Omalizumab for Management of Refractory Urticaria: Experience of a Tertiary Care Centre in Eastern India

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Abstract

Aim: To study the effects of omalizumab in chronic spontaneous urticaria in Indian patients.

Setting and Design: The study was conducted in a tertiary care centre and it was retrospective and descriptive in nature.

Material and Methods: We analysed the data of patients who were administered omalizumab between June 2014 and June 2015 for the management of refractory chronic spontaneous urticaria at our centre. Omalizumab was used in those patients who did not respond to updosing of antihistaminics and cyclosporine. Omalizumab was used in dose of 300 mg per month for 3 doses.

Results: Twenty-four patients were administered omalizumab during the study period. Average age of the patients was 36.54 years, female: male ratio was 1.4:1, mean duration of disease was 20.66 months, and autologous serum skin test was positive in 33% of studied individuals. Ninety six percent of cases showed response to treatment in our study. Remission was seen in 25% of patients, 50% showed satisfactory response, and 20.83% showed partial response. Average UAS7 scoring before starting omalizumab in preceding week was 24.4. Average UAS7, 2 weeks after starting omalizumab was 4 in responsive patients.

Conclusion: Omalizumab is safe and effective treatment for the management of chronic spontaneous urticaria. It can be used in Indian setting after failure to other third-line therapies such as addition of montelukast and cyclosporine due to high cost of treatment.

Key Words: Chronic spontaneous urticaria, eastern India, omalizumab, refractory urticaria

Introduction

Chronic spontaneous urticaria (CSU) is defined as occurrence of wheals or angioedema or both occurring on most of the days in a week and lasting for more than 6 weeks, without any identifiable triggers. It is a common problem with lifetime prevalence of 7.8–22.3%.[1] Symptoms of urticaria are caused by activation of mast cells and release of histamine and other inflammatory mediators. Immunoglobulin E (IgE) binds to high-affinity FcεRI receptor on mast cells, basophils, and eosinophils. Cross-linking of this receptor-bound IgE leads to the degranulation of mast cells and release of inflammatory mediators.[2] The current guidelines recommend the use of non-sedating H1 antihistaminics as the first-line therapy. Dosage of antihistaminics can be increased up to four times the licensed recommendations in case of no response as the second-line treatment.

Omalizumab, cyclosporine, and montelukast form the third line of treatment in patients who do not respond to second-line treatment. Approximately 50% of patients experience inadequate response despite higher doses of antihistaminics.[1]

Omalizumab is a humanised monoclonal IgG antibody against IgE. It binds circulating free IgE and forms tetramers and hexamers of IgE, thereby preventing IgE from binding FcεRI receptor on mast cells and basophils. It was approved by the US Food and Drug Administration (FDA) for the management of CSU in May 2014. It is now a third-line agent for the management of CSU.[3]

Omalizumab is increasingly being used for the management of refractory urticaria; however, data...
Materials and Methods

Case definition

CSU is defined as wheals with or without angioedema present for most of the days in a week for 6 or more weeks.

We analysed the data of patients in whom omalizumab was used in our centre between June 2014 and June 2015. Twenty-four patients were administered omalizumab for CSU during this period. Omalizumab was given to patients who did not respond to first- or second-line therapy. Age, gender, and prior and concomitant drug therapy were recorded. All patients were given injection omalizumab 300 mg every month and patients were followed up for 6 months after the last injection.

Therapeutic response

Response to therapy was recorded with the help of urticaria activity score (UAS) and urticaria control test (UCT).[4,5]

Remission: Patients who did not require any antihistaminics after 3 monthly injections of omalizumab for at least 6 months (UCT score >12).

Complete response: Patients who were asymptomatic (UCT >12) on low-dose antihistaminics (tablet levocetirizine 5 mg or tablet loratadine 10 mg once or twice a day).

Partial response: Patients who required continued omalizumab apart from antihistaminics to remain asymptomatic (UCT >12).

No response: Patients who continued to be symptomatic despite omalizumab monthly injection along with antihistaminics (UCT <12).

Results and Analysis

Altogether records of 24 patients of CSU were found during the study period who were treated with omalizumab for 3 months [Table 1].

Demographics

Age of the patients ranged from 25 year to 52 year with mean age being 36.54 year. Females outnumbered males, and of total of 24 patients, 14 were female and 10 were male.

Disease characteristics

Duration of disease ranged from 6 to 40 months with average being 20.66 months. Autologous serum skin test was positive in 33% (8/24) of tested patients. Comorbidities that were present were chronic kidney disease in one patient and diabetes mellitus and hypertension in two patients each.

Treatment

All patients were initiated on treatment with tablet levocetirizine 5 mg once a day or twice daily. Tablet loratadine was used in those who complained of sedation with tablet levocetirizine. Sixteen patients (66%) were given tablet levocetirizine (5 mg) 2 tablets twice daily and 33% (8/24) could not tolerate higher doses of levocetirizine due to sedation and were given tablet loratadine (10 mg) 2 tablets twice daily. Tablet montelukast 10 mg per day was used in all patients.

