Editorial

The ATAUD Study: The Need to Improve Adherence☆

Estudio ATAUD: la necesidad de mejorar la adherencia

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Compliance is defined as the degree to which a patient adheres to the recommendations agreed with the healthcare professional with regard to taking medication, following a diet, or modifying lifestyle habits.[1]

Hippocrates understood thousands of years ago how difficult it is to achieve adequate adherence to therapeutic indications. The prevalence of poor compliance in asthma patients is higher than 50%, a situation that has not improved significantly for the past 20 years.[2,3] This failure to comply has significant implications, such as worse asthma control, poorer quality of life, and increased incidence of exacerbations and mortality.[4–8]

There are several reasons for non-compliance with medical indications, including simple forgetfulness, deficient healthcare education, fear of side effects, type of inhaler, dosing regimen, overestimation of the degree of control obtained with less treatment, and comorbidities such as ischemic heart disease.[5,7–11]

It is, therefore, essential to identify deficient compliance, understand the reasons for this behavior, and implement strategies to improve this situation.

The ATAUD study ("Assessing adherence to inhaled medication in asthma: Impact of once-daily versus twice-daily dosing frequency") was designed and implemented by the SOGAPAR asthma group. The main objective of this study was to assess whether daily dosing frequency impacts on treatment compliance among asthma patients in routine clinical practice. Secondary objectives included analysis of the effect of compliance on asthma prognosis, and concordance between compliance measured by the Test of Adherence to Inhalers (TAI)[12] and by the electronic prescription refill rate obtained

from the Galician Healthcare Service's electronic prescription system. The study was carried out in the asthma units of 6 community hospitals, and involved a baseline visit and another visit at 6 months.[13]

The main finding of the study is that patients who were prescribed 1 inhalation per day have better compliance, fewer exacerbations, and better asthma control than those who use drugs that require 2 daily doses.

In terms of impact on asthma, better compliance did not correlate with the incidence of exacerbations, asthma control, or changes in lung function, and only a decrease in FeNO values was observed in patients who followed therapeutic indications more closely.

Another interesting finding is that the correlation between compliance assessed from a questionnaire and from prescription refill data collected from pharmacies is only moderate (rho: 0.548). This confirms the difficulty of evaluating this parameter, given the low reliability of patient-reported data. Nor can we consider the prescription refill rate to be completely reliable, because even with this objective data it is impossible to determine precisely how closely the indications of the doctor coincide with the treatment actually taken by the patients. In a recent publication including children aged from 5 to 17 years with severe asthma, compliance was assessed using an electronic device incorporated in the inhaler, and results were compared with the prescription refill rate. The authors reported that only 42% of patients complied with at least 80% of the prescribed doses. Moreover, among patients who refilled 100% of their prescriptions at the pharmacy, compliance with medical indications, according to the records of the electronic device in the inhaler, varied widely, ranging between 27% and 99%.[14]

The ATAUD study has some methodological weaknesses. Firstly, patients were included consecutively, with no consideration given to disease or patient factors that may be relevant to the interpretation of the results, such as baseline severity, educational level, and co-morbidities. Some differences that are likely to influence the results were observed in the baseline visit between the groups. The group treated with 2 inhalations per day presented a higher prevalence of some comorbidities, such as nasal polyposis or sleep apnea syndrome, and a higher eosinophil count in peripheral blood. The use of combinations of inhaled corticosteroids (ICS) with long-acting β-2-agonists was also significantly more frequent in this group, while in the group treated with a single inhalation per day,

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the use of ICS as a single agent was more common. Furthermore, the study duration was limited to 6 months. These differences in the baseline characteristics of the patients, as well as the short follow-up period, could have influenced the incidence of exacerbations, given the impact of seasons and comorbidities on control and on asthma exacerbations.[5,6,15]

The results of the ATAUD study appear to support emerging evidence in this area: the difficulty of correctly assessing compliance among asthmatic patients; the need to improve compliance which is clearly deficient, even in units specialized in the management of this disease; the importance of the type of inhaler and the dosing regimen in improving patient compliance with medical prescriptions and disease course; and, in line with Hippocrates, the possibility that some patients are less than truthful when reporting their use of certain medications.

