New Recommendations in the Treatment of Asthma?

¿Nuevas recomendaciones en el tratamiento del asma?

To the Editor:

In the brilliant 2009 Spanish guidelines for asthma management (GEMA) Long-Acting Beta-Agonists (LABA) are a first-choice medicine in step 3 asthma along with low dose Inhaled Corticosteroid (IC), for example up to 400 mcg/day of budesonide. Another option is to increase budesonide to a medium dosage, up to 800 mcg. The combination of LABA and CI is also the first choice treatment in step 4 treatment. With these guidelines in mind, I believe it is interesting to mention the recent appearance of two noteworthy articles on the role of LABA in the treatment of asthma.[1,2] The debate on the use of these drugs goes back to a long-running controversy that states that LABA are effective but doubts remain on the safety of their prolonged use. There are numerous studies on the efficacy of LABA on asthma that have highlighted the decrease of exacerbations in the course of asthma when LABA are added to IC treatment, without needing to increase the dosage of these steroids. However, the criticism of the definition of exacerbation as a decrease in peak flow and the concomitant use of rescue SABA (Short-Acting Beta-Agonists) in control groups mean that the overall results of these studies are, to say the least, misleading.[3] The problem arises when, over 50 years ago, the use of SABA was banned as a monotherapy in asthma. SABA caused more deaths because they led to a lack of control of this condition, as they hid bronchial inflammation and increased sensitivity to bronchoconstrictor stimuli. The physiopathological basis for this is in the adaptive response of the beta-adrenergic system to the repeated stimulation of the receptors, leading to desensitisation followed by a decrease in the receptor density as well as the gene expression of these receptors.[4] Furthermore, the regular use of beta-agonists increases bronchial hyperresponsiveness, even though it maintains some level of bronchodilation, which along with a long-term reduction in the response to rescue therapy with SABA, is the reason why they can make it harder to control asthma without any prior warning in the form of increased symptoms.[5] That is why LABA, which are basically longer-acting SABA, have also been banned as a monotherapy in persistent asthma and, according to recent large-scale studies, they have brought about a greater number of serious asthma attacks and more asthma-related deaths than in the group of asthmatics who do not use it. The meta-analysis on 19 double-blind and randomised studies on the effects of LABA published in 2006 on more than 33,000 asthmatics, including those belonging to the SMART study, proved that the group that used LABA had an increase in exacerbations that needed hospitalisation compared to the placebo group. They had an absolute increase in hospitalisations of 0.7%, and an increase in the risk of asthma-related death from 0.6% to 0.7%. This means approximately one death per 1000 patients/year of use.[6] The Afro-American population and the group who used LABA versus placebo were the highest-risk subgroups.

The Food and Drug Administration[1] published in the New England Journal of Medicine the recommendations that were adopted in February 2010 stating that LABA must remain as an asthma treatment, but only when asthma cannot be controlled with IC. It also stated that long-term use of LABA should be prescribed only when strictly necessary. Therefore, although in step 3 and 4 the GEMA recommend low or medium dose IC plus LABA as first choice treatment for asthma, and medium dose IC on its own or with antileukotrienes as an alternative treatment, it may be advisable to swap them around and give preference to IC. Also, if the control of asthma is understood as the degree to which the symptoms are minimised in relation to the medication applied, the question is, could IC be administered in even higher doses before having to choose LABA as an additional alternative – never as a monotherapy – alongside IC? The debate goes on.

References

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Adalberto Pacheco-Galván

Unidad de Asma y Tos de Difícil Manejo, Servicio de Neumología, Hospital Ramón y Cajal, Madrid, Spain

E-mail address: apacheco.hrc@salud.madrid.org