

Impact of Omalizumab on Anaphylaxis in Patients Treated for Chronic Urticaria

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Keywords

Anaphylaxis · Omalizumab · Chronic urticaria

Abstract

Background: Anaphylaxis is a life-threatening systemic allergic reaction. Omalizumab (OMA) is an established treatment in chronic urticaria (CU), but experience in anaphylaxis is limited.

Objectives: The objective was to evaluate the efficacy and safety of OMA on anaphylaxis in patients with CU who are resistant to antihistamine therapy and have a history of anaphylaxis.

Method: Patients with antihistamine-resistant CU and a history of anaphylaxis were eligible. OMA was given 300 mg/150 mg every 4 weeks. Urticaria control test (UCT) scores, the episodes of anaphylaxis, and adverse events were recorded during the OMA treatment. **Results:** A total of 7 adults were included. After starting OMA, all of them achieved a complete control (UCT = 16) after 3 months of OMA treatment; 6 of them did not suffer any attack of anaphylaxis in the follow-up periods (5 patients for more than 12 months and 1 patient for 4 months). No adverse events were observed. **Conclusion:** The study indicated the efficacy and safety of OMA for antihistamine-resistant CU patients with a history of anaphylaxis and its potential as a prevention option for anaphylaxis.

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Introduction

Anaphylaxis is a life-threatening systemic allergic reaction, with a lifetime prevalence of 1.6–5.1% [1]. Among its complex underlying mechanisms, the binding of IgE and the high-affinity IgE receptor (FcεRI) on the surface of mast cells and basophils plays a significant role. For its acute episode, prompt intramuscular epinephrine is the first-line treatment; for its prevention, premedication of glucocorticoids and/or antihistamines, despite a lack of evidence, may be appropriate, and omalizumab (OMA) has potentially emerged to cover this condition. As an established treatment in chronic spontaneous urticaria, OMA could bind to free IgE and downregulate FcεRI on basophils and mast cells [2], which may also help with this condition on the basis of limited evidence.

Materials and Methods

The retrospective, observational real-world study was conducted at the Department of Dermatology, Peking University First Hospital, Beijing, China, from November 2018 to March 2022. Patients had to meet the following inclusion criteria: (1) diagnosis of

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Table 1. Demographic and clinical data of patients included in our study

No. Sex/age (y)	CU	diagno- sis	duration of CU	ASST	previous treatment of CU	response to OMA	Anaphylaxis		episodes (time) of anaphylaxis before OMA	treatment of the last episode	episodes of anaphylaxis after OMA	response	Doses, mg/ interval, wk; follow-up, mo*
							symptoms	symptoms					
1	M/65	CSU	12 mo	+	sgAH	Y	Urticaria, hypotension, syncope	Urticaria, hypotension, syncope	2 (3 mo; 4 mo)	GC	0	Y	300/4; 20
2	F/23	CSU	3 y	+	sgAH, GC(IV)	Y	Urticaria, flushing, GI symptoms, hypotension	Urticaria, flushing, GI symptoms, hypotension	2 (2 wk; 5 mo)	GC	0	Y	300/4; 16
3	M/33	CSU	12 mo	+	sgAH, GC(PO)	Y	Urticaria, hypotension	Urticaria, hypotension	1 (1 mo)	Epinephrine	0	Y	300/4; 15
4	F/58	CSU	30 mo	-	sgAH, GC(PO), TCM	Y	Angioedema, urticaria, hypotension	Angioedema, urticaria, hypotension	1 (6 wk)	GC	0	Y	150/4; 20
5	F/65	CSU, SD	5 y	+	sgAH, GC(IV)	Y	Angioedema, urticaria, dyspnea/wheezing, hypotension	Angioedema, urticaria, dyspnea/wheezing, hypotension	2 (1 wk; 6 mo)	Calcium gluconate, sgAH	1 (at month 2)	N	300/4; 13
6	F/43	CSU	5 y	+	sgAH, GC(IV), TCM	Y	Urticaria, GI symptoms, hypotension	Urticaria, GI symptoms, hypotension	1 (5 wk)	GC	0	Y	300/4; 4
7	M/26	CSU	10 y	+	sgAH, GC(PO)	Y	Angioedema, urticaria, dyspnea/wheezing, syncope	Angioedema, urticaria, dyspnea/wheezing, syncope	3 (1 wk; 2 wk; 1 mo)	GC	0	Y	300/4; 17

ASST, autologous serum skin test; CU, chronic urticaria; CSU, chronic spontaneous urticaria; SD, symptomatic dermographism; sgAH, second-generation antihistamine; GC, glucocorticoids; TCM, traditional Chinese medicine; IV, intravenous; PO, per os; OMA, omalizumab; GI, gastrointestinal; wk, week/weeks; mo, month/months; y, year/years; Y, yes; N, no. *Follow-up was from medication initiation to March 2022.

