Quality of life in severe asthmatic patients treated with benralizumab

Juan Carlos Miralles López, Ana Isabel Escudero Pastor, Antonio Carbonell Martínez, Cristina Navarro Garrido, Yaiza Bonilla Pacheco, Yulia Petryk Petryk.

Allergy Section. University General Hospital Reina Sofia. Murcia, Spain.

Juan Carlos Miralles López

Allergy Section. Hospital General Universitario Reina Sofía.

Avda. Intendente Jorge Palacios 1, 30003 Murcia

Spain

Email: jucarmir@telefonica.net

Key words: Quality of life; Severe asthma; Benralizumab; Control correlation; Lung function correlation.

Severe asthma has a great impact on the health related quality of life (HRQoL) of patients and their families (1). Thus, an appropriate asthma control is expected to improve HRQoL. Biologics, primarily monoclonal antibodies, have been developed to target specific pathways and important molecules in the pathogenesis of asthma, and their use has shown some promising effects on the HRQoL of severe asthmatic patients (2).

Benralizumab treatment decreases exacerbations and improves lung function in patients with severe, uncontrolled eosinophilic asthma (3), and we have reported in a real life study of 10 patients with severe asthma (4), that benralizumab decreases the number of exacerbations improving disease control.

The aim of this work is to study the effect of benralizumab in the HRQoL of patients with severe asthma, its different domains, and the relationship of the improvement in HRQoL with the changes in other variables such as asthma control, exacerbations, and lung function. The study was conducted in routine clinical practice, in accordance with the ethical standards established in the Declaration of Helsinki of 1946, and informed consent was obtained from all participants before enrolment in the study.

We have measured epidemiological variables, eosinophilia, HRQoL, number of exacerbations, asthma control (Asthma Control Test questionnaire), and lung function. We have assessed HRQoL by applying the mini AQLQ (Asthma Quality of Life Questionnaire); this questionnaire covers four health domains: symptoms, activity limitation, emotional function, and discomfort due to environmental stimuli.

The nonparametric Wilcoxon signed-rank test has been used for the statistical analysis and the results are described by median and interquartile range (IQR). We have correlated the changes in quality of life data with the changes in other variables such as lung function, asthma control and exacerbations using the Spearman's rank correlation coefficient.

We present data from 15 patients (9 women, 6 men) with severe eosinophilic bronchial asthma who have received treatment with benralizumab for 6 months. The mean age was

58.8 years (range 39-78), nine were never smokers and 6 ex-smokers. Most of them had overweight with an average BMI of 33.14.

Regarding background, 10 patients referred chronic rhinosinusitis, 8 nasal polyposis, and eight were atopic. About Asthma Severity, nine patients were in step 5 of GEMA (Spanish Guide for Asthma Management) (treated with high-dose inhaled corticosteroids and long-term bronchodilators, in addition to antileukotrienes and anticholinergics), and other six patients were in step 6, requiring continuous oral steroids.

Referring to adverse effects, administration of Benralizumab was uneventful for 14 patients, but one developed mild fever controlled with paracetamol. This good tolerance agrees with previous reports on the safety of the drug (3).

Mean eosinophil blood count was 522 cells/µL before the drug and 48 cells/µL after it, with 9 patients presenting 0 eosinophils.

The results of the mini AQLQ are shown in the table I. We have obtained a statistically significant improvement in the Total score: median pre-treatment 2.93 and posttreatment 5.60 ($p<0.001$), and in the four domains: Symptoms: 3.00 and 6.20 ($p<0.001$), Activity limitation 3.00 and 5.75 ($p<0.001$), Emotional function 2.67 and 6.00 (p 0.001) and Environmental stimuli 3.33 and 5.67 (p 0.043).

All the patients achieved the minimal important difference (6) of improvement in the AQLQ Total score. 14 patients in the Limitation Activity domain, 13 patients in the Symptoms domain, 12 in the Emotional Function domain and 8 patients in the Environmental Stimuli domain.

All patients experienced clinical improvement with the treatment. The number of exacerbations decreased in all cases, and the median for the year prior to Benralizumab was 3 (2.00-4.00) and 0 (0.00-0.00) (annualized rate) after the drug (p 0.001).

We also obtained improvements in asthma control: median ACT pretreatment 12 (8.00-16.00), posttreatment 21 (19.00-23.00) (p<0.001) and nonsignificant for lung function: median FEV1 pretreatment 1.6 L (1.14-2.06), posttreatment 1.81 L (1.19-2.93) (p 0.073 NS).

