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Changes in Treatment Adherence During the COVID-19 Pandemic in Patients with Severe Asthma Receiving Biologic Agent Treatment

Biyolojik Ajan Tedavisi Alan Ağır Astımlı Hastalarda COVID-19 Pandemisi Sırasında Tedaviye Uyumdaki Değişiklikler

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Abstract

Aim: This study aimed to evaluate the effects of the COVID-19 pandemic on treatment adherence in patients with severe asthma who were receiving omalizumab and mepolizumab treatment in our clinic.

Material and Method: A total of 53 patients with severe asthma, 45 of whom were using omalizumab and 8 of whom were using mepolizumab, were included in the study. The medical records of the patients were recorded anonymously and retrospectively.

Results: It was seen that the rate of patients using omalizumab in the study population decreased during the pandemic period compared to the 1-year period before the pandemic. It was observed that approximately 51% of the patients using omalizumab missed routine treatment doses. The major factor in skipping treatment doses was the fear of contracting COVID-19 upon admission to the hospital. In the mepolizumab group, the rate of using biologic agents during the pandemic period increased compared to 1 year before the pandemic. Dose skipping was observed among 37.5% of the patients in this group and it was found that the major risk factor for skipping a dose was the fear of contracting COVID-19 upon admission to the hospital.

Conclusion: In this study, it was found that there was a decrease in the duration and rate of use of biologic agent therapies administered in a health institution under the supervision of a healthcare professional among patients with severe asthma during the pandemic.

Keywords: Coronavirus anxiety scale, mepolizumab, omalizumab, SARS-CoV-2

Öz

Amaç: Bu çalışmada, kliniğimizde omalizumab ve mepolizumab tedavisi alan ağır astımlı hastalarda COVID-19 pandemisinin tedaviye uyum üzerindeki etkilerinin değerlendirilmesi amaçlanmıştır.

Gereç ve Yöntem: Çalışmaya 45'i omalizumab ve 8'i mepolizumab kullanan ağır astımlı 53 hasta dahil edildi. Hastaların tıbbi kayıtları isimsiz ve geriye dönük olarak kaydedildi.

Bulgular: Çalışma popülasyonunda omalizumab kullanan hasta oranının pandemi öncesi 1 yıllık döneme göre pandemi döneminde azaldığı görüldü. Omalizumab kullanan hastaların yaklaşık %51'inin rutin tedavi dozlarını kaçırdığı gözlendi. Tedavi dozlarının atlanmasındaki en büyük faktör, hastaneye kabul edildikten sonra COVID-19'a yakalanma korkusuydu. Mepolizumab grubunda pandemi döneminde biyolojik ajan kullanma oranı pandemi öncesi 1 yıl öncesine göre artış gösterdi. Bu gruptaki hastaların %37,5'inde doz atlama gözlemlendi ve doz atlamanın en büyük risk faktörünün hastaneye başvuruda COVID-19 kapma korkusu olduğu bulundu.

Sonuç: Bu çalışmada, bir sağlık kuruluşunda sağlık profesyoneli gözetiminde uygulanan biyolojik ajan tedavilerinin pandemi döneminde ağır astımı olan hastalarda kullanım süre ve oranlarında azalma olduğu saptanmıştır.

Anahtar Kelimeler: Koronavirus anksiyete ölçeği, mepolizumab, omalizumab, SARS-CoV-2

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INTRODUCTION

Asthma is a heterogeneous disease characterized by chronic airway inflammation. Although most patients can keep their asthma under control with standard control treatments, there are patients with severe asthma who cannot keep it under control despite adherence to treatment. Severe asthma is asthma that is aggravated when high-dose medication is reduced or that cannot be controlled despite the treatment of factors contributing to worsened asthma such as wrong inhaler techniques, poor treatment adherence, comorbidities, and risk factors and despite adherence to level 4 or 5 treatment according to the Global Initiative for Asthma (GINA). The prevalence of severe asthma, a subgroup of difficult to treat asthma, is about 3.7%.[1]

