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Home administration of biological treatment in severe asthma in real-life experience: impact on asthma control and quality of life

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Key words

Biological treatment; severe asthma; home administration; self-administration.

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Impact statement

Home administration of biological treatment in severe asthma did not lead to any deterioration of asthma control or quality of life in real-life experience.

Summary

Introduction. *Several biological agents for the treatment of severe asthma have been approved for self-administration on an outpatient basis in the last years. However, data on the impact of home administration in outcomes such as asthma control and quality of life in real-life settings are sparse. Being this knowledge crucial for clinical practice, this study aimed to assess asthma control and quality of life in patients who transitioned from day hospital administration of biological therapy to home administration.* ***Methods.*** *A single-center prospective analysis of 33 patients treated with biologics for severe asthma, who switched from hospital to home treatment was performed. Asthma Control Test (ACT), Control of Allergic Rhinitis and Asthma Test (CARAT), Asthma Life Quality (ALQ) and the number of exacerbations were assessed 3 months before and 3 and 6 months after of home-use.* ***Results.*** *ACT and CARAT did not show statistical differences comparing to the baseline values (21.8 ± 2.7 and 23.8 ± 5.5) within 3 months (22.1 ± 2.4, p = 0.609; 23.2 ± 5.3, p = 0.572) or 6 months (23.4 ± 0.9, p = 0.553; 23.7 ± 6.2, p = 0.149) of home administration. Also, ALQ score did not show meaningful variations between baseline (9.5 ± 3.2) and after 3 months (11.2 ± 4.4, p = 0.275) and 6 months (10.3 ± 3.8, p = 0.209) of home-use. Regarding asthma exacerbations, we did not record a significant difference comparing to the baseline values of 3 months/patient exacerbations (0.2 ± 0.4) and after 3 months (0.2 ± 0.5, p = 0.786) or 6 months (0.2 ± 0.4, p = 1.000) of change in modality treatment. There were no cases of anaphylaxis or other serious adverse effects in those patients treated at home.* ***Conclusions.*** *Transition of day hospital administration of biologic treatment for severe asthma to home administration did not lead to any deterioration of asthma control or quality of life. Our results emphasized the efficacy and safety of home administration of biologic treatment and provide support on changing the paradigm of the administration of biological treatment in severe asthma.*

Introduction

Severe asthma affects approximately 5-10% of all asthmatic patients and it is characterized by an insufficient response to treatment with high doses of inhaled corticosteroids and a second controller (1, 2). In recent years, there has been a remarkable progress in the treatment of asthma due to a better understanding of its complex pathophysiology and the introduction of several biological drugs (3). Recently, four out of five biologics have been approved for patient self-administration at home in Europe. The advantages of self-administration of drugs have already been highlighted in the literature, as well as being clearly recognized in the treatment of rheumatoid arthritis and psoriasis. These studies stated the efficacy and safety of the treatments, besides the greater patient adherence to therapy (4-6). The out-of-hospital administration of biologic agents in severe asthma has been addressed by several studies that evidenced the added-value of this kind of administration (7-9). For instance, some studies demonstrated that patients can safely and effectively self-administer biological agents through proper training and no cases of anaphylaxis, suspected allergic reactions or other serious adverse effects related to biological treatment were reported. Also, patient satisfaction related to self-administration has been reported (10, 11). In the era of

Coronavirus disease 2019 (COVID-19), international respiratory societies (Global Initiative for Asthma, European Respiratory Society, British Thoracic Society and American Academy of Allergy, Asthma & Immunology) updated their guidelines favoring the practice of self-administration of biologics. This recommendation of self-administration of biologics at home was followed by some centers during lockdown periods that revealed to be a success (12, 13). Nevertheless, it is needed to collect more data to clearly state the advantages of patient self-administration of biological drugs at home. Therefore, the aim of this study was to assess asthma control and quality of life in patients who transitioned from day hospital biological therapy administration to home administration at the Pulmonology Department of Centro Hospitalar e Universitário de Coimbra.

Methods

Study design

The current work was a prospective observational real-life study performed on patients treated with biologics for severe asthma, who switched from hospital to home treatment, between May 2020 and July 2021. The study took place in severe asthma unit from Pulmonology Department of Centro Hospitalar e Universitário de Coimbra. The research was conducted in accordance with the ethical standards established in the Declaration of Helsinki and informed consent was obtained from all participants before enrolment in the study.