We have correlated the changes in the Total AQLQ score and the four domains with the changes in asthma control, lung function and exacerbations. The Total AQLQ score shows significant correlation with ACT: r_s = 0.615 (p 0.015) and FEV1: r_s = 0.739 (p 0.002), but not with decrease of exacerbations: r_s = -0.430 (p 0.109 NS) (Figure 1).

Similar results have been obtained by Symptoms, which also correlates with ACT: r_s = 0.535 (p 0.040) and FEV1: r_s = 0.702 (p 0.004), but not with exacerbations: r_s = -0.419 (p 0.120 NS), and Environmental stimuli with ACT: r_s = 0.534 (p 0.040), with FEV1: : r_s = 0.591 (p 0.020), and exacerbations: r_s = -0.349 (p 0.203 NS).

Nevertheless, the domain Activity limitation correlates with the three variables, ACT: r_s = 0.706 (p 0.003), FEV1: r_s = 0.680 (p 0.005), and exacerbations r_s = -0.518 (p 0.048).

Finally, the domain Emotional function does not correlate with any other variable: ACT: r_s = 0.325 (p 0.238 NS), FEV1: r_s = 0.504(p 0.055 NS), and exacerbations r_s = -0.286 (p 0.302 NS).

We have obtained, after treatment with benralizumab, a significant improvement in the patients' HRQoL, both Total AQLQ score and the four domains Symptoms, Activity limitation, Emotional function and Environmental stimuli. This improvement correlates with improvement in asthma control (ACT) and lung function in the case of Total score, Symptoms and Environmental stimuli, and in addition with decrease of exacerbations in Activity limitation.

In accordance with other authors, a correlation was found between improvement in HRQoL and asthma control (7) and lung function improvement. The lack of correlation

of the changes in HRQoL with decrease of exacerbations (but Activity limitation) has also been reported by Enríquez-Matas et al (8), and it could be due to the fact that the short period covered for the AQLQ questionnaire (two weeks) makes more difficult reflecting changes in a variable such as exacerbations. This limitation is more evident considering the long free period there is sometimes between exacerbations.

We conclude that benralizumab significantly improves HRQoL in severe asthmatic patients, globally and by domains: symptoms, activity limitation, emotional function, and discomfort due to environmental stimuli. This improvement is correlated with better asthma control and lung function.

Conflict of Interest: Juan Carlos Miralles López has received lecture fees from Novartis, GSK, Astra Zeneca, Sanofi and Chiesi. The rest of authors declare that they have no conflicts of interest.

The authors have not received any funding for this work.

References

1. Stucky BD, Sherbourne CD, Edelen MO, Eberhart NK. Understanding asthma-specific quality of life: Moving beyond asthma symptoms and severity. Eur Respir J. 2015; 46(3): 680–687.

2. Hossny E, Caraballo E, Casale T, El-Gamal Y and Rosenwasser L. Severe asthma and quality of life. World Allergy Organ J 2017;10(1):28

3. Chipps BE, Newbold P, Hirsch I, Trudo F, Goldman M. Benralizumab efficacy by atopy status and serum immunoglobulin E for patients with severe, uncontrolled asthma. Ann Allergy Asthma Immunol 2018;120(5):504-511.

4. Miralles López JC, Escudero Pastor AI, Carbonell Martínez A, Navarro Garrido C, Bonilla Pacheco Y, Petrik Petrik Y. Benralizumab in real life. J Investig Allergol Clin Immunol 2021; Vol. 31(1) doi: 10.18176/jiaci.0599.

5. Busse WW, Bleecker ER, FitzGerald JM, et al. Long-term safety and efficacy of benralizumab in patients with severe, uncontrolled asthma: 1-year results from the BORA phase 3 extension trial. Lancet Respir Med. 2019;7(1):46-59.

6. Juniper EF, Guyatt GH, Willan A, Griffith LE. Determining a minimal important change in a disease-specific Quality of Life Questionnaire. J Clin Epidemiol 1994; 47: 81-7

7. Howell CR, Thompson LA, Gross HE et al. Association of consistently suboptimal quality of life parallels consistently poor asthma control in children with asthma. Ann Allergy Asthma Immunol. 2017; 119(6): 562–564.

8. Enríquez-Matas A, Fernández-Rodríguez C, Andrés Esteban EM, Fernández-Crespo J. Main Contributory Factors on Asthma Control and Health-Related Quality of Life in Elderly Asthmatics. J Invest Allergol Clin Immunol 2020; 30(4):264-271.