Contents lists available at ScienceDirect

Respiratory Investigation

journal homepage: www.elsevier.com/locate/resinv

Original article

Efficacy of long-term omalizumab therapy in patients with severe asthma

Junko Saji, MD, PhD[a,b,*], *Takahito Yamamoto, MD*[a,b], *Motonaka Arai, MD, PhD*[c], *Masamichi Mineshita, MD, PhD*[b], *Teruomi Miyazawa, MD, PhD*[b]

[a]*Division of Respiratory Diseases, Department of Internal Medicine, Kawasaki Municipal Tama Hospital, 1-30-37 Syukugawara, Tama-ku, Kawasaki, Kanagawa 214-8525, Japan*

[b]*Division of Respiratory Disease, Department of Internal Medicine, St. Marianna University School of Medicine, Kanagawa, Japan*

[c]*Tsurukawa Rehabilitation Hospital, Tokyo, Japan*

ARTICLE INFO

Article history:
Received 4 April 2015
Received in revised form
10 August 2016
Accepted 3 November 2016

Keywords:
ACT
AHQ
Anti-IgE antibody
Omalizumab
Severe asthma

ABSTRACT

Background: The efficacy of omalizumab, an anti-immunoglobulin E (IgE) antibody, has been studied in patients with severe bronchial asthma. We conducted a study to evaluate, on the basis of both objective and subjective measures, the efficacy of omalizumab as a long-term therapy in patients with severe and persistent asthma.

Methods: Omalizumab was administered subcutaneously every two or four weeks. The results of pulmonary function tests, Asthma Control Test (ACT) and Asthma Health Questionnaire (AHQ)-33 scores, the dosage of methylprednisolone during the 12-month treatment period, and the number of emergency visits prior to the start of treatment with omalizumab were compared in patients pre- and post-treatment with omalizumab.

Results: Fourteen patients were enrolled in the study between June 2010 and February 2012. Ten patients completed the study. With omalizumab treatment, there was no improvement in lung function; however, the number of emergency visits (19.3 before treatment vs. 1.2 after treatment, $p=0.020$) and the dosage of methylprednisolone (871.5 mg before treatment vs. 119.0 mg after treatment, $p=0.046$) decreased significantly. ACT and AHQ-33 scores at 16 weeks after treatment were significantly better than baseline scores. Four patients continued treatment with omalizumab for four years, and a reduction in their corticosteroid usage was noted.

Conclusions: Long-term omalizumab therapy in our patients was found to significantly reduce corticosteroid usage and the number of emergency visits. Long-term omalizumab therapy was effective and might have potential to reduce the frequency of asthma exacerbations.

The trial has not been registered because it is not an intervention study.

*Corresponding author at: Division of Respiratory Diseases, Department of Internal Medicine, Kawasaki Municipal Tama Hospital, 1-30-37 Syukugawara, Tama-ku, Kawasaki, Kanagawa 214-8525, Japan. Fax: +81 44 930 5181.

E-mail addresses: j2saji@marianna-u.ac.jp (J. Saji), yam@marianna-u.ac.jp (T. Yamamoto), mara@marianna-u.ac.jp (M. Arai), m-mine@marianna-u.ac.jp (M. Mineshita), miyazawat@marianna-u.ac.jp (T. Miyazawa).

http://dx.doi.org/10.1016/j.resinv.2016.11.002
2212-5345/

Please cite this article as: Saji J, et al. Efficacy of long-term omalizumab therapy in patients with severe asthma. Respiratory Investigation (2016), http://dx.doi.org/10.1016/j.resinv.2016.11.002

1. Introduction

Bronchial asthma is a chronic inflammatory disorder of the airways. An estimated 300 million people worldwide are affected by bronchial asthma to some degree [1]. Although inhaled corticosteroids (ICSs) have been shown to decrease the risk of mortality, approximately 5% of asthma patients have severe asthma that is inadequately controlled by ICS and long-acting β_2-agonist (LABA) therapies [2,3]. The long-term goals of asthma management are good symptom control, prevention of exacerbations, avoidance of fixed airway obstruction, and avoidance of adverse treatment effects. Patients with persistent symptoms or repeated exacerbations despite strict adherence to the Global Initiative for Asthma (GINA) guidelines for ICS therapy should be referred to a specialist with expertise in the management of severe asthma who can monitor step 4 treatment [4]. Anti-immunoglobulin E (anti-IgE) is suggested for patients who need step 5 treatment, especially those with allergic asthma [5]. IgE was discovered by Ishizaka et al., in 1966 and is known to play an important role in the inflammatory cascade triggered by allergen exposure in patients with atopic asthma [6]. After 36 years, the humanized monoclonal anti-IgE antibody omalizumab was approved in Australia for treatment of moderate to severe allergic IgE-mediated asthma. In Japan, omalizumab is now recommended for patients with severe persistent asthma that has been inadequately controlled at step 4 under the Japanese Asthma Prevention and Management Guideline 2009 [7].

