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The efficacy of omalizumab therapy in chronic spontaneous urticaria: A retrospective analysis

Kronik spontan ürtikerde omalizumab tedavisinin etkinliği: Retrospektif değerlendirilme

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Abstract

Background and Design: Omalizumab is recombinant humanized monoclonal antibody that binds to immunoglobulin E (IgE). It inhibits the activation of IgE by binding to the effector cell, thereby inhibiting the release of cellular mediators. Omalizumab is indicated in H1-antihistamine-resistant chronic spontaneous urticaria (CSU) cases and data on successful use in CSU is increasing.
The aim of this study was to evaluate the efficacy and possible side effects of omalizumab, the period from the discontinuation of treatment to the relapse of symptoms, and the clinical and demographic characteristics of patients with refractory CSU.
Materials and Methods: We retrospectively evaluated the data of 130 patients with refractory CSU who received subcutaneous 300 mg/month omalizumab therapy in our clinic.
Results: Complete remission was achieved in 77.8% of the patients. Of the 80 patients who discontinued therapy due to remission, 55% had relapses within 2 months to 1 year. It was observed that the efficacy of the drug was not lost and the efficacy did not change in the patients who started the treatment again. Six percent of the patients did not respond to treatment. Clinical improvement was found to be independent of age, gender, presence of angioedema, high thyroid autoantibody levels and disease duration. No serious side effects were found in the patients.
Conclusion: In patients with refractory CSU, omalizumab is an effective and safe treatment option.
Keywords: Urticaria, therapy, omalizumab

Öz

Amaç: Omalizumab, immünoglobulin E'ye (IgE) bağlanan rekombinant humanize monoklonal antikordur. IgE'nin efektör hücreye bağlanmasını engelleyerek aktivasyonu dolayısıyla da selüler medyatörlerin salınımını inhibe etmektedir. Omalizumab H1-antihistaminiklere dirençli kronik spontan ürtiker (KSÜ) olgularında endikasyon almış olup, KSÜ'de başarılı şekilde kullanımına dair veriler artmaktadır. Çalışmamızda, kliniğimizde takip ettiğimiz tedaviye dirençli KSÜ olgularında omalizumab etkinliği ile olası yan etkilerinin; tedavinin kesilmesinden itibaren semptomların nüks etmesine kadar geçen sürelerin ve olguların klinik ve demografik özelliklerinin değerlendirilmesi amaçlanmıştır.
Gereç ve Yöntem: Kliniğimizde takip ettiğimiz ve 300 mg/ay subkutan omalizumab tedavisi alan 130 KSÜ olgusu retrospektif olarak değerlendirildi.
Bulgular: Omalizumab tedavisi alan 130 hastanın %77,8'inde tam remisyon sağlandı. Remisyon nedeniyle tedavisi sonlandırılmış olan 80 hastanın %55'inde 2 ay-1 yıl içinde relaps gözlendi. Tedaviye tekrar başlanan hastalarda, ilacın etkinliğinde bir kayıp olmadığı ve etkinliğinin değişmediği gözlendi. %6 hastada tedaviye yanıt alınamadı. Klinik iyileşmenin yaş, cinsiyet, anjiyoödem varlığı, tiroid otoantikor yüksekliği ve hastalık süresinden bağımsız olduğu gözlendi. Hastalarda ciddi bir yan etki saptanmadı.
Sonuç: Dirençli KSÜ olgularında omalizumab etkin ve güvenli bir tedavi seçeneğidir.
Anahtar Kelimeler: Ürtiker, tedavi, omalizumab

Introduction

Chronic Spontaneous Urticaria (CSU) is a skin disease characterized by erythematous-edematous papules, angioedema or both that recur for more than 6 weeks and have no apparent external trigger[1,2]. The prevalence of CSU ranges from 0.5% to 1%[2]. Half of the cases are accompanied by angioedema[2].

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Omalizumab is a recombinant humanized monoclonal antibody and inhibits the activation of Immunoglobulin E (IgE) by blocking it from binding to the effector cell, thereby inhibits the release of cellular mediators[3-6]. It has licensed for the treatment of H1-antihistamines-resistant CSU cases and data on its successful use in CSU are increasing. In our study, we evaluate the clinical and demographic characteristics of the CSU patients receiving omalizumab, the effectiveness and the possible side effects of the treatment and the time of the recurrence of symptoms after discontinuation of treatment.