Type 2 inflammation occurs in about half of all patients with severe asthma. Biologic treatment is a good option for patients with severe asthma who need frequent systemic steroids or who have steroid-dependent type 2 inflammation. In these patients omalizumab (anti – IgE), mepolizumab, reslizumab, benralizumab (anti – IL-5), and dupilumab (anti IL – 4/IL – 13) are the available monoclonal antibodies targeting type 2 inflammation.[1-3] Only omalizumab and mepolizumab have been approved for use in severe asthma in Turkey although all of the above have been approved for use in severe asthma in the world. In controlled studies and clinical experiments, both drugs have been shown to be effective in reducing asthma attacks and hospitalizations, maintaining symptom control, reducing the doses of control medication, and improving quality of life.[3-5]

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a highly contagious virus, is a new type of coronavirus first reported in December 2019 in Wuhan, China. Coronavirus disease-2019 (COVID-19), which causes significant morbidity and mortality, was declared a pandemic by the World Health Organization (WHO) on March 11, 2020.[6] The first coronavirus case was announced by the Ministry of Health in Turkey on the same day. During the COVID-19 pandemic, adherence is crucial in treatment with control medications, including biologic agents, for those with respiratory diseases such as asthma.[7,8]

Based on the available data, what is currently recommended in guidelines is to continue regular asthma treatments, including corticosteroids and biologic agents, in asthma patients during the COVID-19 outbreak.[1,9] Real-life data obtained on this topic during the pandemic will support the implementation and development of such recommendations. In this study, we aimed to evaluate the effects of the COVID-19 pandemic on adherence to treatment in patients with severe asthma who were receiving omalizumab and mepolizumab treatment in our clinic.

MATERIAL AND METHOD

Study Design and Patient Recruitment

Patients over the age of 18 with a diagnosis of severe asthma, who started to receive omalizumab or mepolizumab treatment according to the GINA guideline before March 20, 2019 in our clinic and are still receiving these treatments on March 20, 2021, were included in the study. The medical records of the patients were evaluated anonymously and retrospectively.

Demographic characteristics of the patients (age, sex, weight, height, comorbidities, place of residence), asthma diagnosis and follow-up periods, the biologic agent they were taking (omalizumab or mepolizumab), the presence of atopy (skin prick test and/or serum spesific IgE positivity observed for perennial/seasonal allergen sensitivity) were recorded from patient files. In addition, before and during the pandemic, any disruption in treatment with the control therapies that the patients were using for asthma, the reason for the interruption of the treatment if there was any, and the rates of taking biologic agents and the reason for skipped doses if any were also evaluated. Patients' rates of COVID-19 infection during the pandemic and how they were treated (outpatient/hospital) were also evaluated. The Coronavirus Anxiety Scale (CAS) scores of patients who had CAS results in their records were noted.

The study protocol was approved by the Keçiören Training and Research Hospital (Ethics Committee No: 2012-KAEK-15/2248) and an authorization certificate was obtained from the Ministry of Health (Hale Ateş-2021-01-23T08_53_18) to carry out the study.

Omalizumab and Mepolizumab Administration Protocol

Omalizumab is a humanized monoclonal antibody developed against IgE. It is indicated in moderate to severe persistent allergic asthma patients who are inadequately controlled with inhaled corticosteroids. Omalizumab can be administered to patients with uncontrolled asthma despite GINA Step 4-5 treatment, with a pretreatment total serum IgE level between 30 and 1500 IU/mL, and perennial allergen sensitivity as demonstrated by skin prick test and/or specific IgE measurement on the basis of the Turkish Social Security Institution Health Application Communique. It is applied subcutaneously every 2 or 4 weeks, according to patient's pretreatment body weight and initial total serum IgE levels.[3,4]

Mepolizumab is a humanized IgG1 type monoclonal antibody that binds to IL-5. It is indicated as add-on maintenance treatment of patients with severe asthma with an eosinophilic phenotype. Mepolizumab can be administered to patients with blood eosinophil count of ≥300 cells/μL (≥150 cells/μL if the patient is under long term, regular systemic steroid therapy) and patients with uncontrolled asthma (at least 2 exacerbations per year requiring the use of systemic corticosteroids for at least 3 days) although they have been using a third control medication together with a high-dose inhaled corticosteroid-long-acting beta agonist (ICS – LABA) combination for at least 1 year and/or controlled or uncontrolled asthma under regular systemic steroid therapy for at least 6 months on the basis of the Turkish Social Security Institution Health Application Communique. It is applied subcutaneously 100 mg every 4 weeks.[3,4]

The recommended initial duration of treatment with both biologic agents is at least 16 weeks. At the end of this period, the treatment response is evaluated and if a good response has been obtained, the treatment is continued.[3-5]

Routine Treatment Steps

The conventional treatment approach of the current asthma guidelines regarding the pharmacological treatment of asthmatic patients is the "stepwise approach." There are five steps from 1 to 5 in stepwise treatment, in which the treatment is arranged according to the level of asthma control and targeting the treatment that will ensure control. It is applied by reducing the dose and type of medication (step – down) in well-controlled patients (in cases where asthma has been under control for at least 3 months) and increasing the dose and type of medication (step – up) in patients who have uncontrolled asthma.[10] In this study, the control treatments that our patients were receiving for asthma before and during the pandemic were evaluated through stepwise treatment.

