A pragmatic approach to simplifying inhaler therapy for COPD

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A pragmatic approach to simplifying inhaler therapy for COPD

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Conflict of interest

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Current guidelines for COPD recommend a stepwise approach to inhaled pharmacotherapy.[1] The assessment of COPD is based on severity of airflow limitation (spirometric grades 1-4) as well as symptom burden and exacerbation risk (groups A-D). Symptoms and exacerbations are the main drivers of treatment. The greatest health care burden is associated with frequent exacerbations of COPD – i.e. those patients in groups C and D.

The guidelines are rather complicated suggesting moving up the treatment escalator from monotherapy with long acting beta-agonist (LABA) or long acting muscarinic antagonist (LAMA) to combination inhaler therapy with LABA/LAMA or inhaled corticosteroid (ICS) with LABA (ICS/LABA) and then triple therapy with ICS/LABA/LAMA. Currently, triple therapy requires the use of two separate inhalers comprising ICS/LABA and LAMA often via different devices, which in turn may be associated with poorer long term compliance. However single triple therapy inhalers currently in development may soon become available including once daily with fluticasone furoate/vilanterol/umeclidinium, or twice daily with beclometasone/formoterol/glycopyrronium or budesonide/formoterol/glycopyrronium. Given that there are already numerous different inhaler devices for mono and dual therapy, prescribers are understandably becoming increasingly confused especially in primary care.

We therefore propose a less complex and more pragmatic approach to prescribing stratified by exacerbations and eosinophils, whereby there are only two options for patients with COPD, namely single inhalers comprising either LABA/LAMA or ICS/LABA/LAMA (Figure). The rationale for this simplified approach is proposed as follows. Using two long acting bronchodilators is more effective than one in terms of lung function, symptoms and exacerbations.[2] Hence it would appear cogent to use a LABA/LAMA single inhaler combination as the starting point for patients with increased symptoms or more frequent exacerbations. This is also supported by evidence from real life prescribing data where patients often step up from monotherapy to combination therapy, presumably because the latter results in better control.[3] Hence initiating treatment with LABA/LAMA will result in fewer treatment failures than monotherapy, in turn improving the likelihood of patients adhering to their prescribed inhalers along with a lower health care burden.

The use of ICS/LABA has been shown to be more effective in reducing exacerbations in patients with an eosinophilic component to their COPD.[4,5] Moreover patients with COPD who have frequent exacerbations in conjunction with blood eosinophilia (>300 cells/ul) are at higher risk of exacerbating when stepping down from triple therapy upon subsequent withdrawal of ICS.[6 7]

The situation with regards to ICS/LABA is further complicated by the results of the FLAME study[8] which found overall that once daily indacaterol/glycopyrronium was superior to twice daily fluticasone/salmeterol for effects on exacerbations, lung function and quality of life. However in a subsequent post hoc analysis of FLAME it was found that .LABA/LAMA was no better than ICS/LABA on exacerbations in patients with blood eosinophils >300 cells/ul.[9]

Triple therapy via a single or separate inhalers containing ICS/LABA/LAMA has been shown to be superior to ICS/LABA on lung function, quality of life and exacerbations.[10-12] Given the greater benefits of ICS on exacerbations in patients with eosinophilic COPD, there would appear to be a rationale for starting off with triple therapy for individuals with a higher exacerbation risk, without going through the first step of ICS/LABA, especially once the single triple inhalers become available. Pointedly there are at present no head to head comparisons of triple therapy verses LABA/LAMA. However one might expect that triple therapy would be superior to LABA/LAMA but only for effects on exacerbations in patients with eosinophilic COPD with frequent exacerbations. Whether triple therapy should also be considered as step up for non-eosinophilic patients who are exacerbating despite LABA/LAMA remains unclear, especially in view of the pneumonia risk associated with ICS use.

Where does this all leave us moving forwards with regards to simplifying inhaled therapy for COPD especially for those patients in groups C and D with frequent exacerbations? We would suggest a pragmatic approach using single inhaler therapy whereby patients with eosinophilic COPD (i.e. >300 cells/ul) receive ICS/LABA/LABA and those with non-eosinophilic COPD (i.e. <300 cells/ul) receive LABA/LAMA (Figure). For patients in group B the starting point irrespective of eosinophils would be LABA/LAMA since these patients

have more symptoms but infrequent exacerbations and therefore do not need the ICS moiety. We would advocate two blood draws if necessary to identify those patients with eosinophilic COPD. The most suitable inhaler device for an individual patient is the one which they feel comfortable with, can use correctly and will take on a regular basis in the long term. Real life studies are now indicated to test this hypothesis in COPD patients stratified according to exacerbation frequency and blood eosinophils. Such pragmatic studies should also assess whether using a once or twice daily dosing single inhaler regimen is the best way forward.

Figure Legend

Pragmatic approach to using dual (LABA/LAMA) or triple (ICS/LABA/LAMA) single inhaler therapy for COPD stratified according to blood eosinophils (low <300 cells/ul or high >300 cells/ul) and exacerbation risk. The interrupted line between dual and triple therapy indicates the possibility of stepping up or down.

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