



Self-reported satisfaction of patients receiving omalizumab for severe allergic asthma in Malta

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ABSTRACT

Treatment satisfaction is of utmost importance for ensuring adherence. Omalizumab is administered long-term if effective and well-tolerated in a hospital setting. The aim was to evaluate treatment satisfaction with omalizumab in Malta and to identify factors that may influence patients' satisfaction.

A questionnaire was distributed to all asthmatic adult patients receiving omalizumab for at least one year. The questionnaire included demographic data, dosing regimen, asthma control test and the 14-item English version of the Treatment Satisfaction Questionnaire for Medication (TSQM) Version 1.4. The TSQM 1.4 domain scores range from 0 to 100. Higher scores represent higher satisfaction.

Our cohort included 33 patients (52% males), mean age 53.7 ± 11 years, mean baseline IgE level 510.6IU/ml, mean duration of treatment 3.8 ± 1.98 years and mean number of injections per month 4.6 ± 2.6 . Median TSQM scores were as follows: graded effectiveness 78%, graded side effects 100%, graded convenience 74.2% and overall satisfaction 76%. Regression analysis showed that convenience score, effectiveness score and ACT score were significantly associated with global satisfaction.

Global satisfaction scored high among the Maltese cohort of patients despite the inconvenience and side effects associated with receiving omalizumab. This is an add-on beneficial effect to the efficacy and effectiveness already been achieved with this medication.

1. Introduction

Omalizumab, an *anti*-IgE monoclonal antibody, is an approved add-on therapy being utilized by Maltese patients with severe persistent IgE-mediated allergic asthma. Several large international studies have reported the efficacy, safety, tolerability and effectiveness of omalizumab in a real-life clinical setting [1–4]. Patients are selected for treatment by strict well-defined criteria and great commitment is required for receiving medication since it is administered only in a hospital setting at the only main hospital in Malta and is administered every 2 or 4 weeks subcutaneously. Treatment satisfaction is defined as the individual's rating of important attributes of the process and outcomes of his/her treatment experience and has been associated with adherence as well as willingness for patients to continue treatment [5]. The 14-item Treatment Satisfaction Questionnaire for Medication (TSQM) Version 1.4 has been identified as a reliable and valid instrument to assess patients' satisfaction with medication, providing scores on four scales – side effects, effectiveness, convenience and global satisfaction [6]. There is no published literature studying self-reported patient satisfaction with

omalizumab to date.

The aim of this survey was to evaluate treatment satisfaction in patients treated with omalizumab in everyday clinical practice in Malta and to identify factors that may influence their satisfaction.

2. Material and methods

2.1. Materials and method

A questionnaire was distributed to all adult patients receiving omalizumab for at least one year at Mater Dei Hospital in Malta, the only tertiary referral centre in Malta during the month of October 2017. The questionnaire included demographic data, details related to dose and dosage frequency of omalizumab, an asthma control test (ACT) [7] to assess control of asthma at the time of the questionnaire, as well as the 14-item English version of the Treatment Satisfaction Questionnaire for Medication (TSQM) Version 1.4 [6]. Side effects experienced in the past and not experienced recurrently or recently were not taken into consideration. All patients who completed the questionnaire were

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Abbreviations

TSQM	Treatment Satisfaction Questionnaire for Medication
ACT	Asthma Control Test
ACQ	Asthma Control Questionnaire

included in the survey analysis. The participants were all compliant to omalizumab on a regular basis when their hospital appointments were checked.

2.2. Treatment satisfaction

The TSQM 1.4 is a 14-item validated questionnaire that measures perception of four domains of treatment satisfaction, consisting of four scales: the effectiveness scale (questions 1–3), the side effects scale (questions 4–8), the convenience scale (questions 9–11), and the global satisfaction scale (questions 12–14). The TSQM 1.4 domain scores were calculated as recommended by the Questionnaire's authors [12–14]. Effectiveness is calculated as follows: $((\text{Item 1} + \text{Item 2} + \text{Item 3}) - 3) \text{ divided by } 18 \times 100$; side effects: $([\text{Sum of Item 5 to 8}] - 4) \text{ divided by } 16 \times 100$; Convenience: $([\text{Sum of Item 9 to 11}] - 3) \text{ divided by } 18 \times 100$; Overall Satisfaction: $(\text{Item 14} - 1) \times 5/6 \text{ then } ([\text{Sum of Item 12 to 14}] - 3) \text{ divided by } (12) \times 100$. The TSQM 1.4 domain scores range from 0 to 100 with higher scores representing higher degree of satisfaction. The global satisfaction scale is used to evaluate the overall satisfaction of patients with their medications [6].