Evaluation of Treatment Adherence

In our clinic, for patients with the diagnosis of severe asthma, medications are administered by a trained nurse under the supervision of a doctor following all safety precautions, every 2 or 4 weeks according to the dosage table for patients receiving omalizumab and every 4 weeks for patients receiving mepolizumab. The patients are evaluated before the injections, 2 hours after the first three injections, and 30 minutes after the next injections. The findings are recorded in the patients' files at each visit. From the patient records, it was evaluated whether the patients used their daily control asthma medications regularly during the pandemic, whether there were interruptions in biologic agent therapies such as skipping doses, discontinuing the treatment or having it done in another health institution and, if there were any, the reasons behind them were evaluated. These values were compared with the pre-pandemic period and the rates of receiving treatment were expressed as percentages.

Coronavirus Anxiety Scale Evaluation

The CAS was developed by Sherman A. Lee in 2020 to identify possible dysfunctional anxiety cases associated with the COVID-19 crisis, and the Turkish validation of the scale was performed by Biçer et al. in the same year. The scale consists of 5 questions scored from 0 ("never") to 4 ("almost every day in the last 2 weeks"). A total score of ≥9 is accepted as a cut-off score for separating patients with and without dysfunctional anxiety.[11,12] Patients with CAS results in their files were identified, and patients with a CAS score of ≥9 were considered to have dysfunctional anxiety.

Statistical Analysis

Data were analyzed using IBM SPSS Statistics 22.0 for Windows (IBM Corp., Armonk, NY, USA). The Kolmogorov-Smirnov test was used to test the normal distribution of variables. Continuous variables with normal distribution were expressed as mean ± standard deviation, and continuous variables without normal distribution were expressed as median (min-max). Categorical variables were presented as numbers and percentages. Differences in numerical variables between the two groups were evaluated with Student's t-test or the Mann-Whitney U test. Changes in treatment steps before, during, and after the pandemic were evaluated with Kendall's W analysis. Changes in the rate of usage of biologic agents before and after the pandemic were evaluated with the paired sample t-test. Values of $p<0.05$ were considered significant for statistical analyses.

RESULTS

A total of 66 patients were initially included in this study. Thirteen patients, 5 patients whose treatment was continued in another center at the time of the study and 8 patients whose treatment was discontinued for various reasons, were excluded from the study. The data of 53 patients who met the study criteria were thus evaluated. Demographic findings of the study population are given in **Table 1**. Among patients using omalizumab, the number of cases with atopy (42 (93.3%) vs. 1 (12.5%), $p<0.001$) and perennial allergen sensitivity (41 (91.1%) vs. 1 (12.5%), $p<0.001$) were found to be higher and the number of cases with chronic eosinophilic pneumonia (3 (6.7%) vs. 7 (87.5%), $p<0.001$) was found to be lower compared to patients using mepolizumab. The mean year of diagnosis for asthma among patients using omalizumab was 19 years, while it was found to be 10 years in the mepolizumab group ($p=0.006$).

