domains compared to the baseline assessment (Figure 1A). Significant improvement in total PAQLQ scores - >1.5 points [7] was achieved by 47.4% of children after 16-week treatment and by 63.6% of children after 52-week treatment (Figure 2A). The greatest improvement after 16 weeks of treatment was noticed in symptoms domain (52.6% of children), while after 52 weeks of treatment - in emotion domain (63.6% of children). The improvement in activity domain only in 36.8% of children after 16 weeks and in 36.4% after 52 weeks was observed (Figure 2A).

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

Caregivers after 16-week and after 52-week of treatment of their children with omalizumab had higher PACQLQ scores in both domains (Figure 1B). Significant improvement in total PACQLQ scores >1.5 points [8] was achieved by 52.6% of caregivers after 16-week treatment and by all caregivers after 52 weeks (Figure 2B). There was no difference between single domains after 16 weeks. The greatest improvement was noticed in activity domain after 52-weeks (100% of caregivers) (Figure 2B).

We found significant positive correlation between total PAQLQ and total PACQLQ at first ($R=0.59$) and at second ($R=0.52$) visit. At third visit such correlation did not reach the level of significance ($R=0.15$).

ICS dose reduction

After 52-week of therapy, 63.3% of patients achieved reduction in inhaled glucocorticosteroids doses; median ICS dose reduction was 300 mcg/day. There was no relation between PAQLQ nor PACQLQ and steroid sparing effect.

We did not notice significant improvement of FEV1 after 16 and 52 weeks of treatment with omalizumab.

Discussion

Although randomized controlled trials evidence have demonstrated the efficacy of omalizumab on quality of life in children [12-14], clinical trial results do not analyse specific domains in both children and caregivers quality-of-life questionnaires. The main merit of this study was the aim the quality of life in severe asthmatic children and their parents with specific pediatric tools for the first time in a real life situation. Our study has some practical implication of different assessment in children and caregivers. No other than Pediatric Asthma Quality of Life Questionnaire (PAQLQ) by Juniper et al. specifically developed and validated to measure asthma control, refers to typical childhood issues [15]. Our study shows significant improvements in quality of life of children with severe asthma, their caregivers, and great reduction in ICS use.

We noticed a positive correlation between asthma quality of life in parents and children treated with OMB, but only after 16-weeks of treatment. Our results revealed that the parent's assessment of change in quality of life in activity domain were not related to child's assessment.

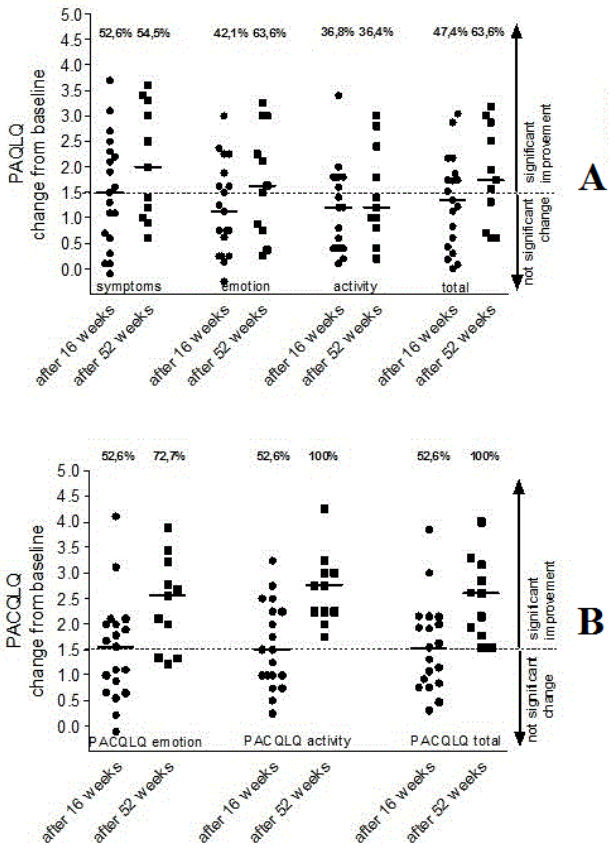

Figure 2: A. Percentage of children with improvement in PAQLQ scores showed in all three domains and in total score after 16- and 52-week treatment with omalizumab. **B.** Percentage of caregivers with improvement in PACQLQ scores showed in all two domains and in total score after 16- and 52-week treatment of their children with omalizumab.

In our previous study we observed that children with better control of asthma had a higher PAQLQ scores in all three domains [10]. However, weak correlations were found between clinical parameters such as asthma diary, FEV1 and PEF, and the activities domain of PAQLQ, between FEV1 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.

The main limitation of our study in which preliminary data is 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 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 UK [16]. This retrospective analysis showed that quality of life improved significantly from baseline, both at 16-weeks and up to 12-moths post-OMB initiation and the improvement in AQLQ scores was better than in the PERSIST study [17].

Reducing ICS use is an important goal of therapy for children with severe asthma. The results presented in Annett et al. study in children with asthma participated in the Childhood Asthma Management Program (CAMP) provided findings on how medication treatment contribute to changes in child or parent quality of life [18]. 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 mcg/day. However, we did not observe any relation between PAQLQ nor PACQLQ and steroid sparing effect, which could be related to the small sample of patients.

In summary, our study showed that improvement in quality of life in asthmatic children and adolescents observed after omalizumab correlates with reduction in ICS use but not with FEV1. Parents' information was different from child observation, therefore both questionnaires for children and their caregivers should be used to evaluate quality of life in children treated with omalizumab. Our interesting finding needs further evaluation in a larger study.

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