Pulmonol. 2020;26(2):63–65

PULMONOLOGY

www.journalpulmonology.org

EDITORIAL

Is adherence to treatment influenced by the ability to use inhaled devices in patients with COPD correctly?

Chronic Obstructive Pulmonary Disease (COPD) is a frequent and disabling disease, and it is responsible for important limitations in daily life and high economic impact on the health system.[1] Patients with moderate to severe COPD are affected by chronic symptoms, poor quality of life and frequent exacerbations, and are at high risk of mortality for respiratory and non respiratory diseases.[2] Pharmacologic treatment, based mainly on bronchodilators and inhaled corticosteroids, is able to modify several outcomes of the disease, although a clear demonstration of the possibility of improving survival is still lacking.[3,4] Unfortunately, the adherence to the long-term use of inhaled drugs is very low, thereby reducing the impact of the pharmacologic treatment on the progression of the disease. While adherence in the randomised clinical trials is high, several observational data from real life have documented that a variable percentage of between 30 and 50% of patients with COPD use regularly inhaled drugs.[5,6]

Several factors have been associated with a poor adherence, some of them related to demographic characteristics such as age and gender, clinical aspects of the disease (severity, comorbidities), socio-economic factors (education, health literacy, social/familiar support, income), characteristics of the inhaled therapy (dose regimen, number and type of inhalers, satisfaction with inhalers), satisfaction with drug efficacy and clinician expertise.[5] In real life, most severe patients have a better adherence to treatment than patients with mild to moderate disease, probably due to the greater limitation in daily life and to the perception of the efficacy of the treatment.

In this issue of Pulmonology, Duarte-de-Araujo and coworkers[7] extended a previous recent observation[8] on a fairly large group of patients with COPD of different severity: they used a specific psychometric tool (Measure of Treatment Adherence), validated for the Portuguese population in 2001, consisting of seven questions leading to a total score ranging from 6 to 42. They demonstrated that 16.5% of the patients examined were classified as non-adherent, and that this percentage was significantly higher in less severe COPD patients. Furthermore, a significant relationship was found between non adherence and FEV1%, also when data were corrected in a logistic analysis by several confounding factors. This relationship may be expected, because the severity of symptoms may promote a more regular use of the inhaled drugs, confirming the positive effect of the pharmacologic treatment. This observation is not new, although the several observational studies in this topic area have not clearly underlined this specific point. In effect, in the usual current clinical practice, low adherence to treatment both in asthma and in COPD is more frequent in less severe patients who do not understand the need for a continuous regular treatment when they only have mild symptoms and limitations. In any case, low adherence to the pharmacologic treatment has been demonstrated to be associated with poor outcomes of the disease, such as increased frequency and severity of symptoms and exacerbations, progressive decline in pulmonary function and even mortality.[9]

A second point considered in the paper[7] is the relationship between performance in using inhalers and adherence to treatment. The authors used a clearly defined checklist for the major critical errors according to the different dry-powder inhalers (DPI), and they found that almost 40% of the patients misused the recommended inhalers; this was lower with DPIs than with metered dose inhalers (MDIs). In a multivariate analysis, misuse of inhalers was only significantly associated with age, gender, and socio-economic level, while no significant relationship was observed between inhaler technique and adherence to medications. This topic has been extensively reported in the literature: several observational studies showed the high prevalence of incorrect use of the inhalers in both asthma and COPD patients, and that this fact was associated with an inadequate control of the disease in many countries, including Italy and Portugal.[10,11] In a recent large survey including almost 3000 patients with COPD selected by the general practitioners (GPs) or pulmonary specialists, more than 50% of the patients made one or more critical errors in the use of different devices, more frequently using MDIs and soft-mist inhalers[12]; the rate of severe COPD exacerbations was twice

https://doi.org/10.1016/j.pulmoe.2020.01.005

greater in patients with poor inhaler technique in comparison with the others.