chronic urticaria (CU) based on the medical history, clinical photographs, and provocation tests (for chronic inducible urticaria); (2) uncontrolled [urticaria control test (UCT) < 12] or partial controlled ($12 \leq \text{UCT} < 16$) disease despite up dosing oral H1-antihistamines; (3) with at least one episode of anaphylaxis with no identified triggers before OMA treatment. Anaphylaxis was defined according to Sampson criteria [3] and diagnosed after the onset of CU by review of medical records. Autologous serum skin testing was conducted to detect autoreactivity [4]. We used the UCT for efficacy assessment for CU, recorded the episodes of anaphylaxis for efficacy assessment for anaphylaxis prevention, and monitored adverse events for safety assessment. The UCT retrospectively assesses the overall control of urticaria during the past 4 weeks with a total of four questions, each with five answer options (scored with 0–4 points) [5]. The UCT score is the sum of the scores of all four individual item scores (0–16 points). Higher scores indicate poorer disease control and severer disease activity. CU is classified, based on UCT scores, as uncontrolled ($\text{UCT} < 12$), partial controlled ($12 \leq \text{UCT} < 16$), and complete controlled ($\text{UCT} = 16$) disease.

Results

In total, 7 patients with antihistamine-resistant CU and a history of anaphylaxis, while no other allergic diseases, were treated with 150 mg ($n = 1$) or 300 mg ($n = 6$) of OMA every 4 weeks for CU. A summary of the patients' characteristics, dosage regimens, and response to OMA treatment is shown in Table 1.

Before OMA treatment, 6 patients had uncontrolled urticaria ($\text{UCT} < 12$) and 1 patient had partial controlled urticaria ($12 \leq \text{UCT} < 16$), despite up dosing antihistamine; all of them had a history of 1–3 episodes of anaphylaxis. After starting OMA, all of them achieved a complete control ($\text{UCT} = 16$) after 3 months of OMA treatment; 6 of them did not suffer any attack of anaphylaxis in the follow-up periods (5 patients for more than 12 months and 1 patient for 4 months); 1 patient experienced anaphylaxis at month 2, after 1 week of injection of OMA, with a trigger of inhalation of flour when cooking. In the study, the treatments were well tolerated during the follow-up periods (4–20 months); 6 of them continued OMA; and 1 (No. 3 in Table 1) stopped the OMA due to well-controlled urticaria and the absence of anaphylaxis.

Discussion

OMA has been reported to cause anaphylaxis in <0.1% of patients, with 44% of reactions occurring more than 1 h after administration and 78% occurring within the first 3 doses [6]. In our study, the only 1 patient with episode

of anaphylaxis during treatment had a specific trigger of strong association. We proposed that the episode is not associated with OMA, so OMA was continued, with no more episodes observed in the following 1-year treatment.

In the recent systematic review, among 35 cases with idiopathic anaphylaxis, 22 (63%), 10 (28.5%), and 3 (8.5%) patients had complete, partial, and no response to OMA, respectively [7]. In addition, OMA has been reported to prevent anaphylactoid reactions to mRNA COVID-19 vaccine in 2 cases [8]. A small-scale double-blind and placebo-controlled study showed no statistically significant difference between OMA and placebo when comparing the number of anaphylaxis events in 6 months after starting OMA, but found a possible benefit of OMA in preventing anaphylaxis episodes after exclusion of episodes before the 60-day time point [9]. Interestingly, the episode of our 1 patient who still suffered anaphylaxis after OMA treatment was within 60-day time point as well. This might be a hint of delayed benefit of OMA in these patients.

In conclusion, although limited in number, the study indicated the efficacy and safety of OMA for antihistamine-resistant CU patients with a history of anaphylaxis and its potential as a prevention option for anaphylaxis. Other limitations included unavailable serum tryptase levels, specific allergens, and short follow-up time. Further studies are needed to confirm the effect of OMA on preventing anaphylaxis.

Statement of Ethics

The study was conducted in accordance with the World Medical Association Declaration of Helsinki. The study protocol was reviewed and approved by the Ethics Committee of Chinese Ethics

Committee of Registering Clinical Trial (ChiECRCT20190208), and informed consent was waived because data were retrospective and deidentified.

Conflict of Interest Statement

Dr. Zhao is the speaker/advisor for and/or has received research funding from Novartis, Pfizer, Astellas, Galderma, Janssen, GSK, BAYER, LEO, MEDA Pharma, and ALK Pharma, outside the submitted work. The rest of the authors declare that they have no relevant conflicts of interest.

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Author Contributions

Xiaoting Song performed data analyses and drafted the manuscript. Bo Liu, Miao Yu, Shuanglu Liao, Tingting Luan, and Changling Li participated in sample collection and interpretation of data. Zuotao Zhao designed the study and reviewed the manuscript. All authors were involved in final approval.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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