International Journal of Inflammation, Cancer and Integrative Therapy

Expert Review Open Access

Malizumab Efficacy and Safety in Adult Patients with Wheat-Dependent Exercise-Induced Anaphylaxis: Reduction in Basophil Activation in Vitro and Allergic Reaction to Wheat

Yoko Chin*

Department of Dermatology, Shimane University Faculty of Medicine, Shimane, Japan

Abstract

Background: Anaphylactic shock occurs frequently in patients with wheat-dependent exercise-induced anaphylaxis (WDEIA), so avoidance of wheat products is advised. The purpose of this study was to assess the efficacy and safety of long-term omalizumab treatment in adult patients with WDEIA [1, 2].

Methods: Twenty adult patients with WDEIA were enrolled in this phase 2 multicenter single-arm trial (UMIN 000019250). All patients received 150-600 mg of omalizumab subcutaneously, and assessments (basophil activation and blood examination) were performed at regular intervals during the administration (0-48 weeks) and observation periods (48–68 weeks). The primary endpoint was the proportion of patients who achieved a basophil activation rate of less than 10% with fractionated wheat preparations, and the secondary endpoint was the proportion of patients who had no allergic reactions after consuming wheat products [3].

Results: During treatment with omalizumab, more than 80% of patients had a basophil activation rate of less than 10% against all fractionated wheat preparations, and 68.8% of patients who met the primary endpoint had no allergic reaction. During the observation period, the proportion of patients with basophil activation rates less than 10% gradually decreased, while the proportion of patients with positive allergic reactions increased gradually and reached a maximum of 46.7%. During the study, no severe adverse events were observed [4].

Conclusions: Long-term omalizumab treatment is safe and effective for adult patients with WDEIA, as measured by basophil activation rate with wheat allergens and allergic reactions after removing wheat restrictions. This, however, is insufficient to achieve desensitisation.

Keywords: Basophil activation test; Efficacy; Omalizumab safety; Wheat-dependent; Exercise-induced anaphylaxis

Introduction

Food-dependent exercise-convinced anaphylaxis (FDEIA) is a distinct type of IgE-intermediated food disinclinations, in which antipathetic symptoms are inspired not just by eating the causative foods but by adding exercise or other secondary factors.FDEIA frequently occurs in grown-ups, and wheat accounts for further than 60 of its causative foods. In cases with FDEIA, anaphylactic shock is a frequent circumstance; thus, avoidance of causative foods is generally recommended in these cases. presently, no effective treatment for FDEIA has been established [5, 6]. FDEIA caused by wheat, i.e. conventional wheat-dependent exercise-convinced anaphylaxis (CO-WDEIA) has been clarified as being acclimatized substantially to ω-5 gliadin, and a recombinant ω-5 gliadin-specific IgE test is suitable to identify further than 90 of adult cases with CO-WDEIA [7]. Still, an outbreak of WDEIA caused by cutaneous sensitization to hydrolyzed wheat protein(HWP) supplemented in a cleaner passed between 2009 and 2012 in Japan. A civil check revealed further than 2000 individualities were affected by sensitization toHWP. After pullout of the HWP-containing cleaner, the absolution rate was 56 at 60 months, though a substantial number of cases still avoid eating wheat products since antipathetic responses sometimes develop when wheat products are ingested [8]. We've preliminarily shown that the basophil activation test (club) is an excellent tool to estimate the sensitization condition of cases with wheat disinclinations, including ω- 5 gliadin-acclimatized subjects and HWP-acclimatized subjects, using several wheat medications includingHWP. SinceCO-WDEIA and HWP-acclimatized wheat-dependent exercise-convinced anaphylaxis (HWP-WDEIA) are IgE- intermediated responses, omalizumab was considered as a good seeker to treat these cases [9]. We reported the results of a primary open study to assess the goods of short- term omalizumab treatment(3 boluses of 150 mg). The results, which were attained by covering club, demonstrated that omalizumab administration significantly inhibited wheat allergen- convinced basophil activation in cases with HWP-WDEIA. still, the inhibition achieved with omalizumab treatment regressed topre-treatment situations 12 weeks after the conclusion of omalizumab treatment. Then, we report the results of a long-term omalizumab study conducted on adult cases with WDEIA. The primary ideal of this study was to demonstrate the efficacity of long-term omalizumab treatment for wheat mislike [10].

