Original paper

Omalizumab improves forced expiratory volume in 1 second in patients with severe asthma

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Abstract

Introduction: Asthma is a multiphenotypic disease, and therapeutic managenment in patients with severe asthma is particulary difficult, with conventional treatment of severe asthma showing poor efficacy.
Aim: To analyse forced expiratory volume in 1 s (FEV_1) following the adminstration of omalizumab.
Material and methods: Six patinents (mean age: 50 ±12.6) with severe, uncontrolled asthma according to the GINA guidelines were enrolled in the study.
Results: Treatment with omalizumab increased in all subjects FEV_1 by 17.28 ±13.4% after months and 18.57 ±13.4% after 12 months of treatment.
Conclusions: These results provides further evidence that therapy with omalizumab improves spiromtric parameters in severe asthma.

Key words: asthma, omalizumab, spirometry, forced expiratory volume in 1 s.

Introduction

Asthma is a disease in which chronic inflammation of the airways and bronchial hyperactivity cause clinical symptoms such as wheezing, dyspnoea, tightness in the chest and cough. A recent study published by GINA experts emphasizes the heterogeneous character of asthma. Based on the type of cells that dominate the inflammatory infiltrate, the following asthma phenotypes have been distinguished: eosinophil, neutrophil and hypocellular one [1]. Meanwhile, a historical classification distinguishes between allergic and non-allergic asthma. Depending on the course and severity of the disease as well as therapeutic efficacy, controlled, partly controlled and uncontrolled types of asthma have been distinguished. Epidemiological studies estimate that uncontrolled asthma affects 26–49% of patients, while partly-controlled asthma occurs in 30–36% of patients. Complete asthma control is achieved in only 15% of patients. The most common consequences of ineffective asthma treatment include poor life quality, frequent and severe exacerbations as well as an increased risk of premature death [2]. Recently, biological therapy has been recommended in patients with severe asthma. Omalizumab – a humanized monoclonal IgG1 antibody directed against IgE – is recommended in the therapy of severe asthma, following GINA guidelines [3].

Aim

The aim of the study was to perform a retrospective assessment of adjunctive omalizumab therapy in patients with severe asthma who had failed to achieve asthma control when on treatment with maximum doses of inhaled agents and systemic corticosteroids. We have analysed selected pulmonary ventilation parameters following the administration of omalizumab.

Material and methods

A total of 6 patients (5 women and 1 man) aged between 32 and 66 (mean age: 50 ±12.6) were enrolled in the retrospective study assessing the effects of omalizumab adjunctive therapy. The baseline demographic data were obtained and a full medical history was taken. Asthma was diagnosed on the basis of GINA criteria.

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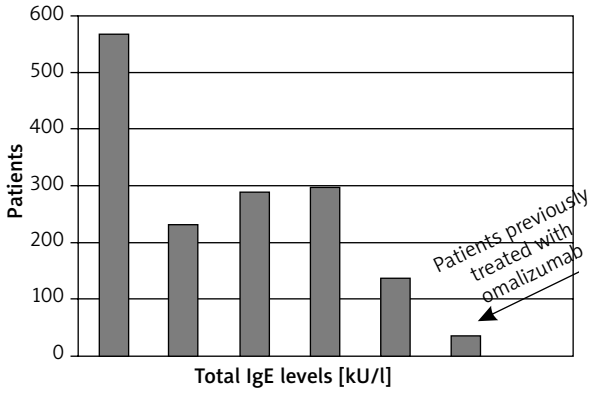

