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Research Article

OMALIZUMAB IN SEVERE-ALLERGIC ASTHMA: THE IMPACT ON REAL LIFE PATIENTS

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A B S T R A C T

Omalizumab has been reported to be a valid therapeutic intervention for the treatment of severe allergic asthma. The aim of this studywas to evaluatethe clinical efficacy of omalizumabandits impact on quality of life (QoL) andemotional sphere.
A retrospective studyon33 adults with severe allergic asthma treated with omalizumabfrom January 2016 to January 2018; patients were divided in group 1 and 2 with age>55 or<55 years, respectively. Exacerbations, FEV1 values,Asthma Control Test (ACT) and Asthma Quality of Life Questionnaire (AQLQ)scores were evaluatedat T0 baseline, T1 1 year and T2 2 years. The Toronto Alexithymia Scale-20 was used to investigate Alexithymia.
Omalizumab induceda significant decrease in exacerbations and increase in FEV1 ,ACT and AQLQ. Alexithymia,in six patients, did not interfere with omalizumab efficacy.From T1 to T2 improvement, even if present, was notsignificant but a reduction of exacerbations in both groups occurred and in group 1 AQLQ increase correlated to environmental stimuli.
Omalizumab was efficacious in different age groups with severe allergic asthma but also improvedtheir QoL. In our study these results were obtained regardless to the presence or not of alexithymia.

INTRODUCTION

Asthma is a heterogeneous disease, characterized by chronic airway inflammation and airway hyper-responsiveness to direct or indirect stimuli, with a clinical history of respiratory symptoms such as wheeze, shortness of breath, chest lightness and cough, together with variable expiratory airflow limitation. Although most asthma patients can achieve good symptom control and minimal exacerbations with regular controller treatment, 5-10% of asthmatic patients suffer from a severe form of asthma that is uncontrolled despite maximal pharmacologic therapy[1].

These patients therefore often have a poor asthma symptom control and experiment exacerbations that may be also life threatening and that need use of oral or systemic corticosteroids, with consequent possible severe side effects[2]. Patients with severe allergic asthma are more at risk of exacerbations because they are sensitive to the triggering action of indoor and/or outdoor inhalant allergens and this can strongly limit normal daily activities and even influence the choice of indoor and outdoor environments, with resulting impairment of their quality of life (QoL).

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QoL of asthmatic patients is not only related to asthma severity and asthma symptom control but is also influenced by psychological factors such as depression, anxiety and alexithymia, which are also often reported as more frequent in patients with severe asthma[3].

Treatment with omalizumab is a valid therapeutic intervention in severe allergic asthma and in our research we wanted to evaluate the impact of this treatment not only on exacerbations but also on different areas of daily life and on the emotional sphere of patients treated with this anti-IgE biological therapy. For this reason we compared the scores of the Asthma Quality of life Questionnaire (AQLQ)[4] before and after one year treatment with omalizumab of patients with severe allergic asthma. In order to investigate if alexithymia was present in this group of patients an appropriate questionnaire, the Toronto Alexithymia Scale-20 (TAS-20)[5], was administered.

Patients and Methods

A 24-month retrospective study on 33 adults with severe allergic asthma, treated with omalizumab, was carried out, in the Allergy Outpatient Unit of the "G. Martino" University Hospital of Messina, from January 2016 to January 2018.

Patients' Characteristics were

- ✓ severe persistent allergic asthma for over 12 months, not controlled by maximum doses tolerated of inhaled glucocorticoids and long-acting beta2-agonists;

- ✓ documented repeated severe asthmatic exacerbations and need for systemic corticosteroids;
- ✓ evidence of positivity for at least a perennial allergen (dust mites and/or parietaria pollens, typical of the Mediterranean area) at skin prick tests and/or RAST
- ✓ levels of total serum IgE ≥ 30 UI/ml and ≤ 1500 UI/ml;
- ✓ basal FEV1 <80% Omalizumab treatment was prescribed according to patients' total IgE levels and body weight.