Conflict of interests

References

1. Adherence to long term therapies: evidence for action. World Health Organization; 2003.
2. Lee J, Tay TR, Radhakrishna N, Hore-Lacy F, Mackay A, Hoy R, et al. Nonadherence in the era of severe asthma biologics and thermoplasty. Eur Respir J. 2018;51, pii: 1701836.
3. Bender BG. Nonadherence to asthma treatment: getting unstuck. J Allergy Clin Immunol Pract. 2016;4:849–51.
4. Gelzer AD, Gao W, Keleti D, Donia T, Megargell L, Kreitman J, et al. Multifaceted interventions improve medication adherence and reduce acute hospitalization rates in medicaid patients prescribed asthma controllers. J Asthma. 2018:1–10, http://dx.doi.org/10.1080/02770903.2018.
5. González Barcala FJ, de la Fuente-Cid R, Alvarez-Gil R, Tafalla M, Nuevo J, Caamaño-Isorna F. Factors associated with asthma control in primary care patients: the CHAS study. Arch Bronconeumol. 2010;46: 358–63.
6. Gonzalez-Barcala J, de la Fuente-Cid R, Tafalla M, Nuevo J, Caamaño-Isorna F. Factors associated with health-related quality of life in adults with asthma. A cross-sectional study. Multidiscip Respir Med. 2012;7:32.
7. Mäkelä MJ, Backer V, Hedegaard M, Larsson K. Adherence to inhaled therapies, health outcomes and costs in patients with asthma and COPD. Respir Med. 2013;107:1481–90.
8. Gemicioglu B, Bayram H, Cimrin A, Abadoglu O, Cilli A, Uzaslan E, et al. Asthma control and adherence in newly diagnosed young and elderly adult patients with asthma in Turkey. J Asthma. 2018:1–9, http://dx.doi.org/10.1080/02770903.2018.
9. Sasaki J, Kawayama T, Yoshida M, Takahashi K, Fujii K, Machida K, et al. Adherence barriers to inhaled medicines in Japanese older patients with asthma evaluated using the "Adherence Starts with Knowledge 20" (ASK-20) questionnaire. J Asthma. 2018:1–10, http://dx.doi.org/10.1080/02770903.
10. González-Barcala FJ, García-Couceiro N, Facal D. Education in asthma [Article in English, Spanish]. Arch Bronconeumol. 2016;52:543–4.
11. Plaza V, Giner J, Calle M, Rytilä P, Campo C, Ribó P, et al. Impact of patient satisfaction with his or her inhaler on adherence and asthma control. Allergy Asthma Proc. 2018;39:437–44.
12. Plaza V, López-Viña A, Cosio BG, en representación del Comité Científico del Proyecto Test of Adherence to Inhalers. Test of adherence to inhalers. Arch Bronconeumol. 2017;53:360–1.
13. de Llano LP, Sanmartín AP, González-Barcala FJ, Mosteiro-Añón M, Abelaira DC, Quintas RD, et al. Assessing adherence to inhaled medication in asthma: Impact of once-daily versus twice-daily dosing frequency. The ATAUD study. J Asthma. 2018;55:933–8.
14. Jochmann A, Artusio L, Jamalzadeh A, Nagakumar P, Delgado-Eckert E, Saglani S, et al. Electronic monitoring of adherence to inhaled corticosteroids: An essential tool in identifying severe asthma in children. Eur Respir J. 2017;50, pii: 1700910.
15. Gonzalez-Barcala FJ, Calvo-Alvarez U, Garcia-Sanz MT, Garcia-Couceiro N, Martin-Lancharro P, Pose A, et al. Asthma exacerbations: risk factors for hospital readmissions. Ir J Med Sci. 2018;187:155–61.