Bronchodilators: the cornerstone of COPD therapy

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Following the GOLD document management of COPD has two major goals: reduction of symptoms and reduction of future risks, in particular prevention of exacerbations. Based on the GOLD 2011 assessment scheme with the categories A-D non-pharmacological and pharmacological interventions have been recommended. Regarding pharmacological therapy long-acting bronchodilators are suggested for the categories B to D as first choice treatment. Both currently available classes of long acting bronchodilators - β2-agonists (LABAs) and anticholinergics (LAMAs) have significant effects on lung function, symptoms, quality of life and exacerbations. There are two major trials that evaluated the effects of a LABA and a LAMA on exacerbations in a head-to-head comparison. Both studies suggest that the LAMA tiotropium is superior to the LABAs salmeterol and indacaterol in this regard. Thus, it seems that a LAMA offers some advantages compared to a LABA. As both classes of drugs seem to be equally well tolerated, at initiation of therapy my first choice is a LAMA.

Recently, in Europe several LABA/LAMA combinations became available - either for once-daily (glycopyrronium/indacaterol, umeclidinium/vilanterol, tiotropium/olodaterol) or twice-daily (aclidinium/formoterol) use. With this as a background, the discussion evolved which patients should start with a mono-bronchodilator treatment and which patients should right away receive a LABA/LAMA combination. There is no evidence base for this decision. The spectrum of opinions goes from “every patient should be started with a single bronchodilator” to “every patient needs a LABA/LAMA combination”. My personal view is that newly-diagnosed patients with moderate symptoms and no history of frequent exacerbations may be treated with a single bronchodilator whereas highly symptomatic patients with frequent exacerbations should receive a dual bronchodilator.

The application of the GOLD recommendations for pharmacological therapies in clinical practice is limited to initial therapy, or in other words: there are no suggestions for escalation or de-escalation of treatment. This shortcoming goes back to a shortage of studies that analyse the consequences of de-escalation and a lack of studies that evaluate escalation strategies. Nevertheless, I do believe that it is logical to escalate to a dual bronchodilator if a patient does not show a relevant improvement when treated with a single bronchodilator.

In patients with frequent exacerbations alternatively an ICS/LABA combination may be used. ICS/LABA combinations have shown to be more effective regarding lung function, quality of life and exacerbations than the single components. Head-to-head comparisons between ICS/LABA and LABA/LAMA combinations in patients without a history of frequent exacerbations showed non-inferiority or superiority (for some endpoints) for the LABA/LAMA combination indacaterol/glycopyrronium versus the ICS/LABA combination fluticasone propionate/salmeterol.

Recently, a study has been finalized that evaluated the same combinations in a head-to-head comparison in highly symptomatic patients (dyspnea grade mMRC ≥2) with moderate to very severe airflow limitation (post-bronchodilator FEV1 25-60% predicted and a significant history of exacerbations (≥ 1 documented COPD exacerbation requiring treatment with antibiotics, systemic corticosteroids or hospitalization within one year of randomisation). The primary objective of the study was that the combination indacaterol/glycopyrronium is at-least non-inferior to fluticasone propionate/salmeterol in terms of rate of COPD exacerbations (mild/moderate/severe) during 52 weeks of treatment. According to a press release indacaterol met the primary endpoint and furthermore demonstrated superiority in reducing the rate of all COPD exacerbations. These results suggest that the exacerbation history alone does not give sufficient guidance as to whether an ICS/LABA combination may be indicated and preferred to a LABA/LAMA combination.
In summary, the available data suggest that long-acting bronchodilators either given as mono- or dual-therapy represent the cornerstone of therapy for COPD patients ranging from newly diagnosed cases with moderate symptoms to highly symptomatic individuals with a relevant history of exacerbations. Which patients may be preferably treated with an ICS/LABA combination or a triple therapy with LAMA/LABA/ICS remains to be established.

References


