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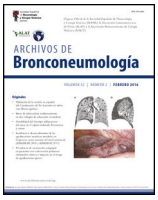

Letter to the Editor

Discrepancies Between GEMA and GINA in the Classification of Inhaled Corticosteroids☆

Discrepancias en la clasificación de los glucocorticoides inhalados entre GEMA y GINA

To the Editor,

We read with interest the letter signed by Doctors Entrenas-Costa and Entrenas-Castillo[1] in which they suggest that the classification of the dose of 100 μg of fluticasone furoate (FF) once a day (OD) that appears in the GEMA guidelines as medium dose[2] should be "corrected" and classified in line with the GINA guidelines as low dose.[1]

GEMA is a clinical practice guideline drawn up by independent experts from 15 different scientific societies.[2] The classification of 100 μg FF OD as a medium dose is evidence-based and consistent with the approved Summary of Product Characteristics (SPC) for FF[3] and with the classifications of other relevant international guidelines, such as SIGN 158 in the UK and the Australian Asthma Handbook. Few direct comparisons are available with FF and other inhaled glucocorticoids, particularly at low doses, so it is difficult to establish the exact equipotent dose (equivalent in efficacy and safety) of FF. According to the SPC, a daily dose of 100 μg of FF in asthma is approximately equivalent to 250 μg of fluticasone propionate (FP) twice a day (BID, medium dose), while 200 μg FF OD is approximately equivalent to 500 μg FP BID (high dose).[3] A low dose of FF is not approved in asthma. Evidence of efficacy and safety with 50 μg of FF OD in mild-moderate asthma is low and inconsistent, although at least one of the published studies indicates greater efficacy than placebo and approximately similar efficacy to that of low-dose FP (100 μg BID) in mild asthma.[4]

With regard to safety, the authors comment that the dose of 100 μg FF does not suppress cortisol, based on a pharmacokinetic/pharmacodynamic model and limited data from a 6-week study.[1] However, in a 52-week study of 503 adults and adolescents with asthma specifically designed to assess safety, 24-h urinary cortisol excretion at the medium dose of 100 μg FF OD was similar to that obtained at the high dose of 500 μg FP BID after 1 year of treatment, and about 10% of patients treated with 100 μg FF had persistently low urinary cortisol levels (<40 nmol/24 h) during treatment.[5] All inhaled glucocorticoids present a risk of systemic (e.g. pneumonia, cortico-adrenal axis suppression, osteoporosis, glaucoma, etc.) and local (candidiasis, etc.) adverse effects, all of which are dose-dependent.

As a result, until new data become available, we believe that the classification of 100 μg FF as a medium dose is the most correct and prudent option. Treatment for asthma maintenance should be administered at the minimum dose required to maintain disease control[2] in order to minimize the risk of adverse effects.

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Response to the GEMA Executive Committee☆

Respuesta al Comité ejecutivo de GEMA

Dear Editor,

We thank the GEMA Executive Committee for their comments on our letter on discrepancies in the classification of inhaled glucocorticoids (IGC) between the GEMA and GINA classifications.[1] As they point out, clinical practice guideline recommendations must be based on solid evidence, something that is lacking in this particular area. GEMA's positioning is therefore in line with the indications of the Summary of Product Characteristics and the therapeutic positioning report recently published by the AEMPS.[2]

In their argument in favor of classifying a dose of 100 μg/24 h fluticasone furoate (FF) as medium, they cite the 2 papers that constitute the few references that compare ICGs in terms of equipotency. In the Bateman study,[3] different doses of FF versus fluticasone propionate (FP) 100 μg/12 h (low dose) were compared over a period of 8 weeks. The dose of FF 100 μg/24 h was not inferior that of FP 100 μg/12 h in terms of FEV_1, and did not produce a significant decrease in cortisol. The study of Busse et al.,[4] specifically designed to assess safety at 52 weeks, showed that urinary cortisol values for FF 100 μg/24 h were normal for 90% of patients at baseline. Throughout the study, urinary cortisol at all visits was normal in 72% of cases, low in 10%, and high in 17%.

GEMA positioning on the medium dose is consistent with most clinical practice guidelines. However, an example of the difficulty that persists in establishing the exact equipotent dose of FF is that the UK guidelines (SIGN 158),[5] published by the British Thoracic Society (BTS), use 3 categories (low, medium and high dose) to classify ICG. Specifically, they situate FF/vilanterol 100 μg/24 h in the medium dose section, while simultaneously including it in half of the low-dose step. The BTS standpoint is a very good reflection of the limitations we still encounter in establishing the exact equipotent dose of FF.

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