Materials and Methods

The effectiveness of omalizumab, side effects, and duration of remission after treatment were investigated retrospectively in 130 CSU patients receiving omalizumab in our clinic followed in 2014-2017. Omalizumab was administered as 300 mg subcutaneous in every 4 weeks, regardless of patient weight and serum IgE levels, in accordance with the urticaria treatment scheme. Demographic and clinical characteristics of patients and Urticaria Activity Scores (UAS7) recorded before the treatment, after the first injection and after the third injection were evaluated. In addition, the Dermatology Life Quality Indexes (DLQI) recorded before treatment and at the third month of treatment was examined. Anti-thyroglobulin and anti-thyroid peroxidase autoantibody panel were examined to evaluate thyroid autoimmunity. No inducible urticaria patients were included in the study. Our study was approved by the Ethics Committee of Health Sciences University İzmir Bozyaka Training and Research Hospital. (approval number: 86-2019). Informed consent was obtained from all patients who participated in our study.

Statistical Analysis

Descriptive statistics used in the study were expressed as mean ± standard deviation, number (n) and percentage (%).

Results

Eighty three of 130 (63,8%) patients receiving omalizumab treatment were female and their ages ranged from 14 to 82 years (mean age: 42.4±15.7), duration of disease ranged from 6 months to 40 years (mean duration: 5, 7±6.5 years). High thyroid autoantibodies were detected in 45 (34.6%) patients. Seventy-two of the patients (55.3%) had angioedema. Demographic characteristics of the patients were summarized in Table 1.

All patients were resistant to doses up to four times the second-generation antihistamines we administered as recommended in the treatment guidelines, and resistant to leukotriene receptor antagonist drugs.

Treatment was discontinued as complete remission was achieved after 3-24 months of treatment in 80 (61.5%) of 130 patients to whom omalizumab was administered. In our patients, complete remission was defined as complete regression of urticaria lesions and angioedema attacks or suppression of urticarial plaque output and itching at the level of minimal symptoms that do not require additional medications (antihistamine, leukotriene receptor antagonist). In 36 (45%) of 80 patients whose treatment were discontinued, no new attack and lesion output was observed in 6-27 months of follow-up. Recurrence of symptoms was observed within 2-12 months (mean 4.5±5.2 months) in 44 (55%) of 80 patients whose treatment was discontinued due to the remission, and the treatment was continued again. It was observed that there was no loss in the effectiveness of the drug and the effect did not change in the patients in whom the treatment was continued again. In 42 of 130 patients included in the study, treatment is continued without interruption. Treatment was discontinued at the request of the patients since no response was received in eight patients after 1-3 doses. Currently, our 42 patients receiving omalizumab treatment at 300 mg subcutaneous dose in every 4 weeks and ongoing treatment times range from 1 to 24 months. A significant decrease in lesions of 42 patients was detected with treatment but the treatment of these patients is ongoing due to the recurrence of lesions a week to ten days before the next injection, or because they need additional medications (antihistamine, leukotriene receptor antagonist, systemic steroid) during the course of treatment, even occasionally, for a short period of time.

Table 1. Demographic characteristics of the patients

Age (yearly/mean)	14-82 (42.4)
Gender	
female/mean	83(63.8%)
male/mean	47 (36.2%)
Duration of disease	6 month-40 year (mean 5.7 year)
Thyroid disease, n (%)	45 (34.6%)
Angioedema, n (%)	72 (55.3%)
UAS (mean+/-standard deviation)	5.34+/-0.88
DLQI (mean+/-standard deviation)	14.6+/-5.6

UAS: Urticaria activity scores, DLQI: Dermatology life quality index

A full treatment response was achieved within 24-72 hours after the first injection at a rate of 77.8% in the patients whose urticarial lesions were suppressed by omalizumab, while UAS7 was calculated as 5.34±0.88 before treatment, the score declined to 0.67±1.1 in the following week after the initial injection. UAS7 calculated after 3-month treatment was also calculated as 0.66±1.3. The DLQI declined to 4.9±3.1 (-9.7) after 3-month treatment while it was 14.6±5.6 before treatment.