Patients were evaluated recording number of exacerbations, pulmonary function, symptoms control, and AQLQscores at 3 intervals of time: before starting treatment with omalizumab (T0), after 1 year (T1) and after 2 years (T2) of treatment. Patients were also evaluated regarding the presence of Alexithymia. Pulmonary function was evaluated measuring the forced expiratory volume in 1 second (FEV1)[6].

Patient's asthma symptoms control was assessed using the Asthma Control Test (ACT)[7], a 5-item questionnaire that assesses asthma impact on home and work activities, shortness of breath, symptoms, rescue medication usage, and overall asthma control. Scores range from 5–25 (higher is better). Scores of 20–25 are classified as well-controlled asthma; 16–19 as not well-controlled; and 5–15 as very poorly controlled asthma.

Patient's QoL was measured by the standardized version of the AQLQ[4]. The AQLQ consists of 4 domains (symptoms, activity limitation, emotional function and environmental stimuli), with a total of 32 items; the overall score is the mean of these 32 items on a scale of 1 to 7 (1 = severe impairment; 7 = no impairment).

The presence of alexithymia was measured by the Toronto Alexithymia scale-20 (TAS 20)[5],a self-report scale that is comprised of 20 items, rated using a 5-point Likertscale whereby 1 = strongly disagree and 5 = strongly agree. There are 5 items that are negatively keyed (items 4, 5, 10, 18 and 19). The total alexithymia score is the sum of responses to all 20 items. The TAS-20 uses cutoff scoring: equal to or less than 51 = non-alexithymia, equal to or greater than 61 = alexithymia. Scores of 52 to 60 = possible alexithymia.

In order to evaluate data among patients of different age groups we divided patients into two groups: Group 1 with age> 55 years (5 males and 10 females with median age of 64 years) and Group 2 with age <55 years (10 males and 8 females with median age of 43,5 years).

All subjects provided written informed consent for processing of personal data according to GDPR 2016/679.

Statistical Analysis

Data are presented as median and interquartile range (IQR). Comparisons between categorical variables (gender difference in the two groups) are performed with the exact Fisher test.

Comparisons between the two groups for T0 variables (exacerbations, ACT, FEV1, AQLQ related to symptoms, activity limitation, emotional function and environmental stimuli, TAS) are calculated using the Mann-Whitney Test.

Comparisons between variables taken into consideration in the two groups (exacerbations, ACT, FEV1, AQLQ related to symptoms, activity limitation, emotional function and environmental stimuli) at T0, T1 and T2 are calculated with the Friedman test, while between T0 and T1 and finally between T1 and T2 are calculated with the Wilcoxon Signed Ranks Test.Statistical significance was set for $p < 0.05$.

RESULTS

No gender differences were observed in the two groups (group 1: 5 males and 10 females, group 2: 10 males and 8 females; $p>0.05$)nor differences in values of exacerbations,FEV1, ACT, AQLQ related to symptoms, activity limitation, emotional function and environmental stimuliat T0.

In both groups there was a statistically significant decrease in the number of exacerbations ($p<0.0001$)while there was a statistically significant increase of FEV1 ($p=0.002$ vs $p=0.005$in group 1 and 2 respectively) and of ACT ($p<0.0001$), AQLQ related to symptoms ($p<0.0001$), activity limitation ($p<0.0001$), emotional function ($p<0.0001$) and environmental stimuli ($p<0.0001$) in both groups (Fig. 1-7).

Both groups showed a marked improvement in all the parameters and there were no substantial differences in the trend of the single variables in the two groups for the three intervals of time considered.

There was a statistically significant improvement fromT0 to T1 in both groups for all the parameters taken into consideration, while between T1 and T2 the improvement even if present was not statistically significant, if not, in the reduction of exacerbations in both groups and in the increase of the AQLQ related to environmental stimuli only in group 1 ($p = 0.01$).

Regarding TAS-20,it resulted positive for alexithymia in 6 patients only from group 2.These six patients presented a significant improvement of all the parameters (exacerbations, FEV1, ACT, AQLQ scores) such as non-alexithymic patients.