Materials and Methods

Subjects

A phase 2, multicentre single- arm study was completed at six spots across Japan Shimane University Hospital, Hiroshima University Hospital, Kobe University Hospital, Tokyo Medical and Dental

***Corresponding author:** Yoko Chin, Department of Dermatology, Shimane University Faculty of Medicine, Shimane, Japan, E-mail: ychin@med.shimane-u.ac.jp

Received: 25-Jan-2023, Manuscript No. ijm-23-89688; **Editor assigned:** 28-Jan-2023, PreQC No. ijm-23-89688; **Reviewed:** 11-Feb-2023, QC No. ijm-23-89688; **Revised:** 21-Feb-2023, Manuscript No. ijm-23-89688(R); **Published:** 28-Feb-2023, DOI: 10.4172/2381-8727.1000206

Citation: Chin Y (2023) Malizumab Efficacy and Safety in Adult Patients with Wheat-Dependent Exercise-Induced Anaphylaxis: Reduction in Basophil Activation in Vitro and Allergic Reaction to Wheat. Int J Inflam Cancer Integr Ther, 10: 206.

University Hospital, Hyogo Prefectural Kakogawa Medical Center, and Okabe Allergy Clinic. The subjects with WDEIA fulfilled either the individual criteria by the Special Committee for the Safety of Protein Hydrolysate in Cosmetics5(opinion of HWP- WDEIA was given) or the individual criteria by the study group of Health Labour Sciences Research Grant(opinion ofCO- WDEIA was given); aged than 20 times of age; avoiding wheat products because of a history of anaphylaxis after wheat ingestion within 1 time or positive results of an IgE test against wheat and/ or gluten performed within 4 weeks. We attained written informed concurrence from the actors at the time of enrollment. The study was approved by the ethics commission of Shimane University and the Dean of the Faculty of Medicine and preregistered to a public registry.

Dose of omalizumab administration

The cases were administered 150 – 600 mg of omalizumab(Xolair ®, Novartis Pharma, Tokyo, Japan) by subcutaneous administration 12 times at four- week intervals or 24 times at two- week intervals according to the administration protocol recommended by omalizumab for bronchial asthma. Evaluations(club and blood examination) were performed at regular intervals during omalizumab administration(at 0, 12, 20, 28, 36, and 44 weeks), and these were followed- up with regular compliances(at 48, 52, 56, 60, 64, and 68 weeks). Antipathetic symptoms were estimated after 12 weeks using the scoring system described.

Basophil activation test

An allergen-convinced CD203c expression- grounded basophil activation test (club) was performed using supplemental blood basophils. The activation agents used for the club were as follows HWP (final attention0.1 and 1 μg/mL); PBS answerable bit of wheat protein (PBS) (final attention 1 and 10 μg/mL); ethanol birth bit of wheat protein (EtOH) (final attention 1 and 10 μg/mL); alkali birth bit of wheat protein (Alkali) (final attention 1 and 10 μg/mL); and purified ω-5 gliadin (final attention0.1 and 1 μg/mL). After activation with these agents, CD203c expression on the basophil face was covered by luminescence-actuated cell sorting. The activation rate was assessed in comparison withanti-IgE activation, and the final value was expressed as a chance ofanti-IgE activation.

Outcomes

The primary endpoint of the study was the proportion of the cases who achieved an activation rate below 10 (as determined from the club) with all wheat medications (either HWP, PBS, EtOH, and Alkali for the HWP- WDEIA group, or ω- 5 gliadin, PBS, EtOH, and Alkali for theCO-WDEIA group) during and/ or after the omalizumab treatment. former report showed that the cases with wheat mislike displayed activation rates lesser than 10 on CD203c expression- grounded club, on the other hand, the cases with tolerant to wheat displayed activation rates lower than10.8 thus, we decided the activation rate lesser than 10 in the club was positive in this study. We preliminarily reported that a drop in activation rate to lower than 10(grounded on CD203c expression) was achieved in 40 of cases with active wheat mislike, following treatment with three boluses of omalizumab (150 mg/ month).8 A major secondary endpoint was the proportion of the cases with an antipathetic score of 0 when wheat products were consumed after lifting of restrictions on wheat input. The wheat input restriction was lifted and a regular diet containing wheat products was started if a basophil activation position below 10 was achieved after omalizumab treatment. Several croakers were involved in determining anaphylactic symptoms, including croakers other than those in the study. Other secondary endpoints involved a safety assessment and included adverse events**,** supplemental blood, and biochemical tests**(**circumstance rate of abnormal values for each test).