Figure 1. Total IgE levels in patients prior to omalizumab enrolment

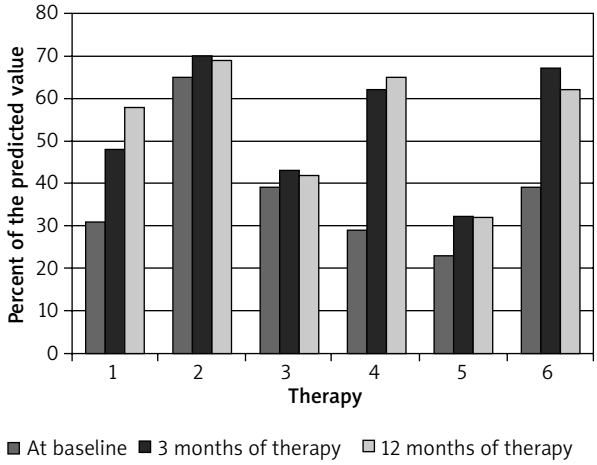

Figure 2. Effects of omalizumab therapy on FEV_1

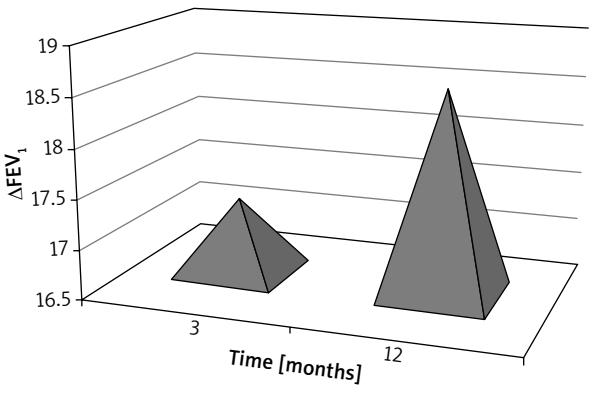

Figure 3. Increase in FEV_1 in patients treated with omalizumab

During the screening visits, subjects first had measurements of height, weight, blood pressure, heart rate, oxygen saturation, a physical examination and the subjects also completed the Asthma Control Test questionnaire (ACT) and Asthma Quality of Life (AQOL) questionnaire. The subjects then underwent spirometry. The spirometries were performed before the morning dose of inhaled corticosteroids and bronchodilatory drugs. Blood samples were analysed for total and specific IgE levels.

The qualification for omalizumab therapy was in line with Novartis and National Health Fund guidelines. Patients with severe uncontrolled asthma, who had been receiving therapy recommended by GINA, were qualified for the therapy [1]. The dose of omalizumab was selected in accordance with drug manufacturer's recommendations and depended on the patient's body mass and baseline total IgE levels (Figure 1).

The doses administered ranged between 150 and 900 mg per month. All patients who qualified for omalizumab therapy had allergic asthma. Allergy to perennial allergens, mainly to house dust mites (*Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*) was confirmed in the evaluated patients.

Results

The analysis of forced expiratory volume in 1 s (FEV_1) values in patients treated with omalizumab showed increased FEV_1 in all patients in the first 3 months of therapy. The highest increase (100%) in FEV_1 was observed in 2 patients (Figure 2).

Comparative analysis of the increase in average ΔFEV_1 in patients receiving omalizumab showed an increase by 17.28 ±13.4% and 18.57 ±13.7% after 3 months and 1 year of treatment, respectively.

Discussion

The analysis conducted demonstrated improved spirometric parameters in all patients receiving omalizumab for 1 year. Our findings are consistent with the observations of other researchers who conducted their studies in large groups of patients, allowing for statistical analysis of the results obtained [4]. Thorough meta-analysis by Lai *et al.* [5] showed that biological therapy with omalizumab is, most of all, safe and also reduces exacerbations, improves the quality of life and increases FEV_1 in patients with severe asthma. It is worth noting that a clear increase in FEV_1 occurs already in the first 3 months of treatment (Figure 3).

The mechanism of action of omalizumab involves IgE binding followed by elimination of this antibody from circulation [6]. The patients subject to evaluation demonstrated high total IgE levels prior to enrolment (Figure 1), except for one patient who had already been treated with omalizumab in phase III clinical trial (Novartis) in

2009. Omalizumab therapy reduces the levels of free IgE circulating in the serum up to 99% and causes a radical reduction in FcεRIs (by approx. 97%) on the surface of basophils [7, 8]. High levels of IgE are a factor increasing bronchial hyperresponsiveness. Omalizumab-induced reduction in antibody levels improves spirometric parameters in patients with asthma [9–11].

It was also shown that omalizumab reduces bronchial tree inflammation in patients with asthma [12]. Therapy using this antibody reduces both eosinophil infiltration in the respiratory epithelium as well as eosinophil count in the sputum. Furthermore, it was noted that this type of treatment decreased the number of B-CD19+, CD3+ and CD4+ lymphocytes infiltrating the bronchial walls as well as suppressor/cytotoxic CD3+ and CD8+ lymphocytes [13]. According to Riccio *et al.* [14], reduced inflammation in the bronchial epithelium inhibits bronchial tree remodelling. It was demonstrated that a 12-month therapy with omalizumab reduces the number of collagens deposited in the reticular layer of the bronchial epithelial basement membrane, thus improving bronchiolar elasticity and patency [15, 16]. Other studies have shown that omalizumab has beneficial effects also on bronchiolar smooth muscles [17]. According to Mauri *et al.*, omalizumab inhibits muscle remodelling and blocks the accumulation of excess extracellular matrix proteins (ECM), mainly galectin [18].

Further studies are needed to perform longer clinical observations and spirometry tests with statistical analysis.

Conclusions

The analysis conducted along with the observations in patients treated with omalizumab suggest the beneficial effects of this drug in patients with severe asthma. In addition to safety and improvement in the general condition of patients, an increase in FEV_1 has been noted at 3 and 12 months. The results confirmed earlier observations.

Conflict of interest

The authors declare no conflict of interest.

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