Cyclosporine was used in 83% (20/24) of patients. In patients with chronic kidney disease and hypertension, cyclosporine was not used. One patient refused to take cyclosporine and was administered omalizumab after updosing of antihistaminics. Omalizumab was administered at the dose of 300 mg per month for 3 months in all patients. All patients were advised to continue tablet levocetirizine 5 mg or loratadine 10 mg once a day. Patients were followed up for 6 months after the last of the three injections.

Treatment response [Chart 1]

Twenty five percent (6/24) of patients underwent remission and continued to remain asymptomatic (UCT >12) despite stopping antihistaminics. Patients are still on follow-up and longest remission period has been 9 months. Fifty percent (12/24) of patients had satisfactory response and required tablet levocetirizine or loratadine once or twice daily for control of symptoms during intermittent period. Five (20.83%) patients continued to be symptomatic after three injections of omalizumab and concomitant antihistaminics. Four out of these five patients were continued on injection omalizumab 150 mg per month.

Table 1: Clinical parameters of urticaria patients treated with omalizumab

| Clinical characteristic | (n=24) |
|------------------------|--------|
| Mean age (year)        | 36.54  |
| Female: male           | 1.4:1  |
| Duration of disease (months) | 20.66 |
| ASST (%)               | 8/24 (33) |
| Comorbidities          |        |
| Chronic kidney disease | 1      |
| Hypertension           | 2      |
| Diabetes mellitus      | 2      |
| Previous treatment     |        |
| Levocetirizine 5 mg (2 BD) | 16    |
| Loratadine 10 mg (2 BD) | 8     |
| Montelukast 10 mg      | 24     |
| Cyclosporine - 3 mg/kg | 20     |

ASST: Autologous serum skin test
and one patient was given injection omalizumab 300 mg/month. One patient did not respond to therapy despite omalizumab 300 mg monthly and higher than licensed dose of antihistaminics. They were managed with oral steroids and methotrexate along with antihistaminics to maintain remission.

Monitoring
Patients on antihistaminics were monitored by asking questions about sedation such as daytime sleepiness or dryness of mouth. Patients on cyclosporine were evaluated by baseline blood urea, serum creatinine, and blood pressure; renal function and blood pressure were repeated on every visit. Patients on omalizumab were made to wait for at least 2 h after first injection and 1 h after subsequent injections. They were also asked questions regarding pain at injection site, headache, or development of any symptoms after omalizumab injection.

Urticaria activity score and urticaria control test
UAS was performed on every visit and UAS7 record was analysed on every visit. We taught patients how to perform UAS7 on first visit and insist that patients bring records of UAS during all subsequent visits. Average UAS7 scoring before starting omalizumab in preceding week was 24.4. Average UAS7, 2 weeks after starting omalizumab was 4 in responsive patients and 18 in unresponsive patients. Most of the patient felt relief of symptoms on day 4 and day 5. Average UCT score for a month before starting omalizumab injection was 6 and average UCT a month after injection omalizumab was 14 in patients who responded to therapy. This UCT was sustained at >12 in all responsive cases (23/24).

Adverse effect
None of the patients complained of any adverse effect on omalizumab. None of our patients developed any injection site reaction or anaphylaxis.

Discussion
Omalizumab is a safe and effective treatment for the management of CSU. It was seen to be effective in majority of cases at the dose of 300 mg every month. It was also seen to be effective in those cases who did not respond to treatment with cyclosporine 3 mg/kg, montelukast and updosing of antihistaminics. Similar result was seen when data from three pivotal studies on omalizumab, namely, GLACIAL, ASTERIA I, and ASTERIA II, were compiled that omalizumab 300 mg per month was effective irrespective of background therapy.[6]

Our study showed response to treatment in 96% cases. Remission was seen in 25% of patients, 50% showed satisfactory response, and 20.83% showed partial response. In a similar study conducted in Israel, it was shown that 86% of patients responded to treatment with omalizumab, while 14% did not respond; this higher rate of failure to treatment was possibly because of the use of single 150 mg omalizumab injection in these patients.[7]

We used 300 mg monthly injection of omalizumab and 96% (23/24) of patients responded to treatment within 1 week of initiation of treatment. A study published by Maurer et al also concluded that omalizumab 300 mg per month was more effective as compared to 150 mg per month.[8] A study published by Godse et al in Indian patients used dose of omalizumab based on body weight and IgE levels as per dose schedule of asthma.[9]

No adverse effect was noticed in any of our patient on omalizumab during therapy or follow-up period. Other study has shown serious adverse event in 6% of cases on 300 mg monthly injection while 1% in 150 mg monthly injection. No anaphylaxis was reported which was same as in our study.[4]

Conclusion
Omalizumab is first in class anti-IgE monoclonal antibody and is FDA approved for the treatment of CSU. It is effective in refractory urticaria and almost all patients who do not respond to therapy with antihistaminics and cyclosporine responds to treatment with omalizumab. It is a safe drug and no major side effect was seen in our study. Finally, it leads to lasting remission in one-fourth of patients after three doses 1 month apart.

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Nil.

Conflicts of interest
There are no conflicts of interest.

What is new?
• Omalizumab is effective in patients not responding to combination of updosing of antihistaminics, montelukast, and cyclosporine
• It can result in remission in one-fourth of patients with refractory urticaria
• It is relatively safe drug as we did not notice any adverse effect of therapy in our experience though in a small number of patients.
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