This study included 18-year-old patients or older with severe asthma who were receiving treatment with biologic agents for at least 6 months. We used a protocol to support the process of self-administration, which comprised: 1) a questionnaire to the patients aiming to evaluate their acceptance level of the home administration modality, the patient perception of the advantages and drawbacks of this kind of administration, as well as to give the opportunity to the patients expose their concerns; 2) the decision of the coordinator of severe asthma unit on the patient overall conditions to comply with the modality treatment; 3) a teaching/training period of self-administration in the day hospital by the nurses team. Furthermore, patients were asked what kind of support information they would prefer regarding self-administration (video, written information). Patients received two or three doses under supervision with training on how to self-administer (according to the ability of the patient), followed by home self-administration for the remainder of the follow-up time. Telephone calls were made by the nurse to check if the auto-administration was performed at the correct time and reinforce adherence to therapy.

Clinical monitoring and patient follow-up after home treatment initiation was performed at least twice: at 3/4 months and at 6 months of treatment. At each patient visit the following parameters were recorded and comparatively evaluated: asthma control, asthma-related quality of life, number of exacerbations and adverse effects. The determination of these parameters is described in detail in the next sections. The technique was reviewed by the nurse.

Study measurements

Asthma control

Symptom control was assessed using the Asthma Control Test (ACT) and the Control of Allergic Rhinitis and Asthma Test (CARAT) at baseline, at 3 months and at 6 months after home treatment initiation. Scores at 3 and 6 months were compared to baseline.

The ACT is a self-administered five-item tool for identifying patients with poorly controlled asthma with a score ranging from 5 to 25. A score of 20 to 25 means that the asthma is well controlled; a cut off score of ≤ 19 indicates poorly controlled asthma in which a score of 16 to 19 is considered partially controlled asthma; and < 16 indicates uncontrolled asthma (14). Individual ACT score changes of ≥ 3 were considered to be clinically meaningful (15). A validated Portuguese-language version of the ACT was used (16).

CARAT is a brief self-administered Portuguese questionnaire divided into two sections: the first part evaluates the symptoms of allergic rhinitis through four questions, in which a total > 8 means good control; and the second part evaluates the symptoms of asthma in six questions, with good control defined as values > 16. Asthma was considered controlled for CARAT global score above 24 (17, 18).

Asthma-related quality of life

The quality of life was measured by Asthma Life Quality (ALQ) test, a self-administered questionnaire that comprises 20 questions in yes/no answer format. It addressed six dimensions of asthma's impact in patients' lives: activity and sleep, symptoms, triggers, unscheduled health care use, medication and psychological. All questions had equal weight and the total ALQ score is calculated as the sum of all positive (yes) responses, ranging from 0 to 20 (19). Lower scores reflect greater quality of life impairment. The Portuguese version of the ALQ was previously translated, adapted and validated (20).

Exacerbations

An exacerbation was defined as worsening of asthma symptoms, requiring the administration of oral corticosteroids (OCS) for at least 3 days or if the patient had visited an emergency department or was hospitalized. Exacerbation rates in the 3 months before home transition were compared to the number of exacerbations at 3 and 6 months following home treatment.

Adverse events

Safety was assessed by the collection and description of drug-related adverse events (AEs) during the study. The investigators determined the relationship of the AE to the different biologic agents.

Statistical analysis

Data at baseline were expressed as mean ± standard deviation (SD) for continuous variables and in terms of number and percent (n, %) for categorical variables. The normality of data distribution was assessed using Kolmogorov-Smirnov test. The statistical analysis used to assess the results obtained after transition to home administration was the Paired samples t-test for paired samples. A statistical significance level of 0.05 was used. Statistical analysis was performed by using the SPSS 25.0 software.

Results (figure 1)

Baseline patients' characteristics

A total of 33 patients from a population of 57 patients (57.9%) with severe asthma receiving biologic treatment were selected by the assistant physician to home administration and were enrolled in this study. Two patients were excluded because they did not adhere to the therapy on home modality and, subsequently, they were transferred back to the day hospital administration.

