

## Letter to the Editor



### OPEN ACCESS

**Received:** Jan 30, 2020

**Revised:** Mar 26, 2020

**Accepted:** Apr 6, 2020

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# Omalizumab Treatment in Patients With Cholinergic Urticaria: A Real-World Retrospective Study in Korea

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To the editor,

Cholinergic urticaria (CholU), a subtype of chronic inducible urticaria (CIndU), is characterized by pinpoint, highly pruritic wheals with surrounding erythema caused by increased core body temperature.<sup>1</sup> CIndU does not respond well to H<sub>1</sub>-antihistamines (H<sub>1</sub>AH).<sup>2,3</sup> Omalizumab, a monoclonal antibody against immunoglobulin E, is a new therapeutic option for not only recalcitrant chronic spontaneous urticaria (CSU) but also various types of CIndU, including dermographism and cold urticaria.<sup>2-4</sup> Omalizumab treatment for CholU has been reported mostly in Western countries.<sup>3,4</sup> Here, we retrospectively analyzed omalizumab efficacy and its association with clinical characteristics in 27 H<sub>1</sub>AH-refractory CholU patients in Korea.

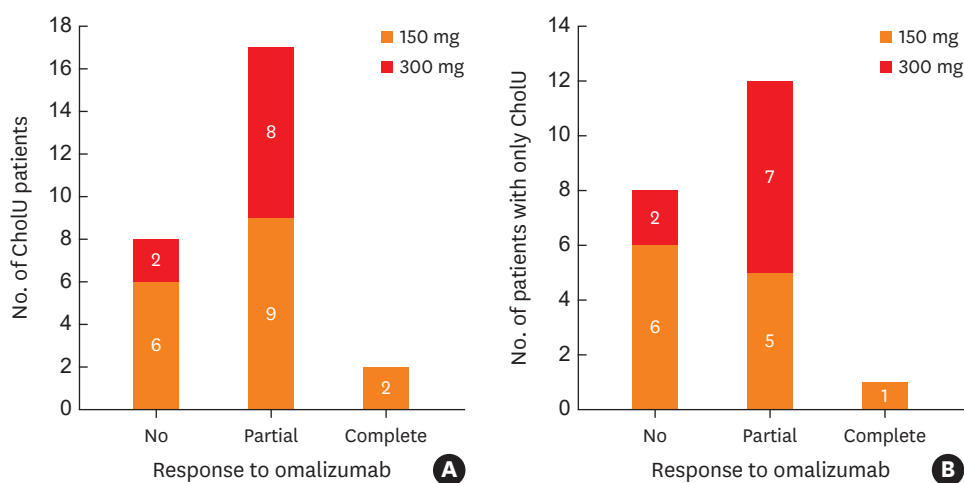
Twenty-seven CholU patients (mean age, 32.48; range, 17–69 years; male patients, 23 [85.2%]) were enrolled at the Department of Allergy of 3 university hospitals in Korea (**Supplementary Methods**). Six patients had combined CSU (21 had only CholU), and they were grouped into complete responders, partial responders, and non-responders according to their response to omalizumab using the visual analogue scale (VAS).

The clinical characteristics and omalizumab treatment of each patient are described in **Supplementary Table S1**. The 27 patients comprised 2 complete responders (7.4%), 17 partial responders (63.0%), and 8 non-responders (29.6%). Among 17 partial responders, 9 (52.9%) received 150 mg omalizumab and 8 (47.1%) received 300 mg. Out of 8 non-responders, 2 was administered 300 mg omalizumab (25.0%). The 2 complete responders responded to 150 mg omalizumab (**Figure A**). The 21 patients with CholU only comprised 1 complete responder (4.8%), 12 partial responders (57.1%), and 8 non-responders (38.1%) (**Figure B**). Twenty-one patients (77.7%) started at a dose of 150 mg and 4 were up-dosed to 300 mg because of no response to 150 mg. All of them were partially responsive after up-dosing. Regardless of dose changes, 10 patients (37.0%) received a maximal dose of 300 mg, of which 8 (75%) were partial responders and 2 (25%) were non-responders, while 17 patients received a maximal

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#### Disclosure

There are no financial or other issues that might lead to conflict of interest.



