

Mini Review

COPD, Where is the Research in Inhaled Therapy Going?

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***Corresponding author:** Antonio L. Aguilar-Shea, Family Physician, E.A.P. Puerta de Madrid, Avda del Ejército 61, Zip Code 28802, Alcalá de Henares, Spain**Received:** November 19, 2019; **Accepted:** January 28, 2020; **Published:** February 04, 2020**Abstract**

A review in COPD therapy was conducted to analyze the comparative studies in inhaled long-acting bronchodilators to know where the research is leading and to see if there is any treatment superior to others. The most relevant findings were the drift towards long lasting triple therapy in severe non-controlled patients and the superiority of LABA/LAMA versus LABA/ICS in double therapy in stable patients. Regarding LABA/ICS fixed combinations, budesonide/formoterol was associated with fewer exacerbations than fluticasone/salmeterol.

Keywords: Chronic obstructive pulmonary disease; Exacerbations; Primary care; Inhaled corticosteroids; Long-acting β_2 -agonist; Long-acting muscarinic antagonist; Inhaled therapy

Review

Chronic obstructive pulmonary disease (COPD) is not a curable disease and the goal of treatment is to maximize the lung function that remains. The lung function that is lost cannot be recovered. The main symptoms in COPD are coughing, excessive sputum production and dysnea. Treating these symptoms is the main objective in COPD management with the absolute avoidance of smoking [1,2].

COPD exacerbations, when symptoms become worse rather quickly, are associated with rapid decline in lung function, life quality decrease, increase in hospitalization and increase of death [3]; avoiding these flare-ups are critical in these patients. Inhaled therapy and the absolute avoidance of smoking are the first steps in COPD management. Inhaled long-acting bronchodilators are the initial treatment in maintenance COPD therapy [1,2]; different options include long-acting muscarinic antagonist (LAMA), long-acting beta2 agonist (LABA) and inhaled corticoids (ICS); as single therapy or in combination. Practice guidelines describe different scenarios and propose different treatment options, with no drug or drug combination preference [1,2].

In order to know where the research in COPD therapy is leading and if there is any treatment superior to others, a search in Medline (Pubmed) was conducted analysing the comparative studies in inhaled long-acting bronchodilators, especially focused on the last 5 years to review the most recent data.

When comparing a fixed combination of LABA/LAMA versus LABA/CI in people with stable COPD, the fixed combination of LABA/LAMA proved to offer a better control of the disease [4-12]. Cochrane [13] review in 2017 supported this finding and was in the lines of the recent GOLD guideline [1]. Recent data comparing indacaterol/glicopirronium vs fluticasone/salmeterol, reaffirmed this conclusion and also concluded to be a more cost-effective option [14-17].

Research comparing fixed combinations within the same treatment group were also reviewed, in order to find out if there was a combination better than the other ones. In LABA/ICS fixed combinations, no combination was better than other [18-22], but recent data in Italian [23] and Spanish [24] populations revealed

that budesonide/formoterol combination was associated with fewer exacerbations than fluticasone/salmeterol. The review of the data in LAMA therapy revealed that there was no difference in the devices, handihaler or respimat, containing tiotropium and that glicopirronium could be considered more cost-effective than tiotropium [25-27]. Data comparing LABA versus LAMA revealed that tiotropium offered better control in COPD than salmeterol [28] and that indacaterol was more effective and tiotropium [29,30]. The review of ICS/LABA versus LAMA data, just revealed one study concluding that budesonide/formoterol proved a better control of COPD compared to tiotropium [31]. Regarding LAMA/LABA fixed combinations, Cochrane review reported that indacaterol/glicopirronium offered better results in exacerbation prevention and life quality when compared to umeclidinium/vilanterol [13]. In another study, umeclidinium/vilanterol proved more lung function improvement when compared to tiotropium/olodaterol [32].

As COPD progresses in severity the inevitable is to try to control the disease with all available inhaled therapy options, drifting to triple therapy (LAMA/LABA/ICS) [1,2,33]. Triple therapy as proved to offer a better COPD control than double and single therapy, which would be the obvious conclusion. TRILOGY study [34] concluded that beclometasone/formoterol/glicopirronium was better than double therapy with corticoid beclometasone/formoterol, TRINITY study [35] concluded that it was also better than LAMA monotherapy with glicopirronium, TRIBUTE study [36] concluded that it was better than double therapy without corticoid indacaterol/glycopyrronium; further research also concluded that fluticasone/umeclidinium/vilanterol was better than double therapy with corticoid budesonide/formoterol [37] and fluticasone/vilanterol [38] or double therapy without corticoid umeclidinium/vilanterol [38]. Adding different inhaled agents is the proposed and logical recommendation by COPD guidelines in non-controlled patients [1,2] and by recent studies towards long-acting triple therapy [39-41]. Currently there is no data comparing the different triple therapy options with each other, so we will have to wait to see if any long-lasting triple therapy proves superiority over the rest.

In conclusion, the most relevant recent changes are the superiority of LABA/LAMA versus LABA/ICS in double therapy in stable

patients and the drift towards long lasting triple therapy in severe non-controlled patients. Regarding LABA/ICS fixed combinations, budesonide/formoterol was associated with fewer exacerbations than fluticasone/salmeterol.

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