Correctly using the inhaler devices is crucial for a good result of the therapy, independently of a possible but not clearly demonstrated effect on drug compliance. Some general recommendations should be remembered: (a) if possible, avoid the use of different devices with a single patient, in order for them to have to learn only one inhalation technique; we have now different drugs and combinations (ICS/LABA or LABA/LAMA or ICS/LABA/LAMA) administered with the same device, allowing movement from one combination to another based on the clinical assessment, without changing the inhalation technique; it has been already demonstrated that switching from one device to another, if not accompanied by appropriate training for the patient, can be associated with poor clinical outcomes and increased use of health care resources[13]; (b) monotherapy with a single inhaler, possibly administered once daily, has been reported to be more effective in the control of the disease that multiple devices used at different time of the day[14]; (c) education on the use of inhalers and practical demonstrations of the inhalation technique at each visit is crucial in order to have a correct interpretation of the results of the pharmacologic treatment. Recently new ''intelligent'' devices have been developed, to simplify the inhalation technique (like new breath-actuated MDIs)[15] or to check for the correct inhalation technique and adherence.[16,17] On the other hand, the contribution of the inhaler misuse to general adherence to the maintenance therapy is still controversial, as suggested by some authors[18] but not confirmed by the paper from Duarte-de-Araujo et al.[7]

The final point of the manuscript by Duarte-de-Araujo et al.[7] is related to the adherence of GPs to the recommendations derived from international guidelines or documents, like the Global Initiative for Chronic Obstructive Pulmonary Disease (GOLD) guidelines. As reported in previous surveys,[19,20] overtreatment is the most frequent situation, with less severe patients receiving frequently regular ICS where there is reduced use of bronchodilators. This fact has some historical reasons (ICS/LABA combinations were the first drugs showing a positive effect on many clinical and functional outcomes of COPD) and it is related to prescription feasibility (in some countries, like Italy for example, more recent LABA/LAMA combinations may only be prescribed by pulmonary specialists) and also to the lack of appropriate clinical assessment of the patients. This tendency to overtreat COPD patients has not greatly changed in recent years despite the wide diffusion of GOLD guidelines, which suggests that in real life many physicians believe that in a disease poorly responsive to pharmacologic treatment, it is better to use all available drugs independently of the baseline disease severity, in order to try to prevent the progressive deterioration of the disease.

In summary, we have several demonstrations that in the last 10 years adherence to inhaled therapy is very poor in COPD patients, and the paper from Duarte-de-Araujo et al.[7] confirms this assumption. There are several determinants of this poor adherence, and this paper adds to the many factors also the level of disease severity as assessed by FEV1. In any case, all potential determinants may together only explain a minor part of the total variance, suggesting that other personal factors may have a strong influence on adherence to treatment. As an example, the adherence to the prescribed therapy is strongly influenced by the individual patient's general behaviour and personality, and it may be independent of the real efficacy of the drugs, as demonstrated by the post-hoc analysis of the TORCH study[21] where adherence was associated to a reduction in mortality and in hospital admissions due to severe exacerbations independently of the specific treatment arm, including the placebo arm. Strategies for implementing and reinforcing adherence should be promoted, although the efficacy of these intervention has not been definitely proven.[5,22]

Conflicts of interest

The authors have no conflicts of interest to declare.