**Figure.** Number of patients with CholU according to response to omalizumab treatment and omalizumab dosage (A). Number of patients with only CholU according to response to omalizumab treatment and omalizumab dosage (B). Response to omalizumab was assessed by patient global assessment using VAS (0–10 scale): a complete responder (0), a partial responder (VAS: 1–5), a non-responder (VAS: 6–10). CholU, cholinergic urticaria; VAS, visual analogue scale.

dose of 150 mg comprised 2 complete responders (12%), 9 partial responders (53%), and 6 non-responders (35%). Fourteen of 19 partial or complete responders (73.7%) had the response within 4 weeks after the final effective dose. There were no significant differences in clinical characteristics according to omalizumab responses (**Supplementary Table S2**).

Several case series have reported that CholU patients (from 62% to 75%) showed good response to omalizumab.<sup>4</sup> Recently, larger case series involving 16 CholU patients reported 6 (37%) complete responders, 5 (31%) major responders, and 2 (13%) partial responders, where most patients had the responses within 6 weeks.<sup>5</sup> Furthermore, 5 of 9 patients with CholU only (56%) were complete or major responders. In a randomized clinical trial involving 22 CholU patients, the negative rate of exercise challenge test was 31.3% at week 48, and daily symptoms score and VAS score progressively improved week 16 after treatment with 300 mg omalizumab.<sup>6</sup> Our study showed that 19 (70.4%) of 27 CholU patients and 13 (61.9%) of 21 patients with CholU were partial or complete responders, providing indirect evidence for the good efficacy of omalizumab for H<sub>1</sub>AH-refractory CholU in an Asian country. Moreover, of 8 non-responders, 6 received only 150 mg omalizumab without up-dosing, and 5 received omalizumab only for 2 months. Three partial responders had their response at least 3 months after omalizumab treatment. Thus, higher dose and longer duration of omalizumab treatment may improve the outcome of omalizumab treatment in CholU.

In conclusion, this is the first study with the largest number of CholU in Asia, suggesting that omalizumab can be a good treatment option for H<sub>1</sub>AH-refractory CholU.

## ACKNOWLEDGMENTS

This work was supported by the National Research Foundation of Korea (NRF) grant funded by the Korea government (MSIT) (No.2018R1A2B6009178).

## SUPPLEMENTARY MATERIALS

### Supplementary Data S1

Methods

[Click here to view](#)

### Supplementary Table S1

Clinical characteristics and omalizumab treatment of the study subjects

[Click here to view](#)

### Supplementary Table S2

Comparison of clinical characteristics according to response to omalizumab treatment

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## REFERENCES

1. Fukunaga A, Washio K, Hatakeyama M, Oda Y, Ogura K, Horikawa T, et al. Cholinergic urticaria: epidemiology, physiopathology, new categorization, and management. *Clin Auton Res* 2018;28:103-13.  
[PUBMED](#) | [CROSSREF](#)
2. Zuberbier T, Aberer W, Asero R, Abdul Latiff AH, Baker D, Ballmer-Weber B, et al. The EAACI/GA<sup>3</sup>LEN/EDF/WAO guideline for the definition, classification, diagnosis and management of urticaria. *Allergy* 2018;73:1393-414.  
[PUBMED](#) | [CROSSREF](#)
3. Dressler C, Werner RN, Eisert L, Zuberbier T, Nast A, Maurer M. Chronic inducible urticaria: a systematic review of treatment options. *J Allergy Clin Immunol* 2018;141:1726-34.  
[PUBMED](#) | [CROSSREF](#)
4. Maurer M, Metz M, Brehler R, Hillen U, Jakob T, Mahler V, et al. Omalizumab treatment in patients with chronic inducible urticaria: a systematic review of published evidence. *J Allergy Clin Immunol* 2018;141:638-49.  
[PUBMED](#) | [CROSSREF](#)
5. Altrichter S, Chuamanochan M, Knoth H, Asady A, Ohanyan T, Metz M, et al. Real-life treatment of cholinergic urticaria with omalizumab. *J Allergy Clin Immunol* 2019;143:788-791.e8.  
[PUBMED](#) | [CROSSREF](#)
6. Gastaminza G, Azofra J, Nunez-Cordoba JM, Baeza ML, Echechipia S, Gaig P, et al. Efficacy and safety of omalizumab (Xolair) for cholinergic urticaria in patients unresponsive to a double dose of antihistamines: a randomized mixed double-blind and open-label placebo-controlled clinical trial. *J Allergy Clin Immunol Pract* 2019;7:1599-1609.e1.  
[PUBMED](#) | [CROSSREF](#)