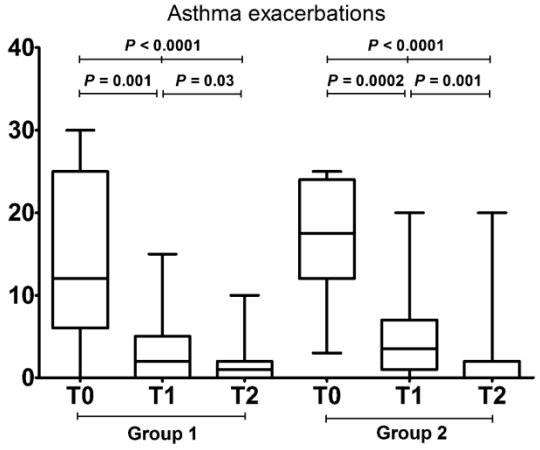

Figure 1 Asthma exacerbations decreased significantlyin both groups during Omalizumab treatment ($p<0.0001$).

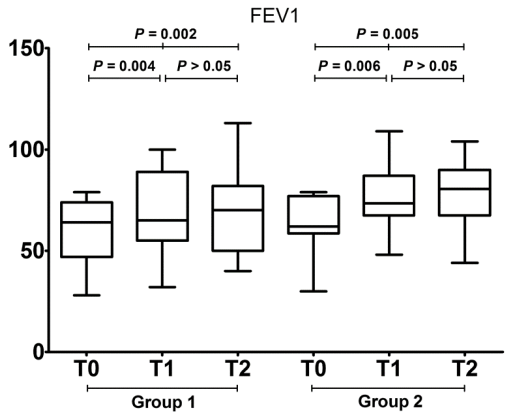

Figure 2 FEV1 significantly increased in both groups during Omalizumab treatment (p=0.002 vs p=0.005 in group 1 and 2 respectively)

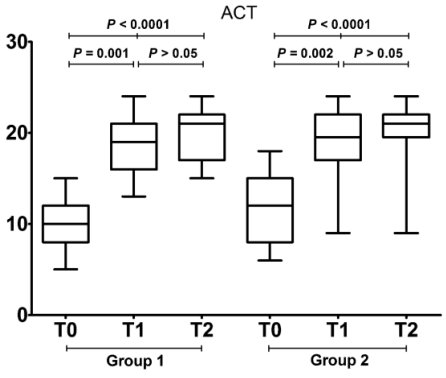

Figure 3 ACT scoresincreased significantly during Omalizumab treatment (p<0.0001)

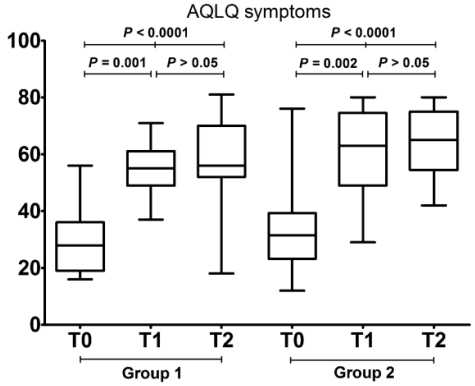

Figure 4 AQLQ scores related to symptomsincreased significantly during Omalizumab treatment (p<0.0001)

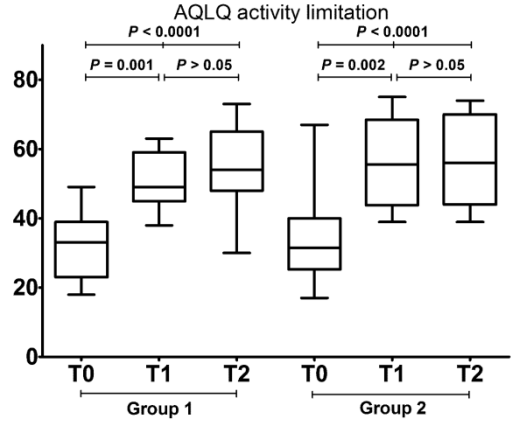

Figure 5 AQLQ scores for activity limitation increased significantly during Omalizumab treatment (p<0.0001)