Clinical characteristics of the study population are shown in **table I**. The mean age of the population was 43.6 ± 16.3 years with a predominance of women (69.7%).

Before home administration, mean ACT scores were 21.8 ± 2.7 points. Mean CARAT score in the upper airways was 8.6 ± 3.1 and in the lower airways 15.1 ± 3.5, with mean of total CARAT score of 23.8 ± 5.5. The initial mean value for ALQ was 9.46 ± 3.2. The mean number of exacerbations in the past 3 months varied between 0 and 1, with most of the patients (84.8%) having none.

Concerning the biologic treatment administrated, 51.5% of patients were treated with omalizumab, 24.2% with mepolizumab, 15.2% with benralizumab and 9.1% with dupilumab. The mean duration of the biologic treatment as an add-on maintenance therapy was 3.0 ± 2.9 years. No patients were on OCS.

Symptom control

Asthma control based on the ACT scores did not show statistical differences comparing to the baseline (21.8 ± 2.7) at both 3 months (22.1 ± 2.4, p = 0.609) and 6 months of home treatment (23.4 ± 0.9, p = 0.553). No patients showed a decrease of 3 or more points in ACT score at 3 and 6 months of home modality, representing a stability in asthma control. Regarding CARAT total score, there were no significant variation comparing the baseline (23.8 ± 5.5) with the mean score at 3 months (23.2 ± 5.3, p = 0.572) and at 6 months (23.7 ± 6.2, p = 0.149). Similarly, baseline CARAT score of the upper airways (8.7 ± 2.8) and of the lower airways (14.3 ± 4.2) did not show significant difference after 3 months of home-use (8.7 ± 3.8, p = 0.876 and 15.1 ± 2.6, p = 0.145) and also after 6 months (8.8 ± 3.7, p = 0.855 and 14.6 ± 2.9, p = 0.118).