Omalizumab has been reported to significantly reduce the frequencies of severe exacerbations and emergency medical visits and to improve both forced expiratory volume in 1 s (FEV1.0) (% predicted) and mean morning peak expiratory flow (PEF) [8]. However, Holgate et al., reported that omalizumab improves asthma control in the first 16 weeks of treatment without significant improvement in FEV1.0 [9]. It is possible that the efficacy of omalizumab for the prevention of asthma exacerbations is not reflected in the improvements in respiratory function.

It is important to evaluate patients not only on the basis of their asthmatic symptoms, but also their social activities and emotions, which are not covered by standard questionnaires [10]. The Asthma Health Questionnaire (AHQ)-33 (Fig. 1) was developed and validated in Japan specifically to evaluate Japanese asthma patients' subjective health status, including both physiological and psychological symptoms [11]. We conducted a single-institution prospective study to evaluate the long-term efficacy of omalizumab in patients with severe and persistent asthma as assessed by pulmonary function test results, Asthma Control Test (ACT) and AHQ-33 scores, the dosage of methylprednisolone, and the number of emergency visits per year.

2. Patients and methods

2.1. Patients

Fourteen patients were enrolled in the study between June 2010 and February 2012. Enrollment criteria included the presence of severe and persistent asthma, defined according to the Japanese Asthma Prevention and Management Guideline 2009 [6] as treatment with high-dose ICS and one or more of the following additional medications: LABA, sustained-release theophylline, leukotriene receptor antagonist, or oral corticosteroid. In addition, patients must have shown reactivity to at least one perennial aeroallergen, have had a serum total IgE level of 30–1500 IU/mL, and have had a body weight of 30–150 kg. Patients must also have shown insufficient asthma control, which is defined as the presence of one or more of the following: asthma symptoms that interfere with

- I have a cough.
- I have phlegm.
- I wheeze.
- I have asthma attacks.
- I get headaches.
- I have shortness of breath.
- My chest or shoulders feel heavy.
- My chest feels tight.
- My asthma keeps me awake at night.
- Exercise brings on asthma symptoms.
- Fatigue brings on asthma symptoms.
- Having a cold triggers my asthma.
- Inhaling substances like tobacco smoke, dust, cold air, exhaust fumes, pollen or cosmetics brings on asthma symptoms.
- Consuming certain food, alcohol, or non-asthma medications (fever-reducing medications, analgesics, etc.) brings on asthma symptoms.
- Contact with pets brings on asthma symptoms.
- Changes in the weather or atmospheric pressure brings on asthma symptoms.
- I feel depressed because I have asthma.
- I feel upset because I have asthma.
- I feel anxious because I have asthma.
- I feel irritable because I have asthma.
- My asthma makes it difficult for me to concentrate.
- My asthma prevents me from feeling refreshed.
- I am worried about having asthma.
- I am worried about having to continue taking asthma medication.
- My asthma symptoms limit my ability to walk.
- My asthma symptoms limit my ability to run or go uphill.
- My asthma symptoms limit my household activities, such as housework.
- My asthma symptoms limit my social and professional activities.
- My coworkers, classmates and other people have difficulties understanding my asthma problems.
- I am reluctant to meet people who don't know I have asthma.

My asthmatic condition and it's treatment are financially burdensome.

- I am worried that my asthma is a burden to my family.
- Considering the past 7 days, how is your overall of quality of life (QOL) ? Please choose one of the following faces which is considered to express your QOL best.

RESPONSE ITEMS: 0. Not at all, 1. A bit, 2. Somewhat, 3. Quite a bit, 4. Very much

Fig. 1 – Asthma Health Questionnaire-33.

Please cite this article as: Saji J, et al. Efficacy of long-term omalizumab therapy in patients with severe asthma. Respiratory Investigation (2016), http://dx.doi.org/10.1016/j.resinv.2016.11.002