Table1. Demographic findings of the study population

Variables	All population n=53	Omalizumab n=45	Mepolizumab n=8	p
Age, (year)	50.8 ±11	51.1 ±11.4	49.1 ±8.5	0.649
Gender, n(%)				
Female	38(71.7)	33(73.3)	5(62.5)	0.841
BMI, (kg/m²)	29 ±4.9	29.3 ±5	27.6 ±4.3	0.374
Comorbidity, n(%)				
Atopy	43(81.1)	42(93.3)	1(12.5)	<0.001*
Perennial allergen	42(79.2)	41(91.1)	1(12.5)	<0.001*
Seasonal allergen	10(18.9)	10(22.2)	0(.0)	0.322
Allergic rhinitis	8(15.1)	8(17.8)	0(.0)	0.448
Nasal polyp	20(37.7)	15(33.3)	5(62.5)	0.241
CEP	10(18.9)	3(6.7)	7(87.5)	<0.001*
Drug allergy	13(24.5)	12(26.7)	1(12.5)	0.68
Food allergy	0(.0)	0(.0)	0(.0)	-
Venom allergy	3(5.7)	3(6.7)	0(.0)	0.999
Hypertension	9(17.0)	8(17.8)	1(12.5)	0.999
Diabetes Mellitus	3(5.7)	3(6.7)	0(.0)	0.999
OSAS	10(18.9)	9(20.0)	1(12.5)	0.993
Asthma				
Diagnosis time, (year)	15(2-60)	19(2-60)	10(7-23)	0.006*
Follow–up time, (year)	8(2-15)	8(2-15)	6(2-11)	0.321

Abbreviations: BMI: Body Mass Index, OSAS: Obstructive Sleep Apnea Syndrome, CEP: chronic Eosinophilic Pneumonia,

It was seen that the patients using omalizumab had received treatment for 67 months and the patients using mepolizumab had received treatment for 36 months. In terms of standard treatment steps, no difference was detected in the 1-year period before the pandemic and during the pandemic. While the percentage of patients who received biologic agents in the year before the pandemic was 89.0±18.8% in the omalizumab group and 94.9±6.2% in the mepolizumab group, these rates during the pandemic were respectively 82.8±24.8% and 97.0±4.1%. During the pandemic, it was found that 7 (15.6%) patients in the omalizumab group and 1 (12.5%) in the mepolizumab group received their treatment in an external center. During the pandemic, 23 (51.1%) patients in the omalizumab group and 3 (37.5%) patients in the mepolizumab group were found to have missed their treatment doses. The reason for skipping the dose was due to insurance problems in 3 (6.7%) cases in the omalizumab group and in 1 (12.5%) case in the mepolizumab group. Twenty (44.4%) patients in the omalizumab group and 2 (25%) patients in the mepolizumab group had skipped doses by not going to the hospital for fear of contracting COVID-19. Nine (20%) patients were diagnosed with COVID-19 infection in the omalizumab group, whereas no cases of COVID-19 were detected in the mepolizumab group. While four of the patients diagnosed with COVID-19 had severe cases, five had mild cases. The CAS scores in both groups were <9 in all cases (**Table 2**).

Demographic and clinical findings of patients who missed doses during the pandemic are shown in detail in **Tables 3** and **4**. Biologic agent usage rates were found to be lower among patients who missed doses in the year before the pandemic compared to those who did not skip doses (82.6±22.1% vs. 97±6.2%, p=0.003). The rates of COVID-19infection(p=0.663) and CAS scores (p=0.220) were found to be similar among those who skipped doses and those who did not.

Table 2. Clinical findings of the study population

Variables	All population n=53	Omalizumab n=45	Mepolizumab n=8	p
Treatment time, (month)	59(11-142)	67(11-142)	36.5(11-44)	0.003*
Treatment step 1 year before the pandemic				
Step 1	0	0	0	
Step 2	0	0	0	
Step 3	7(13.2)	6(13.3)	1(12.5)	0.149
Step 4	28(52.8)	26(57.8)	2(25.0)	
Step 5	18(34.0)	13(28.9)	5(62.5)	
The treatment step during the pandemic				
Step 1	0	0	0	
Step 2	0	0	0	
Step 3	3(5.7)	1(2.2)	2(25.0)	0.079
Step 4	38(71.7)	33(73.3)	5(62.5)	
Step 5	12(22.6)	11(24.4)	1(12.5)	
Rate of BA received in the 1 year before the pandemic, (%)	89.9 ±17.5	89.0 ±18.8	94.9 ±6.2	0.388
Rate of BA received during the pandemic, (%)	84.9 ±23.4	82.8 ±24.8	97.0 ±4.1	0.001*
Rate of receiving BA at a different center during the pandemic	8(15.1)	7(15.6)	1(12.5)	0.999
Has there been a dose skipping in the pandemic?, n(%)				
Yes	26(49.1)	23(51.1)	3(37.5)	0.704
No	27(50.9)	22(48.9)	5(62.5)	
Reason for skipping dose, n(%)				
Worry about being infected with Covid-19	22(41.5)	20(44.4)	2(25.0)	
Transportation problem	0	0	0	0.415
Insurance problem	4(7.5)	3(6.7)	1(12.5)	
Regular intake of asthma control therapy in the previous 1 year	53(100.0)	45(100.0)	8(100.0)	-
Regularly taking asthma-controller therapy during the pandemic	52(98.1)	44(97.8)	8(100.0)	0.999
Rate of being diagnosed with Covid-19, n(%)	9(17.0)	9(20.0)	0	0.38
Severity of Covid 19, n(%)				
Non severe	5(9.4)	5(11.1)	0	0.781
Severe	4(7.5)	4(8.9)	0	
Coronavirus anxiety scale score	0(0-8)	0(0-8)	0(0-4)	0.427
<9	53(100.0)	45(100.0)	8(100.0)	-
>9	0	0	0	