2.3. Statistical analysis

Parametric numerical data were expressed as mean $\pm$ SD, whereas nonparametric numerical data were expressed as number and percentage. Factors associated with TSQM-14 global satisfaction domain scores were examined using Pearson's correlation test. Multiple step-wise linear regression analysis with 95% confidence intervals was performed to identify the independent predictors of treatment satisfaction. Statistical significance was set at a *p*-value less than 0.05. Statistical analyses were performed utilizing statistical package for the social sciences software version 23.

3. Theory/calculation

Despite physicians ensuring compliance with omalizumab of all our patients at the biologic clinic at our local hospital, the researchers deemed it necessary to analyse patients' satisfaction when receiving omalizumab, keeping in mind that once omalizumab is clinically effective and efficacious with tolerable side effects, it will most likely be continued indefinitely. The authors hypothesize that patients are overall satisfied with their omalizumab treatment and that the benefits with this medication outweigh the risk in the patients' eyes since omalizumab is an effective and well tolerated medication. The inconvenience associated with receiving the medication may however render patients unsatisfied with this medication and since not questioned directly at follow up clinics, may not volunteer such information and might default appointments and become non-compliant in the future. Hence the need for patients to complete the questionnaire and provide us with real-life results.

4. Results

Our cohort included a total of 33 patients (52% males). Table 1 shows the demographic details of all the patients who completed the questionnaire. Of the total 43 adult patients who received omalizumab in Malta, 5 (12.5%) of patients failed to complete the questionnaire for unknown reasons and 5 (12.5%) of patients had not completed one year

of treatment. A total of 14 (42.4%) patients were experiencing 5 different adverse drug events as shown in Table 1. A total of 3 patients had treatment stopped previously due to intolerable arthralgias and myalgias. No serious or life-threatening adverse events were reported. Table 2 shows the mean score per question in each domain of the TSQM as well as the mean score for each domain. Table 3 shows the total median score of each domain of the TSQM. Median TSQM scores were highest (indicating greatest satisfaction) for the side effects domain followed by the rest of the domains, which were equal on average. Table 4 shows the factors that influence global satisfaction with omalizumab. The mean drop in number of exacerbations when comparing one year prior to starting treatment and the most recent year prior to the survey was from 4.51 ± 3.7 to 1.06 ± 1.83 ($p < 0.05$) and the mean drop in systemic corticosteroid requirement during the same time frame was from 3.93 ± 3.96 to 0.54 ± 1.09 ($p < 0.05$). Regression analysis showed that the convenience score, effectiveness score and ACT score were significantly associated with global satisfaction whereas the age, gender, dosing regime, duration of treatment, side effects score as well as the reduction in asthma exacerbations systemic corticosteroid requirement were not.

5. Discussion

Omalizumab is a recombinant, DNA-derived, humanized IgG_{1κ} monoclonal antibody that selectively binds to human IgE and is approved for management of moderate-to-severe allergic asthma [8]. Guidelines recommend the addition of omalizumab for patients with allergic asthma who have inadequately controlled symptoms despite high-dose inhaled corticosteroids together with a long-acting β_2 -agonist [9,10].

Treatment satisfaction is useful to provide insights into the patient's perspective on their current treatment and to monitoring patient outcomes in clinical practice. Treatment satisfaction represents an important outcome since it has been associated with adherence as well as

Table 1
Demographic data of patients who completed the survey (n = 33).

Demographic data	
Number of patients	33
Number of males, n (%)	17 (52)
Hometown	
less than 15 min away from hospital, n (%)	5 (15)
more than 15 min away from hospital, n (%)	29 (85)
Mean age, years ($\pm$ SD)	53.7 $\pm$ 11
Mean baseline IgE level, IU/ml ($\pm$ SD)	510.6 $\pm$ 518
Mean duration of treatment, years ($\pm$ SD)	3.8 $\pm$ 1.98
Dosing regimen	
mean number of injections/month, n ($\pm$ SD)	4.6 $\pm$ 2.6
every 2 weeks, n (%)	15 (45)
every 4 weeks, n (%)	18 (55)
Transport method	
self-driven, n (%)	17 (48.6)
driven by relatives, n (%)	8 (23.5)
public transport, n (%)	7 (20.5)
Mean ACT score, n (SD)	20 $\pm$ 5.4
Compliance to ICS and LABA	
always	28 (85)
very often	3 (9)
often	2 (6)
hardly ever	0
never	0
Side effects experienced, n (%)	
weight gain	11 (33)
myalgias	3 (9)
arthralgias	2 (6)
lethargy	1 (3)
dizziness	1 (3)

ICS = Inhaled corticosteroid, LABA = long-acting B₂ agonist.