References

1. López-Campos JL, Tan W, Soriano JB. Global burden of COPD. Respirology. 2016;21:14–23.
2. Global Initiative for Chronic Obstructive Pulmonary Disease (GOLD), update 2019, http://goldcopd.com.
3. Calverley PM, Anderson JA, Celli B, Ferguson GT, Jenkins C, Jones PW, et al. Salmeterol and fluticasone propionate and survival in chronic obstructive pulmonary disease. N Engl J Med. 2007;356:775–89.
4. Lipson DA, Barnhart F, Brealey N, Brooks J, Criner GJ, Day NC, et al. Once-Daily Single-inhaler triple versus dual therapy in patients with COPD. N Engl J Med. 2018;378:1671–80.
5. López-Campos JL, Quintana Gallego E, Carrasco Hernández L. Status of and strategies for improving adherence to COPD treatment. Int J Chron Obstruct Pulmon Dis. 2019;14:1503–15.
6. Ingebrigtsen TS, Marott JL, Nordestgaard BG, Lange P, Hallas J, Dahl M, et al. Low use and adherence to maintenance medication in chronic obstructive pulmonary disease in the general population. J Gen Intern Med. 2015;30:51–9.
7. Duarte-de-Araújo A, Teixeira P, Hespanhol V, Correia-de-Sousa J. COPD: analysing factors associated with a successful treatment. Pulmonology. 2019;pii: S2531-0437(19):30121–7. Jun 17.
8. Duarte-de-Araújo A, Teixeira P, Hespanhol V, Correia-de-Sousa J. COPD: understanding patients' adherence to inhaled medications. Int J Chron Obstruct Pulmon Dis. 2018;13:2767–73.
9. 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.
10. Melani AS, Bonavia M, Cilenti V, Cinti C, Lodi M, Martucci P. Inhaler mishandling remains common in real life and is associated with reduced disease control. Respir Med. 2011;105:930–8.
11. Maricoto T, Rodrigues LV, Teixeira G, Valente C, Andrade L, Saraiva A. Assessment of inhalation technique in clinical and functional control of asthma and chronic obstructive pulmonary disease. Acta Med Port. 2015;28:702–7.
12. Molimard M, Raherison C, Lignot S, Balestra A, Lamarque S, Chartier A. Chronic obstructive pulmonary disease exacerbations and inhaler handling: real-life assessment of 2935 patients. Eur Respir J. 2017;49, pii. 1601794.
13. Braido F, Lavorini F, Blasi F, Baiardini I, Canonica GW. Switching treatments in COPD: implications for costs and treatment adherence. Int J Chron Obstruct Pulmon Dis. 2015;10:2601–8.
14. Vestbo J, Leather D, Diar Bakerly N, New J, Gibson JM, Salford Study Investigators. Effectiveness of fluticasone furoate-vilanterol for COPD in clinical practice. N Engl J Med. 2016;375:1253–60.
15. Usmani O, Roche N, Marshall J, Danagher H, Price D. An innovative corticosteroid/long-acting β2-agonist breath-

triggered inhaler: facilitating lung delivery of fluticasone propionate/formoterol fumarate for the treatment of asthma. Expert Opin Drug Deliv. 2019;16:1367–80.
16. Carpenter DM, Roberts CA, Sage AJ George J, Horne R. A review of electronic devices to assess inhaler technique. Curr Allergy Asthma Rep. 2017;17:17.
17. Sulaiman I, Greene G, MacHale E, Seheult J, Mokoka M, D'Arcy S, et al. A randomised clinical trial of feedback on inhaler adherence and technique in patients with severe uncontrolled asthma. Eur Respir J. 2018;51, pii: 1701126.
18. Braido F, Chrystyn H, Baiardini I, Bosnic-Anticevich S, van der Molen T, Dandurand RJ, et al. ''Trying, But Failing'' - the role of inhaler technique and mode of delivery in respiratory medication adherence. J Allergy Clin Immunol Pract. 2016;4:823–32.
19. Corrado A, Rossi A. How far is real life from COPD therapy guidelines? An Italian observational study. Respir Med. 2012;106:989–97.
20. Brusselle G, Price D, Gruffydd-Jones K, Miravitlles M, Keininger DL, Stewart R, et al. The inevitable drift to triple therapy in COPD: an analysis of prescribing pathways in the UK. Int J Chron Obstruct Pulmon Dis. 2015;10:2207–17.
21. Vestbo J, Anderson JA, Calverley PM, Celli B, Ferguson GT, Jenkins C, et al. Adherence to inhaled therapy, mortality and hospital admission in COPD. Thorax. 2009;64:939–43.
22. Vanhaecht K, Lodewijckx C, Sermeus W, Decramer M, Deneckere S, Leigheb F, et al. Impact of a care pathway for COPD on adherence to guidelines and hospital readmission: a cluster randomized trial. Int J Chron Obstruct Pulmon Dis. 2016;11:2897–908.

Manuela Latorre[a,b], Giulia Parri[a], Pierluigi Paggiaro[a,*]
[a] *Department of Surgery, Medicine, Molecular Biology and Critical Care, University of Pisa, Italy*
[b] *Pulmonary Unit, Nuovo Ospedale Apuano, Massa, Italy*

* Corresponding author.
E-mail addresses: manuela.latorre@yahoo.it (M. Latorre), giuliaparri@gmail.com (G. Parri), pierluigi.paggiaro@unipi.it (P. Paggiaro).

7 January 2020
Available online 6 February 2020