Abbreviations: BA: Biological Agent

Table 3. Relationship between demographic characteristics and dose skipping

Variable	Dose skipping in treatment Yes n=26	No n=27	p
Age, (year)	53.5 ±12.3	48.2 ±8.9	0.076
Gender, n(%)			
Female	19(73.1)	19(70.4)	0.999
BMI, (kg/m2)	28.9 ±4.6	29.1 ±5.2	0.891
Comorbidity, n(%)			
Atopy	24(92.3)	19(70.4)	0.091
Perennial allergen	23(88.5)	19(70.4)	0.175
Seasonal allergen	7(26.9)	3(11.1)	0.263
Allergic rhinitis	4(15.4)	4(14.8)	0.999
Nasal polyp	10(38.5)	10(37.0)	0.999
CEP	4(15.4)	6(22.2)	0.776
Drug allergy	8(30.8)	5(18.5)	0.352
Food allergy	0(.0)	0(.0)	-
Venom allergy	1(3.8)	2(7.4)	0.999
Hypertension	5(19.2)	4(14.8)	0.950
Diabetes Mellitus	1(3.8)	2(7.4)	0.999
OSAS	4(15.4)	6(22.2)	0.728
Asthma			
Diagnosis time, (year)	21.5(2-60)	15(4-33)	0.068
Follow–up time, (year)	7(2-14)	8(2-15)	0.431

Abbreviations: BMI: Body Mass Index, OSAS: Obstructive Sleep Apnea Syndrome, CEP: chronic Eosinophilic Pneumonia,

Table 4. Relationship between clinical features and Dose skipping

Variable	Dose skipping in the treatment Yes n=26	No n=27	p
Biological agent, n (%)			
Omalizumab	23(88.5)	22(81.5)	0.704
Mepolizumab	3(11.5)	5(18.5)	
Treatment time, (month)	46.5(11-142)	68(11-135)	0.413
Treatment step 1 year before the pandemic			
Step 1	0(.0)	0(.0)	
Step 2	0(.0)	0(.0)	
Step 3	2(7.7)	5(18.5)	0.170
Step 4	12(46.2)	16(59.3)	
Step 5	12(46.2)	6(22.2)	
The treatment step during the pandemic			
Step 1	0(.0)	0(.0)	
Step 2	0(.0)	0(.0)	
Step 3	1(3.8)	2(7.4)	0.425
Step 4	17(65.4)	21(77.8)	
Step 5	8(30.8)	4(14.8)	
Rate of BA received in the 1 year before the pandemic, (%)	82.6 ±22.1	97 ±6.2	0.003*
Rate of BA received during the pandemic, (%)	69.2 ±25.3	100	-
Has there been a dose skipping in the pandemic?, n(%)			
Yes	26(100.0)	0(.0)	-
No	0(.0)	27(100.0)	
Reason for skipping dose, n(%)			
Worry about being infected with Covid-19	22(84.6)	0(.0)	-
Transportation problem	0(.0)	0(.0)	
Insurance problem	4(15.4)	0(.0)	
Regular intake of asthma control therapy in the previous 1 year	26(100.0)	27(100.0)	-
Regularly taking asthma-controller therapy during the pandemic	25(96.2)	27(100.0)	0.985
Rate of being diagnosed with Covid-19, n(%)	5(19.2)	4(14.8)	0.950
Severity of Covid 19, n(%)			
Non severe	2(7.7)	3(11.1)	0.663
Severe	3(11.5)	1(3.7)	
Coronavirus anxiety scale score	0(0-8)	0(0-4)	0.220
<9	26(100.0)	27(100.0)	-
>9	0(.0)	0(.0)	