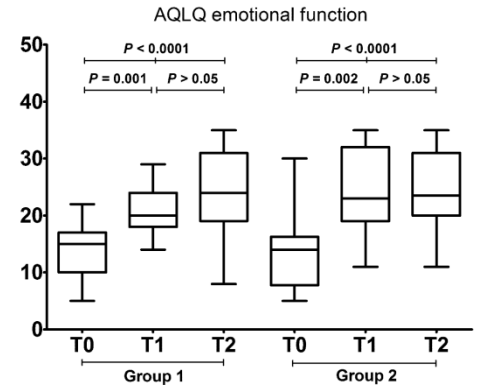

Figure 6 AQLQ scores for emotional function increased significantly during Omalizumab treatment (p<0.0001)

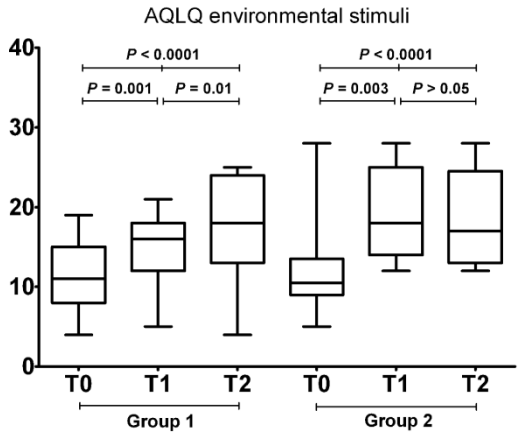

Figure 7 AQLQ scores for environmental stimuli increased significantly during Omalizumab treatment (p<0.0001)

DISCUSSION

As reported in numerous clinical trials and observational studies in real life, omalizumab is an effective and well tolerated add-on therapy used for over ten years in the treatment of severe allergic asthma[8].

The results of our study confirm the efficacy of omalizumab in adult patients, regardless of their age. Asthmatic patients presented a statistically significant decrease in the number of exacerbations from T0 to T2 as well as an increase in asthmatic symptoms control proved by the increase in the ACT scores maintained over time[9].

Respiratory function, monitored measuring the FEV1, improved significantly in both groups from T0 to T1. Nevertheless, younger patients (group 2), presented a further increase of FEV1 from T1 to T2 compared to older patients (group 1). In this group FEV1 decreased, even if not to previous omalizumab treatment values, probably due to systemic corticosteroid discontinuation as already reported[10]; our results, therefore, confirm the steroid sparing effect of omalizumab [11].

In our study we focused not only on the efficacy of omalizumab in patients with severe allergic asthma but mostly on the impact of this treatment on their QoL. Data reported in this study are from patients in real life; it has been widely reported the strong impact that severe allergic asthma has in the daily life of those affected[12].Patients with severe asthma often report that asthma interferes with sports, normal physical exertion, social activities, sleep; their QoL is, therefore, overall affected as they also have a great percentage of emergency

room visits, hospitalizations and absence from school or days lost from work[13, 14].

QoL improved in all our patients after starting treatment with omalizumab. The AQLQ scores related to symptoms, to activity limitation and to emotional function increased significantly, regardless of the age of the patients,during the first year of treatment remaining stable over time.The AQLQ scores related to environmental stimuli,instead, increased significantly in both groups during the first year of treatment (from T0 to T1), continuing to increase from T1 to T2in the group of older patients (group 1) and remaining unchanged in the younger patients (group 2). Different trends between groups of patients could be related to the different lifestyle among age groups: younger patients have, usually, a more active social and working life and are, therefore, more exposed to environmental stimuli such as allergens and pollutants[15].
Unlike what reported in the literature we did not find a significant presence of alexithymia in our patients: only 6 patients presented TAS-20 scores positive for alexithymia. Furthermore, this psychological condition did not affect the response to treatment with omalizumab; it can be suggested that the close clinical follow-up,after severe asthma diagnosis in our Asthma Unit, counteracted the negative effects on the patients'asthma management. It has been previously reported that asthmatic patients with alexithymia find it difficult to recognize and express symptoms' intensity and frequency, have poor treatment adherence and underestimate the risk of exacerbations [3].

In conclusion this study reports not only the positive clinical results obtained with Omalizumab treatment of different age group patients with severe allergic asthma, but also the improvement of their QoL. These results were obtained in all patients regardless to the presence or not of alexhitymia.

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