Table 2
TSQM individual items (n = 33).

TSQM items	Item means (SD)
Effectiveness	
Prevents or treats/7	5.7 (1.4)
Relieves symptoms/7	5.6 (1.3)
Time to start working/7	5.2 (1.3)
Side effects	
Bothersome side effects/5	4.5 (1)
Interfere physical function/5	4.2 (1.3)
Interfere mental function/5	4.5 (1.1)
Side effect impact on satisfaction/5	4.6 (0.7)
Convenience	
Easy to use/7	5.2 (1.3)
Plan when to use/7	5.7 (1)
Convenient to take/7	5.4 (1.4)
Overall satisfaction	
Confident in benefits/5	4.2 (0.9)
Good outweighs the bad/5	4.0 (0.97)
All things into account/7	5.2 (1)

Table 3
Median score for each domain of TSQM (n = 33).

TSQM scale and items	Item scale median/100
Graded Effectiveness	78
Graded Side effects	100
Graded Convenience	74.2
Overall satisfaction	76

Table 4
Regression analysis showing factors that influence global satisfaction.

	r	p-value
Age	-0.029	0.873
Gender	-0.126	0.484
Number of injections	0.1656	0.357
Frequency of injections	-0.1243	0.231
Duration of treatment	0.1472	0.157
Side Effects Score	0.214	0.232
Convenience Score	0.3465	0.048
Effectiveness Score	0.6601	0.003
ACT Score	0.6213	0.0001
Reduction in exacerbations	0.1125	0.533
Reduction in OCS courses required	-0.0614	0.723

willingness to continue treatment [5]. Adherence to treatment is one of the most important factors that guarantee the success of treatment in obstructive lung diseases [11]. Although the importance of medication adherence and treatment satisfaction has become well recognized in recent years with the availability of current guidelines for obstructive lung diseases emphasizing their importance, the rates are consistently low in real-life settings [11]. Improved adherence could be associated with better asthma control [12].

Results from a validation study suggest that the TSQM is a psychometrically robust instrument, which brings out the most important dimensions of patients' experiences with their medication [6]. This self-reported questionnaire was designed to assess patient treatment satisfaction in chronic diseases [13] and has recently also been utilized to study satisfaction with asthma treatment [11].

5.1. Effectiveness

The mean effectiveness score for each question in this domain

showed that the patients were either satisfied or very satisfied with the ability of omalizumab to treat their asthma, with the ability of medication to reduce symptoms and with the amount of time for the medication to start working. Since approval of omalizumab for severe allergic asthma, a total of 25 studies including 9213 asthma patients have evaluated the effectiveness of omalizumab under "real-life" conditions. A meta-analysis was conducted to evaluate the effectiveness of omalizumab documents the real-life pharmacotherapeutic effectiveness of omalizumab, as add-on treatment to improve outcomes in patients with results showing an improvement in the ACT score and ACQ score, a reduction in asthma exacerbations as well as a reduction in systemic corticosteroid requirements. The results mirrored, complemented, and extended the efficacy data from randomized controlled trials [14]. A local study too has identified omalizumab to be effective in reduction of exacerbations, improving asthma control and decreasing requirements of corticosteroids [15], which has been reconfirmed in this survey.

5.2. Side effects

In a number of recent internationally published studies, the overall safety profile of treatment with omalizumab is reported as being acceptable, remarkably safe and well tolerated in real-life. Most adverse events were mild-to-moderate and patients continued the treatment despite the side-effects [2,16,17]. In our cohort of patients, bothersome side-effects were reported as being minimal with minimal interference on physical and mental function. The score calculating the effect of side effects on satisfaction was reported to be close to nil. This survey excludes patients in whom treatment was discontinued in view of intolerable side-effects. However, for those patients who agreed to continue treatment despite the side-effects experienced, patients were not concerned about their impact. The most common side-effect was weight gain in a third of patients, possibly since patients had a better appetite associated with better asthma control. However, this is also contradictory since less systemic steroids were required for asthma control. Other less common side-effects included myalgias and arthralgias, which were minimal and well-tolerated. Otherwise, the drug would have been stopped during routine out-patient follow-up appointments, during which such issues are usually addressed.