Results

An aggregate of 20 cases- 12 cases with HWP- WDEIA and 8 cases withCO-WDEIA fulfilled the individual criteria by the Special Committee for the Safety of Protein Hydrolysate in Cosmetics and by the study group of Health Labour Sciences Research Grant, independently- were enrolled in this study, and their characteristics are described. Five cases had pollinosis, one had antipathetic rhinitis and antipathetic conjunctivitis, and another two had atopic dermatitis as comorbidities. The mean age of the cases was51.3 times(range, 22 – 75), mean body weight was56.7 kg(range, 45 – 74), and mean serum total IgE was316.4 IU/ mL(range, 17 – 1229). Overall, 19 out of 20 cases completed the protocol. One case with HWP- WDEIA discontinued the study eight weeks after starting omalizumab administration due to an bothered lip sensation. Since the symptom appeared previous to inception of the study, this symptom was judged not to be an adverse event of omalizumab. After starting long- term omalizumab treatment, of the 19 cases included in the analysis, the primary endpoint of a basophil activation rate below 10 against all fractionated wheat medications(PBS, EtOH, Alkali, and HWP/ ω- 5 gliadin) was achieved in 8 of 11 cases with HWP- WDEIA(72.7) and 8 of 8 cases withCO-WDEIA(100), for a aggregate of 16 cases(84.2 achievement rate), between Weeks 12 and 4 [11]. A club repression over 70 was achieved for both groups of HWP- WDEIA andCO-WDEIA following long-term omalizumab treatment. Multiple comparisons using the paired sword's system revealed that mean basophil activation dropped below 10 with all wheat medications except HWP for the cases with HWP-WDEIA during omalizumab- treatment. The proportion of the cases who achieved basophil activation rate below 10 dropped gradationally after 48 weeks until 68 weeks(end of the observation), with a table at 60 weeks in both the HWP- WDEIA group and theCO-WDEIA group.

Discussion

In this single-arm open trial of long-term omalizumab treatment, omalizumab was shown to be safe and effective for adult patients with WDEIA in the primary endpoint and the secondary endpoint. The primary endpoint was the proportion of patients who achieved an activation rate below 10% in CD203c expression-based BAT, an objective parameter to evaluate sensitization conditions in IgE-mediated allergy. The activation rate was set to less than 10% based on our previous observation that patients with wheat allergy displayed activation rates greater than 10% on CD203c expression-based BAT, while patients who were tolerant to wheat displayed activation rates lower than 10%. In addition, HWP-WDEIA patients and CO-WDEIA patients demonstrated distinct reaction patterns during CD203c expression-based BAT. This result is well compatible with our previous observation that HWP-WDEIA patients reacted to HWP but mostly not to purified ω-5 gliadin, whereas CO-WDEIA patients mostly reacted to purified ω-5 gliadin but not to HWP [11].

In recent years, the results of several clinical trials of oral immunotherapy with omalizumab for food allergy have been reported. A pilot study of 11 patients with milk allergy (7–17 years old) showed that oral immunotherapy combined with omalizumab achieved rapid desensitization to milk. Wood et al. conducted a double-blind placebo-controlled trial on 57 patients with milk allergy (7–32 years old), randomised 1:1 with omalizumab or placebo plus milk oral immunotherapy. The study concluded that the use of

omalizumab in conjunction with milk oral immunotherapy reduced adverse events. A clinical study of peanuts oral immunotherapy combined with omalizumab in 13 patients with peanut allergy (8–16 years) demonstrated that omalizumab prevented severe allergic reactions associated with peanuts ingestion. More recently, MacGinnitie **et al.**, conducted a double-blind placebo-controlled trial on 37 patients with peanut allergy (8–16 years old) by peanut oral immunotherapy in the presence or absence of omalizumab. While 85.2% patients in the omalizumab combination group tolerated 250 mg peanuts, only 12.5% achieved tolerance in the oral immunotherapy alone group. These findings are compatible with our present findings that the occurrence of allergic symptoms was maintained below 10% during the omalizumab treatment in adult patients with WDEIA. Together, these results provide evidence of the efficacy of omalizumab in reducing the occurrence rate and severity of allergic reactions in patients with food allergies [12].

Next, we evaluated whether omalizumab treatment combined with wheat ingestion elicits desensitization to wheat. Although omalizumab administration improved BAT response and proportion of allergic symptoms after wheat ingestion, after cessation of omalizumab the BAT response and the incidence of allergic reaction per every 4 weeks increased to more than 45%. The results of our present study are consistent with those of previous studies in that omalizumab administration combined with food ingestion did not improve desensitization rate and maintenance. However, in the MacGinnitie **et al.** study, a high tolerance to peanuts was maintained even after completion of omalizumab treatment. This can be contrasted with our finding of increase in allergic reactions after cessation of omalizumab treatment. These findings parallel the observed increase in basophil activation rates with wheat preparations. Thus, long term omalizumab therapy combined with ordinal wheat ingestion is not enough to achieve desensitization for adult wheat allergy. A well-planned oral immunotherapy rather than an ordinary wheat meal may maintain desensitization to wheat after omalizumab administration was discontinued [13].