Abbreviations: BA: Biological Agent

DISCUSSION

In this study, we examined adherence to treatment during the COVID-19 pandemic among severe asthma patients using biologic agents. It was seen that the rate of patients using omalizumab in the study population decreased during the pandemic period compared to the 1-year period before the pandemic. It was observed that 51% of the patients who were using omalizumab missed the doses in routine treatment. The major factor in skipping the treatment dose was the fear of contracting COVID-19 during hospital admission. In the mepolizumab group, the rate of using biologic agents during the pandemic period increased compared to the 1-year period before the pandemic. Dose skipping was observed in 37.5% of the cases in this group, and it was found that the major risk factor for skipping a dose was the concern of contracting COVID-19 during hospital admission.

In severe asthma patients, treatment adherence during the COVID-19pandemic should be considered by both patients and healthcare professionals because COVID-19infection may progress asymptomatically or as a serious disease that may result in pneumonia and severe acute respiratory distress syndrome in the lower respiratory tract.[13-15] Although studies in asthmatic patients showed different results regarding the course of COVID-19 infection and mortality rate compared to the normal population, it has been reported that non adherence to treatment or continuous oral steroid use in these patients may increase the risk of contamination with COVID-19 and mortality.[16-18] Thus, it is necessary for asthma patients to adhere to treatment at an optimal level and to avoid situations that may cause asthma attacks. According to a study by Kaye et al., among patients with asthma and chronic obstructive pulmonary disease, the rate of using inhaler treatment increased from 53.7% to 61.5% after COVID-19 was declared a pandemic by the WHO. Kaye et al. emphasized that this change was due to the efforts of patients to keep their respiratory tract diseases under control during the pandemic.[7] In the present study, there was no significant change in adherence to inhaler treatment during the pandemic period compared to the period before the pandemic.

Biologic treatments are treatments performed at regular intervals in health institutions under the supervision of healthcare professionals. We have all observed that during the pandemic process patients in all chronic disease groups have delayed appointments at hospitals for routine checkups and other treatments for fear of contracting COVID-19.[19] Thus we also found this in patients using biologic agents. In this study, the rate of medication use in the 1-year period before the pandemic in patients receiving omalizumab treatment was found to be lower than the rate during the pandemic period. However, during the pandemic process, it was observed that treatment doses were skipped significantly more often compared to the period before the pandemic. When the patients were questioned one by one, it was determined that the decreased rate of omalizumab use and skipped treatment doses were mostly due to the fear of contracting COVID-19 during hospital admission. An interesting aspect of this study is that although a decrease was observed in the rate of regular use of biologic agents, there was no increase in the use of standard inhaler therapy in these cases. We think that this is due to the fact that patients constantly wore masks, paid attention to social distancing, did not enter crowded environments, and stayed away from other risk factors that would trigger asthma attacks for fear of contracting COVID-19. The number of cases in the mepolizumab group was limited but the rate of treatment in this group increased compared to the period before the pandemic. Compared with patients receiving omalizumab, patients receiving mepolizumab may have a shorter duration of treatment and a shorter time to have asthma under control, and so they may have greater anxiety about loss of control asthma. It is thought that this situation increased the adherence to treatment in this group. However, among patients using this treatment, it was also observed that treatment doses were skipped during the pandemic and this was again due to the fear of contracting COVID-19 in the hospital.

Although it was seen that the major reason for the decreases in the rates of using biologic agents and receiving regular doses during the pandemic compared to the period before the pandemic was the fear of contracting COVID-19 during hospital admission, the results of the CAS scores were <9 for all patients. Based on these results, it is thought that the patients were not anxious but rather were acting in a cautious manner.

The major limitation of this study is that it was conducted with a small number of cases.

CONCLUSION

In this study, it was found that there was a decrease in the duration and rate of the use of biologic agent therapies administered in a health institution under the supervision of a healthcare professional among severe asthma patients during the pandemic. It was observed that the major risk factor for the decrease in treatment adherence was the fact that these treatments were given in the hospital and the patients were worried about admission to hospital for fear of contracting COVID-19.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study protocol was approved by the Keçiören Training and Research Hospital (Ethics Committee No: 2012-KAEK-15/2248) and an authorization certificate was obtained from the Ministry of Health (Hale Ateş-2021-01-23T08_53_18) to carry out the study.

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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