

RESEARCH NOTE

Impact of omalizumab on pollen-induced seasonal allergic rhinitis: An observational study in clinical practice

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KEYWORDS

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INTRODUCTION

Seasonal allergic rhinitis (SAR) caused by Japanese cedar and cypress pollen (SAR-JCP) is a highly prevalent disease and a serious social concern in Japan.¹

Omalizumab, a recombinant humanized monoclonal anti-immunoglobulin E (IgE) antibody, decreases the serum-free IgE levels by 84%–99%² and eventually downregulates the FcεRI expression in basophils and mast cells.³ Thus, omalizumab improves the allergic response regardless of the allergen type.^{4,5} The efficacy of omalizumab against cedar pollinosis has been demonstrated in previous studies.^{6,7} Thus, in Japan, omalizumab was approved for SAR pollinosis in 2019.

The main purpose of this research was to investigate whether omalizumab administered even after the peak period of pollen dispersal improves the symptoms of SAR-JCP.

METHODS

Study design

This research was a prospective, observational study of patients with SAR-JCP who received omalizumab. This study was conducted between February 2020 and May 2020, and was approved by the Ethics Committee on Research Involving Human Subjects, Showa University School of Medicine (Approval number: 3192). We obtained written informed consent from all participants before commencing the study.

Participants

SAR-JCP was diagnosed based on the history of cedar pollen-induced clinical symptoms for at least two consecutive years; the serum-specific IgE antibody against the cedar pollen antigen was class ≥ 3 [≥ 3.5 UA/mL

or ≥ 13.5 lumicount (kU/L)]. We enrolled patients who fulfilled the following inclusion criteria: (i) age, > 12 years; (ii) serum total IgE levels, 30–1500 IU/mL; (iii) baseline body weight, 30–150 kg; and (iv) those who were treated with histamine H_1 receptor antagonists (various types), nasal corticosteroids (fluticasone propionate 110 $\mu\text{g}/\text{day}$), and ophthalmic antihistamines (epinastine hydrochloride ophthalmic solution 0.05% four times/day) but confirmed that their severe nasal symptoms persisted. The patients who had all the symptoms of sneezing, itchy nose, runny nose, and stuffy nose were included; one or more of these symptoms had to have a symptom rating score of ≥ 3 (e.g., in the example sneezing 1, itchy nose 1, runny nose 1, and stuffy nose 3, the symptom stuffy nose has a score of 3).¹ Patients who were taking oral steroids were excluded. A total of 18 participants received omalizumab after the peak period of pollen dispersal and were evaluated at week 4 after treatment. All 18 participants completed the protocol. The peak period of cedar and cypress pollen dispersal was defined as the start day when 30 grains/ cm^2 was counted.⁶

Dosage and administration of omalizumab

Omalizumab was subcutaneously administered to patients every 2 or 4 weeks based on the total serum IgE levels and baseline weight (Supplementary Materials). The doses were the same as those for asthma cases.

Assessment of efficacy

All patients were asked to fill in the patient form to describe the visual analog scale (VAS) score of their overall symptoms: four nasal symptoms (i.e., sneezing, itchy nose, runny nose, and stuffy nose) and the symptom of itchy eyes based on the five-point scale (0: none, 1: mild, 2: moderate, 3: severe, and 4: very severe). We assessed allergic rhinitis-related quality of life using the Japanese Rhinoconjunctivitis Quality of Life Questionnaire (JRQLQ).^{1,8}

Statistical analysis

All statistical analyses were performed using JMP software (version 15.0) by two-tailed nonparametric Wilcoxon signed-rank test prior to and post treatment. We considered p values of < 0.05 statistically significant.

RESULTS

The patients' characteristics are shown in Table 1. All 18 participants were evaluated at week 4. The evaluation

TABLE 1 Patient characteristics

	Mean $\pm$ SD or n
Sex (female)	9
Age, mean $\pm$ SD (range)	26.7 $\pm$ 9.5 (12–45)
Comorbidity	
Perennial allergic rhinitis	12
Bronchial asthma	3
Hay fever dermatitis	3
Serum total IgE levels at baseline (IU/mL)	407.3 $\pm$ 449.6
Serum total eosinophils levels at baseline (cells/ μL)	227.0 $\pm$ 275.3
Specific IgE levels against cedar pollens (CAP-RAST*)	
Class 2 (0.70–3.49 UA/mL)	0
Class 3 (3.50–17.49 UA/mL)	8
Class 4 (17.50–49.99 UA/mL)	5
Class 5 (50.00–99.99 UA/mL)	1
Class 6 (≥ 100 UA/mL)	4
Specific IgE levels against cypress pollens (CAP-RAST*)	
Class 2 (0.70–3.49 UA/mL)	6
Class 3 (3.50–17.49 UA/mL)	8
Class 4 (17.50–49.99 UA/mL)	1
Class 5 (50.00–99.99 UA/mL)	3
Class 6 (≥ 100 UA/mL)	0

Abbreviations: CAP-RAST*, capsulated hydrophilic carrier polymer radioallergosorbent test; IgE, immunoglobulin E; SD, standard deviation.

day was also within the peak period of cedar and cypress pollen dispersal. VAS scores improved from 64.4 ± 20.8 to 12.7 ± 9.4 after administration of omalizumab, which was statistically significant ($p < 0.001$). The total nasal symptom scores were significantly improved from 2.8 ± 0.7 to 0.8 ± 0.6 ; individual symptoms and JRQLQ also improved with significant differences ($p < 0.001$) (Figure 1). Five patients complained of pain at the injection site, but all of them were mild. No other adverse reactions occurred.