Due to the recurrence of lesions in two patients in the last two weeks, 300 mg of omalizumab was administered once every 2 weeks and clinical remission was achieved with this treatment scheme in both patients.

A 14-year-old child was also included in our study and no side effects were observed while complete remission was achieved with a treatment of 300 mg/month omalizumab.

While headache was observed in 9 patients (6.9%), no other side effects were encountered.

Discussion

Omalizumab is a recombinant humanized monoclonal antibody binding to IgE. This antibody, which binds to free IgE in circulation, prevents its activation and release of cellular mediators by preventing the binding of IgE to the effector cell. The effect of omalizumab is thought to be performed through rapid decrease in free IgE and downregulation of high-affinity IgE receptor on basophils and mast cells[5-8]. In our study, it was observed that omalizumab was a safe and effective treatment option in resistant CSU and these results support the literature data to date. The approval

of omalizumab and guide recommendations are based on double-blind, placebo-controlled study results in over one thousand patients.

In a phase 3, randomized, double-blind, multicenter study conducted by Maurer et al.[9] in 2013 and in a 4-year retrospective analysis by Metz et al.[10], it was concluded that the omalizumab treatment is a fast, highly effective and reliable treatment option in patients with both CSU and chronic inducible urticaria. In a retrospective review of 110 patients diagnosed with CSU resistant to conventional treatments, omalizumab treatment was also found to be successful in suppressing symptoms[11].

In clinical studies, it is reported that the effect of omalizumab has usually occurred in the early period, within the first week after the beginning of treatment[12,13]. In our study, in accordance with the literature, a significant decrease was detected in the lesions of patients within 24-72 hours after the first injection at a rate of 77.8%. However, treatment should be continued for at least 24 weeks and then the decision on the non-responsiveness should be made as there are also those responding to treatment in the 12-24th weeks.

In the literature, it was emphasized that the effectiveness of omalizumab is independent of serum IgE levels and stated that the determination of IgE levels before treatment was not necessary[14-17]. In our study, patient's serum IgE levels were not taken into evaluation before and after treatment.

In studies conducted, it was reported that the symptoms recurrenced after treatment in 70-80% of patients who achieved complete recurred and duration of relapse ranged from three weeks to 4-5 months[10,17,18]. In our study, while the rate of relapse in patients after discontinuation of treatment was determined as 55%, this period was determined to be 4.5 months on average.

In accordance with the literature, clinical improvement was observed to be independent of age, gender, presence of angioedema, thyroid autoantibody height and disease duration[5,9,11]. A significant improvement was determined in the DLQI of patients and UAS7 with omalizumab treatment.

In the literature, it was revealed that the side effects of omalizumab are equivalent to placebo and the most common effect is headache[6,9-11]. In our study, 9 patients had a complaint of tolerable headache and no other side effects were observed.

Data on the use of omalizumab in the pediatric age group are limited. In the studies conducted, omalizumab was administered at doses of 150-300 mg/month in a group of pediatric patients over 7 years old and it was reported that the drug was effective and reliable[19]. In our study, 300 mg/month omalizumab was administered to a 14-year-old patient and no side effects were observed while complete remission was achieved. In our country, omalizumab is approved for use in CSU patients over 12 years of age.

Study Limitation

We consider the single-centered study as the limitation of our study.

Conclusion

In accordance with current literature data and our clinical observations, we believe that the treatment of omalizumab is an approved, effective and reliable treatment option in CSU patients who have persistent symptoms despite treatment with high-dose antihistamines.

Ethics

Ethics Committee Approval: Our study was approved by the Ethics Committee of Health Sciences University İzmir Bozyaka Training and Research Hospital. (approval number: 86-2019).

Informed Consent: Informed consent was obtained from all patients who participated in our study.

Peer-review: External and internal peer-reviewed.

Authorship Contributions

Concept: M.T., Data Collection or Processing: M.T., M.Ç., S.D., F.U., İ.H.S. Analysis or Interpretation: M.T., Literature Search: M.T., Writing: M.T.

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