Table I *- Baseline patients' characteristics enrolled in this study.*

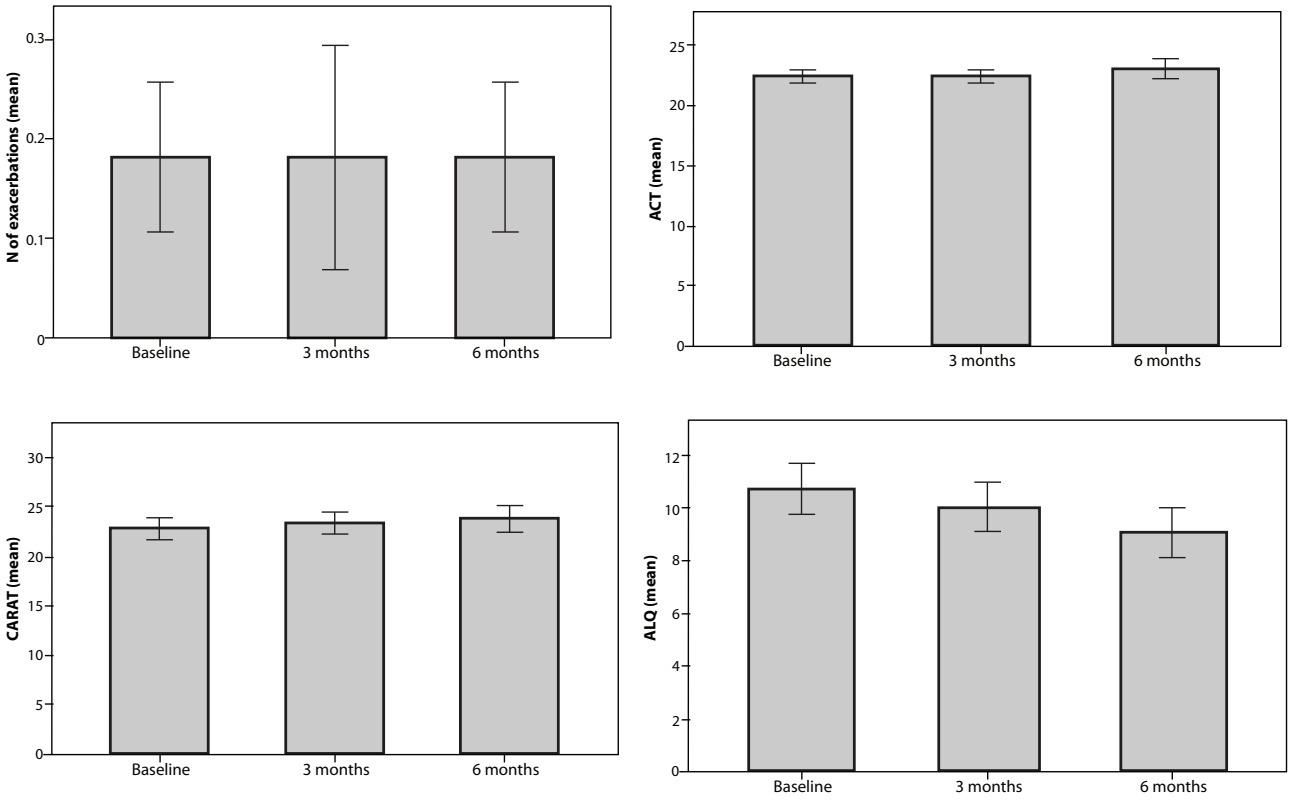
Variable	n = 33
Gender	
Female: n (%)	23 (69.7%)
Male: n (%)	10 (30.3%)
Age (years)	
Mean ± SD	43.6 ± 16.3
Range	19-70
Age group (years): n (%)	
18-34	9 (27.3%)
35-64	19 (57.6%)
≥ 65	5 (15.1%)
BMI (Kg/m^2): mean (SD)	27.9 ± 6.6
ACT	
Total score: mean (SD)	21.8 ± 2.7
Well-controlled asthma (score ≥ 20): n (%)	22 (66.6%)
Partly controlled asthma (score 19-16): n (%)	13 (39.4%)
Uncontrolled asthma (score < 16): n (%)	0 (0%)
CARAT	
Total score: mean ± SD	23.8 ± 5.5
Control asthma (score > 24): n (%)	18 (54.5%)
Upper airway: mean ± SD	8.6 ± 3.1
Control upper airway (score > 8): n (%)	17 (51.5%)
Lower airway: mean ± SD	15.1 ± 3.5
Control lower airway (score > 16): n (%)	18 (54.5%)
Exacerbations in the previous 3 months	
Median (range)	0 (0-1)
0: n (%)	28 (84.8%)
1: n (%)	5 (15.2%)
ALQ	
Total score: mean ± SD	9.46 ± 3.2
Spirometry	
Pre-BD FEV1 (ml): mean ± SD	2.73 ± 0.8
Pre-BD FEV1 (%): mean ± SD	88.0 ± 18.6
FEV1/FVC (%): mean ± SD	74.2 ± 13.6
Post-BD FEV1 (ml): mean ± SD	2.79 ± 0.8
Post-BD FEV1 (%): mean ± SD	91.1 ± 17.1
Biologic treatment: n (%)	
Omalizumab	17 (51.4%)
Mepolizumab	8 (24.2%)
Benralizumab	5 (15.2%)
Dupilumab	3 (9.1%)

ACT: Asthma Control Test; ALQ: Asthma Life Quality; BD: bronchodilator; BMI: body mass index; CARAT: Control of Allergic Rhinitis and Asthma Test; FEV1: forced expiratory volume at 1st second; FVC: forced vital capacity.

Exacerbations

There was no significant difference in exacerbation rate comparing to the baseline value of 3 months/patient exacerbations (0.2 ± 0.4) at both 3 months (0.2 ± 0.5, p = 0.786) and 6 months of home treatment (0.2 ± 0.4, p = 1.000).

Figure 1 *- Evolution of the number of exacerbations and ACT, CARAT and ALQ scores from baseline to 3 and 6 months after transition to home administration of biologic treatment.*



ACT: Asthma Control Test; ALQ: Asthma Life Quality; CARAT: Control of Allergic Rhinitis and Asthma Test.

Quality of life

There were no meaningful variations in ALQ score after 3 months (9.5 ± 3.2 *vs* 11.2 ± 4.4, p = 0.275) or 6 months (10.3 ± 3.8, p = 0.209) of home treatment.