DISCUSSION

This study demonstrated that omalizumab was well tolerated and highly effective in controlling nasal conjunctival symptoms caused by SAR-JCP. One of the novel findings of this study was that omalizumab was effective on SAR-JCP even after the peak period of pollen dispersal and after severe symptoms had appeared in all cases. Intriguingly, the effects of omalizumab were observed within a few days after administration; 15 participants noticed the

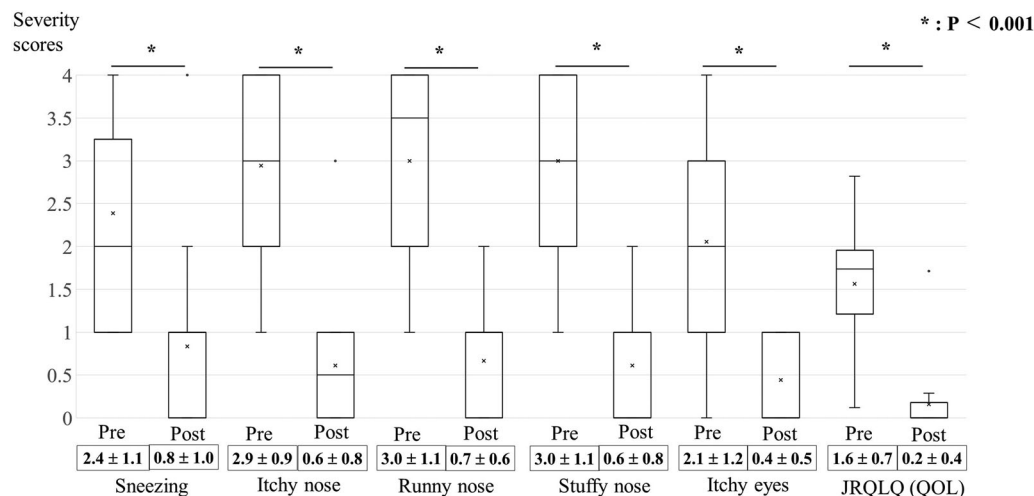


FIGURE 1 Total nasal symptom scores were significantly improved from 2.8 ± 0.7 to 0.8 ± 0.6 ($p < 0.001$); sneezing, from 2.4 ± 1.1 to 0.8 ± 1.0 ($p < 0.001$); itchy nose, from 2.9 ± 0.9 to 0.6 ± 0.8 ($p < 0.001$); runny nose, from 3.0 ± 1.1 to 0.7 ± 0.6 ($p < 0.001$); stuffy nose, from 3.0 ± 1.1 to 0.6 ± 0.8 ($p < 0.001$); itchy eyes, from 2.1 ± 1.2 to 0.4 ± 0.5 ($p < 0.001$). The patients' overall Japanese Rhinoconjunctivitis Quality of Life Questionnaire (JRQLQ) scores were also improved from 1.6 ± 0.7 to 0.2 ± 0.4 ($p < 0.001$)

effects within a week of the administration, thereby establishing the immediate effect of omalizumab on SAR-JCP. The results showed that a single administration of omalizumab during exacerbation is sufficient to control symptoms without prophylactic administration as in previous reports,^{6,7} and provided a hint for the successful use of this highly effective but expensive drug. SAR-JCP is a disease that deteriorates rapidly; thus, immediate effect of omalizumab can be an invaluable advantage in a clinical setting.

We observed the positive effects of omalizumab in all patients. Compared with asthma, which has various phenotypes, omalizumab showed positive results against SAR, suggesting that SAR-JCP is more IgE-dependent.^{9,10}

This study has some limitations worth acknowledging. First, the study sample was small, and the comorbidities of the cases were different. Second, it is still unclear if there was a difference in efficacy between the prophylactic administration as in previous studies and the administration after the onset of symptoms as in this study.

In conclusion, omalizumab treatment, administered after the peak period of pollen dispersal, dramatically improved symptoms in patients with SAR. Moreover, these effects were obtained within a few days in most cases. Hence, omalizumab could offer a promising reliever therapy for patients with SAR.

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CONFLICT OF INTEREST

All authors declare that there are no enterprises, etc. with which they have a conflict of interest to be disclosed pertaining to the article.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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Supplementary Materials. Omalizumab dosage

IgE (serum) (IU/mL)	Weight (Kg)									
	≥20-25	>25-30	>30-40	>40-50	>50-60	>60-70	>70-80	>80-90	>90-125	>125-150
≥20-100	75	75	75	120	150	150	150	150	300	300
>100-200	150	150	150	300	300	300	300	300	450	450
>200-300	150	150	225	300	300	450	450	450	600	375
>300-400	225	225	300	450	450	450	600	600	450	525
>400-500	225	300	450	450	600	600	375	375	525	600
>500-600	300	300	450	600	600	375	450	450	600	
>600-700	300	225	450	600	375	450	450	525		
>700-800	225	225	300	375	450	450	525	600		
>800-900	225	225	300	375	450	525	600			
>900-1000	225	300	375	450	525	600				
>1000-1100	225	300	375	450	600					
>1100-1200	300	300	450	525	600					
>1200-1300	300	375	450	525						
>1300-1500	300	375	525	600						

□ : Administered every 4 weeks

■ : Administered every 2 weeks