Asthma: ICS as a rescue approach - following the patients' preferences

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After 30 years, the annual recommendations of GINA proceeded to a major update in the stepwise therapeutic approach to asthma, affecting the way patients diagnosed with asthma are treated. More specifically, for Steps 1 and 2 treatment, the recommended use of SABA as a reliever therapy has been replaced by the use of low dose ICS-formoterol as a rescue medication. SABA inhalers can be entirely omitted for most patients with asthma, although GINA does not entirely eliminate their use as an add-on reliever therapy. Moreover, it is suggested the starting treatment to be directly with ICS-LABA even in patients with mild asthma, excluding the "step-up" process of ICS alone to ICS-LABA. In this way, most patients with asthma can be prescribed just one inhaler that can be used as both a maintenance (preventive) and rescue treatment: an inhaled corticosteroid-and-long-acting beta agonist, that is formoterol (ICS-LABA). All patients with asthma should receive at minimum an ICS-containing controller treatment either as needed or daily low dose (in mild asthma) for exacerbation prevention[1].

The explanation behind this change is based on a multiyear effort to provide evidence for new treatment strategies for as-needed asthma therapies, focusing on the use of a single inhaler. There is also evidence that frequent use of SABA-only increases the risk of exacerbations instead of protecting patients from them, despite of short-term relief of asthma symptoms, leading even to death[2,3]. The combination of a fast-acting β_2-agonist and inhaled glucocorticoid on an as-needed basis — an anti-inflammatory reliever approach — has been proposed as a potential alternative strategy than SABA reliever alone[4-6]. Several multicenter randomized trials aimed to show the effectiveness of combination products (ICS-SABA/LABA) compared with SABA treatment, both used as needed.

Papi et al found that symptom-driven rescue use of a combination of ICS-SABA in a single inhaler for 6 months is equivalent to regular treatment with inhaled beclomethasone in controlling mild persistent asthma, suggesting that mild persistent asthma may only require as-needed use of an inhaled corticosteroid and an inhaled bronchodilator, rather than regular treatment with inhaled corticosteroids[7].

Budesonide-formoterol as needed in mild asthma was investigated in two double-blind randomized studies, SYGMA 1 and 2, comparing budesonide-formoterol as needed with budesonide plus SABA and SABA alone. SYGMA 1[8] showed that as-needed budesonide-formoterol (ICS-LABA) provided

superior asthma symptom control to as-needed SABA terbutaline, but with a slight superiority (34.4% vs 31.1% of electronically recorded weeks, OR 1.14, p=0.046 within the statistical significance limits). However, as-needed budesonide-formoterol, it was inferior to budesonide maintenance therapy in asthma control (34.4% vs 44.4%, OR 0.64, 95% CI 0.57-0.73). Regarding exacerbations, budesonide-formoterol showed superiority to as-needed terbutaline, while it had similar exacerbation rates with budesonide maintenance group. SYGMA 2[9] concluded that budesonide-formoterol as needed was non-inferior to twice daily budesonide with respect to the rate of severe asthma exacerbations but was inferior in symptom control. In the budesonide-formoterol as needed group patients had lower ICS exposure -approximately one quarter- than those in the budesonide maintenance group.

Another study, Novel START, complementary of SYGMA 1 and 2 tried to implement more real-life conditions and showed that in patients with mild asthma budesonide-formoterol as needed was superior to albuterol for the prevention of asthma exacerbations. However, regarding asthma control budesonide maintenance treatment group was superior to budesonide-formoterol as needed, a finding that favors this option in a patient whose asthma symptoms are the most bothersome[10].

A following study (PRACTICAL), which is a 52-week open label multicenter superiority trial examined as a primary outcome the number of severe asthma exacerbations per patient per year in two treatment groups: ICS-LABA as needed vs ICS maintenance. Severe exacerbations per patient per year were lower with as-needed budesonide-formoterol than with budesonide maintenance plus terbutaline as-needed, although the authors concluded that the study provided "modest" evidence for the superiority of budesonide-formoterol to the reduction of exacerbation rates[11].

When it comes to clinical practice, several factors such as patient preference, or the possibility of poor adherence should also be taken into consideration. It is common that patients are usually concerned about the adverse effects of ICS, even with low doses and the potential risks of treatment resulting in overreliance on SABAs and poor adherence to ICS maintenance treatment[6,12,13]. Even more common, an asthmatic with minor symptoms is vulnerable in stopping his regular treatment despite the doctor' s advice. In addition, although in mild asthma symptoms may be tolerable, airway inflammation usually exists and the risk for severe exacerbations still remains for these patients[14]. Another consideration is the treatment target: symptom control or reduction in the risk of exacerbations, an issue that poses again dilemmas about adherence and clinical status. The answer is to target both. Nevertheless, further studies are needed on this matter as all these studies still leave unanswered questions about the long-term impact of these strategies on airway inflammation, hyper-responsiveness, remodeling and asthma mortality compared with regular ICS usage[15,16].

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CONFLICTS OF INTEREST

No conflicts of interest to declare.

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