The present long-term open study demonstrated a greater inhibitory effect on basophil activation with wheat preparations than our previous pilot study using short-term 150 mg fixed dose omalizumab, since more than 80% of the patients achieved basophil activation below 10% with all four wheat preparations in the present study. These results indicate that dose and duration in omalizumab treatment are key factors for achieving satisfactory inhibition of wheat allergen-sensitized basophils/mast cells. The present study also demonstrated that omalizumab is effective for both HWP-WDEIA, involving sensitized percutaneous and/or rhino-conjunctival routes, and CO-WDEIA, which is assumed to involve sensitization through the gastrointestinal tract[14]. The limitations of our present study include the absence of a randomised placebo-controlled study for omalizumab, and the low number of patients included.

Conclusion

In summary, this study provides precious information on omalizumab treatment for adult cases with WDEIA who avoid wheat in their diet and demonstrates the efficacity and safety of omalizumab when used according to the administration protocols of Xolair ® for bronchial asthma.

Acknowledgement

None

Conflict of Interest

None

References

1. Morita E, Kunie K, Matsuo H (2007) Food-dependent exercise-induced anaphylaxis. J Dermatol Sci 47: 109-117.
2. Morita E, Matsuo H, Chinuki Y, Takahashi H, Dahlström J, et al. (2009) Food-dependent exercise-induced anaphylaxis-Importance of omega-5 gliadin and HMW-glutenin as causative antigens for wheat-dependent exercise-induced anaphylaxis. Allergol Int 58: 493-498.
3. Chinuki Y, Morita E (2012) Wheat-dependent exercise-induced anaphylaxis sensitized with hydrolyzed wheat protein in soap. Allergol Int 61: 529-537.
4. Fukutomi Y, Itagaki Y, Taniguchi M, Saito A, Yasueda H, et al. (2011) Rhinoconjunctival sensitization to hydrolyzed wheat protein in facial soap can induce wheat-dependent exercise-induced anaphylaxis. J Allergy Clin Immunol 127: 531-533.
5. Yagami A, Aihara M, Ikezawa Z, Hide M, Kishikawa R, et al. (2017) Outbreak of immediate-type hydrolyzed wheat protein allergy due to a facial soap in Japan. J Allergy Clin Immunol 140: 879-881.
6. Hiragun M, Ishii K, Yanase Y, Hiragun T, Hide M (2016) Remission rate of patients with wheat allergy sensitized to hydrolyzed wheat protein in facial soap. Allergol Int 65: 109-111.
7. Chinuki Y, Kaneko S, Dekio I, Takahashi H, Tokuda R, et al. (2012) CD203c expression-based basophil activation test for diagnosis of wheat-dependent exercise-induced anaphylaxis. J Allergy Clin Immunol 129: 140-146.
8. Chinuki Y, Yagami A, Adachi A, Matsunaga K, Ugajin T, et al. (2020) In vitro basophil activation is reduced by short-term omalizumab treatment in hydrolyzed wheat allergy. Allergol Int 69: 284-286.
9. Tokuda R, Nagao M, Hiraguchi Y, Hosoki K, Matsuda T, et al. (2009)Antigen-induced expression of CD203c on basophils predicts IgE-mediated wheat allergy. Allergol Int 58: 193-199.
10. Dantzer JA, Wood RA (2018) The use of omalizumab in allergen immunotherapy. Clin Exp Allergy 48: 232-240.
11. Nadeau KC, Schneider LC, Hoyte L, Borras I, Umetsu DT (2011) Rapid oral desensitization in combination with omalizumab therapy in patients with cow's milk allergy. J Allergy Clin Immunol 127: 1622-1624.
12. Wood RA, Kim JS, Lindblad R, Nadeau K, Henning AK, et al. (2016) A randomized, double-blind, placebo-controlled study of omalizumab combined with oral immunotherapy for the treatment of cow's milk allergy. J Allergy Clin Immunol 137: 1103-1110.
13. Schneider LC, Rachid R, LeBovidge J, Blood E, Mittal M, et al. (2013) A pilot study of omalizumab to facilitate rapid oral desensitization in high-risk peanut-allergic patients. J Allergy Clin Immunol 132: 1368-1374.
14. MacGinnitie AJ, Rachid R, Gragg H, Little SV, Lakin P, et al. (2017)Omalizumab facilitates rapid oral desensitization for peanut allergy. J Allergy Clin Immunol0 139: 873-881.