5.3. Convenience

Treatment satisfaction is of utmost importance when prescribing a drug such as omalizumab primarily due to the commitment required since it is only administered in a hospital setting. This implies that patients need to travel to receive treatment sometimes depending on relatives or friends, and employed patients needing to take time off work on a regular basis, in addition to planning appointments around travel and work/family commitments. Our cohort of patients reported that on average, they found it easy or very easy to use, to plan appointments to receive treatment as well as the convenience associated with the treatment. The long-term requirement with treatment to maintain asthma control has also been published recently, emphasizing that omalizumab needs to be continued long-term since deterioration of asthma symptoms return on stopping treatment. In the XPORT trial, recently published, it was concluded that continuation of omalizumab after long-term treatment resulted in continued benefit, as evidenced by improved symptom control (asthma control test and asthma control questionnaire) and reduced exacerbation risk (time to first protocol-defined exacerbation), when compared to the placebo group, in whom omalizumab had been discontinued [18]. In addition, consistent omalizumab treatment was associated with significant reductions in emergency department visits and hospitalizations [19]. This emphasizes the fact that patients receiving treatment should ensure commitment in the indefinite term, no matter the inconvenience associated with receiving the medication.

5.4. Global satisfaction

Ideally, patients should be satisfied with their treatment and be convinced of its efficacy, otherwise this would encourage non-compliance as well as drop-outs. In this survey, Maltese patients were very convinced about the benefits received from the omalizumab, when taking all factors into account. They responded by saying that they were very confident of the benefits achieved by the medication and were also very convinced that the benefits outweigh the risks. In randomized controlled trials, the drop-out rate of omalizumab ranged from 7.1 to 19.4%. When reported, patient decision and adverse events were the most frequently reported causes. In real-life studies the drop-out rate ranged from 0 to 45.5%. Patient decision and lack of efficacy accounted for most treatment withdrawals [20]. Treatment adherence is crucial in patients with severe asthma when one considers the clinical impact of uncontrolled disease and the cost of non-adherence. The risk associated with treatment discontinuation has to be carefully considered both in experimental and real-life settings. Increased knowledge regarding the main reasons for patient withdrawal is important so as to find ways to improve adherence in clinical practice [20].

5.5. Factors which influence patient satisfaction

Analysis of our results revealed that age, gender, frequency and number of injections received and duration of treatment did not influence global satisfaction associated with the treatment. In a study of 289 patients performed to evaluate adherence in patients initiating omalizumab in the Epidemiologic Study of Xolair (omalizumab): Evaluating Clinical Effectiveness and Long-term Safety in Patients with Moderate to Severe Asthma (EXCELS) observational study, assessed over 5 years, more frequent dosing, that is 2-week dosing regimen was associated with a larger number of missed doses when compared to patients receiving the 4-week dosing regimen [12]. Neither did the side-effect score influence global satisfaction further confirming that experienced side-effects were well tolerated. Surprisingly, the documented reduction in asthma exacerbations and systemic corticosteroid requirements did not influence global satisfaction. This could be explained by the fact that patients tend to forget the severity of asthma prior to receiving treatment, hence the importance of close monitoring and data recording for this vulnerable group of patients.

Limitations of this study include a small number of patients from a single centre. Despite being a small sample size, patients are representative of the Maltese population since the cohort included all patients receiving omalizumab in Malta for at least one year, who agreed to participate. The service received at the department where the subcutaneous injections are received, such as staff approach and waiting times could also possibly influence the satisfaction with the treatment. However, such factors were not studied. Treatment satisfaction was assessed using subjective self-reported questionnaires. The questionnaires were completed in the absence of the investigator. This eliminated the possibility of bias from the investigator, however, this could have led to misunderstanding of certain, not so comprehensible questions. In addition, quantification of steroid doses required and severity of exacerbations were not recorded for comparison.

Despite the inconvenience associated with receiving omalizumab, mainly its available formulation and the fact that it is administered in a hospital setting, as well as the side effect profile experienced by some patients, patients' global satisfaction still scored high. This is an add-on beneficial effect to the efficacy and effectiveness that has already been achieved with this medication. High treatment satisfaction with one's medication would encourage adherence in clinical practice. For those patients who scored low in the global satisfaction, the benefit of omalizumab needs to be re-assessed. It would be ideal for this questionnaire to be repeated and compared in the future, following an additional number of years of receiving this medication.

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Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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