A Real-World Analysis of Relapse Rate and Efficacy of a Restricted Monthly Dose of Omalizumab in Recalcitrant Chronic Spontaneous Urticaria in India

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Sir,

Omalizumab is a third-line drug for chronic urticaria but financial constraints limit its long-term use. An expert group of dermatologists under the aegis of Ministry of Health and Family Welfare– Government of India had stipulated that three doses of omalizumab should be administered in relevant cases of chronic spontaneous urticaria (CSU).[1] The dosimetry recommended was injection omalizumab 300 mg every month for 3 months, in case a patient did not achieve a 50% decrease in UAS score at 4 weeks after the first dose, the next dose was not administered. In exceptional cases where there was 50% reduction in UAS score more than 3 doses were administered. As there is paucity of data on the real-world experience with this drug, especially in central government institutes in India, we undertook a retrospective evaluation of patients with CSU treated with omalizumab in 2016–2018 with this regimen. Eighteen patients of refractory CSU were divided in 3 groups based on the number of doses of omalizumab given. Ten patients (56%) received 3 doses, 5 (28%) received less than 3 doses, and 3 (17%) received more than 3 doses. The follow-up records were evaluated and response to treatment and relapses were noted. Demographic data were recorded, including age, sex, duration of disease, prior and concurrent treatment [Table 1]. The severity of disease was recorded as weekly "urticaria activity score" (UAS7). Response to treatment was assessed by using visual analog scale (VAS) and was graded as follows: Complete response (CR): more than 90% reduction of symptoms (VAS = 4-5), Partial response (PR): 30–80% reduction of symptoms (VAS = 2–3), and no response (NR): less than 30% reduction of symptoms (VAS = 0–1). Data was presented as number (%) or Mean ± SD. Changes in continuous outcome measures were evaluated using means, SDs, *P* values, and 95% confidence intervals (CIs). *P* values for continuous outcome measures were generated via t tests (one-way analysis of variance; ANOVA) and to compare proportions between groups *z* test was used. Statistical significance was declared when *P* was less than 0.05.

The results revealed complete response (CR) in all 10 cases (100%) who were given 3 doses of omalizumab. Of the 5 cases with less than 3 doses of omalizumab, 1/5 (20%) had CR, 2/5 (40%) had PR and 2/5 (40%) had NR and among those with more than 3 doses, 2/3 (67%) had CR and 1/3 (33%) had PR [Table 2]. The mean VAS of patients who were given 3 doses, less than 3 and more than 3 doses of omalizumab were 4.8 ± 0.4, 3 ± 1.3 and 4 ± 1.4, respectively, and the difference was statistically significant ($P = 0.008$) [Table 2]. Relapse after stopping omalizumab was observed in 9 (56%) patients out of 16 patients who responded [Table 2]. The relapse rate was 40% for patients who received 3 doses and 33.3% for patients more than 3 doses and the difference was not found to be statistically significant ($P = 0.8336$). Out of these, 1 (11%) patient relapsed within 6 months, 2 (22%) within 2 months, 4 (44%) within 1 month, and 2 (22%) within 15 days of stopping therapy.

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Access this article online

Website: www.idoj.in

DOI: 10.4103/idoj.IDOJ_499_19

Quick Response Code:

How to cite this article: Sardana K, Dixit N, Arora P. A real-world analysis of relapse rate and efficacy of a restricted monthly dose of omalizumab in recalcitrant chronic spontaneous urticaria in India. Indian Dermatol Online J 2020;11:835-7.

Received: 02-Oct-2019. **Revised:** 15-May-2020. **Accepted:** 03-Jul-2020. **Published:** 19-Sep-2020.

Although many studies including the large multicenter, randomized, double-blind, placebo-controlled phase III trials (ASTERIA I, ASTERIA II, and GLACIAL) have shown that omalizumab significantly improved CSU compared with placebo, recurrence of disease after stopping treatment has been a problem and very few studies have commented upon the real-world experience on relapses with this drug in CSU specially in India.[2-4] Relapse after omalizumab has been found to be dependent on two important factors: high baseline UAS7 and slow initiation of response.[5,6] In our study, 9 of the 16 cases experienced relapse. In previous studies the relapse rates range from as low as 5% to as high as 87.5%, but the mean relapse rate was 54.6 ± 29.5%.[5,6] The variable relapse rate reflects the variable doses and intervals of the drug in different studies.[5,6] Our relapse rate of 56% was subanalyzed and it was found that it was dependent on the number of doses, with a relapse rate of 40% at 3 doses which reduced to 33.33% with more than 3 doses. In the XTEND-CIU trial (Xolair Treatment Efficacy of LoNger Duration in Chronic Idiopathic Urticaria), a relapse rate of 43.4% and 45.1% was observed during the 12 weeks after withdrawing omalizumab in patients treated for as long as 24 or 48 weeks.[7] Preliminary results from the OPTIMA study also showed a 44.4–50% relapse rate after 6 months of treatment.[8] Furthermore, a real-life study of 280 patients reported that it was rarely possible to stop omalizumab even after 1–2 years of treatment.[9] The significant analogy is that our relapse rate (56%) with limited doses of the drug is similar to these longer duration trials which suggests that while extending therapy to 6 or 12 months might be more effective but the relapse rates do not differ. The implications are that while taking a decision on administering the drug prolonging the duration is not necessarily curative and does not obviate the relapse rates. The limitations of the study include small number of patients and unavailability of the tests predicting the responsiveness to omalizumab. Further studies with large sample size are required to expound our work.

Table 1: Demographic profile, previous treatment, mean UAS7 (Pre and Post-omalizumab)

Feature	Number (%age)
Age, years	
Mean (range)	45±10 (25-60)
Gender, *n* (%)	
Female	8 (44.45%)
Male	10 (55.55%)
Duration of urticaria	
Mean (years)	6.5±3
Medications prior to omalizumab assumption, *n* (%)	
H_1 antihistamine	
Conventional dose	18 (100%)
High dose (four-fold)	9 (50%)
Methotrexate	7 (39%)
Cyclosporine	2 (11%)
Mean UAS7 (range)	
Pre-omalizumab	36.9±5.8 (28-42)
Post-omalizumab	11.7±14 (0-35)

n- Number of patients, UAS7- Weekly "urticaria activity score"

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

Table 2: A comparison of response parameters and severity of relapsed disease in patients with different doses of omalizumab

Duration	3 doses	<3 doses			>3 doses	
No. of patients (%)	10 (56%)	5 (28%)			3 (17%)	
Response	**CR 10 (100%)**	**CR**	**PR**	**NR**	**CR**	**PR**
		1 (20%)	2 (40%)	2 (40%)	2 (66.67%)	1 (33.33%)
Pre-UAS7	35.7±5.8	28	38.5±3.5	42±0	38.5±3.5	42
Post-UAS7	4.9±5.5	0	31.5±3.5	35±0	0	28
VAS (mean±SD)	4.8±0.4	3±1.3			4±1.4	
Time of best response	Fast responders	1 (Fast responder), 4 (slow responders)			2 (Fast responders), 1 (slow responder)	
Relapse (No. of patients)	4 (40%)	4 (80%)			1 (33.33%)	
Mean (±SD) UAS7 of patients with relapse before omalizumab	40±3.5	40±3.5			42±0	
Mean (±SD) UAS7 of patients with relapse	23±13.2	42±0			28±0	
Severity of relapsed disease as compared to previous disease	less	Same			Less	

UAS7 - Weekly "urticaria activity score," VAS - Visual analog scale, CR- Complete response, PR- Partial response

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