Adverse events

There were no cases of anaphylaxis or other serious adverse effects in the patients treated at home. The related adverse effects were headaches (two cases), pain at the injection site (one case), hair loss (one case) and arthralgia (one case). Two patients discontinued home biologic treatment for non-compliance to the drug and none of the patients discontinued because of adverse effects. There was no difference in adverse effect frequency/severity seen between the home-treated and hospital-treated patients.

Discussion

In this study, we report a real-world experience of use of different biologic agents in home administration in patients with severe asthma. We observed that transition to home administration had no negative impact on adherence and did not lead to any deterioration of asthma control or quality of life, as highlighted by the absence of modification in the ACT, CARAT and AQLQ scores. Additionally, we did not record an increase in the number of reported exacerbations.

Adherence to home treatment in our study appears to be excellent, with only two patients discontinuing this modality of treatment for non-compliance reasons. Overall results of this study indicate that almost all patients were adequately trained to administer the treatment at home and that communication with the patient and confirmation of administration is crucial to enhance adherence to therapy. Additionally, understanding the individual preferences and concerns regarding self-administration at home may also improve adherence to therapy and well-being of the patient (21). These results corroborated previous results (12, 22) that reported self-administration can be a useful tool to maintain adherence to biological therapies. This is notable as it is well recognized that adherence to asthma inhaled

therapy tends to be very poor, with the reported rates of nonadherence ranging from 30 to 70% (23).

The asthma control assessed with validated tools did not show any deterioration when the treatment was switched to home administration. This finding corroborated the results of other previous studies. In 2007, Liebhaber *et al.* (9) reported their experience on 25 patients with allergic asthma undergoing long-term at home treatment with omalizumab demonstrating for the first time that patients can effectively self-administer omalizumab at home. Although efficacy measures were not a primary endpoint of the study of Liebhaber *et al.*, patients showed clinical improvement in symptoms of asthma. More recently, the GREGALE study assessed the functionality of an accessorized pre-filled syringe to administer a fixed dose of benralizumab both in a healthcare setting and at home, in patients with severe uncontrolled asthma (8). This study showed an improvement in asthma control as represented by the decreased in the mean Asthma Control Questionnaire 6 score compared with the baseline values. Several studies performed during COVID-19 lockdown also show that self-administration of biologics at home did not induce any significant change related to severe asthma control or exacerbations rate (12, 13).

In this present study, we did not record a worsen in patient's perception quality of life, since there was no statistically significant difference in the ALQ score in patients who transitioned to home administration. Although in our study we did not directly explore the patient satisfaction with home administration, the medication and psychological perception assessed by ALQ allowed us to infer about it.

In our study, no anaphylaxis was reported with biologic administration in an at-home setting and the safety profile was comparable to that observed in other studies (7-9, 24-27). This is an encouraging aspect for the at-home self-administration of biological drugs for severe asthma. Nevertheless, a longer duration study will be important to assess long-term safety of biologic administration in an at-home setting.

The main findings of our study are quite encouraging about home administration of biological treatment in severe asthma; however, we are aware of some methodological limitations. First, our study was based in a heterogenous asthmatic population under the treatment of four different biologic agents, but we believe that these biases had a low impact in our conclusions as we proved the absence of deterioration of asthma control in every single patient. Second, the sample population size was small, but this was the representation of a real-life experience in a dedicated single-center. To increase the population size, more centers should be involved. Third, even though this study was conducted in a real-life setting with a longer follow-up period (6 months), more extended follow-up times would be necessary to establish the efficacy and safety for longer observation times.

Apart from its limitations, this study presented relevant strengths. To the best of our knowledge, this is the first real-life study of home administration of different biologic agents in treatment of severe asthma addressing the benefit of biological treatment in terms of important clinical aspects, such as symptom control and quality of life, that are the most perceived results by the patient.

Conclusions

In conclusion, our real-life experience supported the efficacy and safety of home administration of biologics agents in the treatment of severe asthma. Larger home therapy studies are needed to provide the evidence necessary to adequately reinforce the efficacy and safety of home administration of biologic treatment in severe asthma and therefore change the paradigm of the administration of biological treatment in severe asthma.

Fundings

None.

Conflict of interests

The authors declare that they have no conflict of interests.

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