

Correspondence

Asthma control differences between inhaled corticosteroids likely related to differences in patient severity

To the Editor:

Price et al¹ used a retrospective observational cohort study to assess prescribing of hydrofluoroalkane-beclomethasone (BDP) and fluticasone propionate (FP) on asthma control and exacerbations using the General Practice Research Database from approximately 500 United Kingdom primary care practices. They concluded that patients prescribed BDP had a similar or better likelihood of achieving asthma control at equivalent or lower dose than FP.

There are methodologic challenges in using observational studies to test for clinical differences between treatments. A major concern is selection bias caused by confounding by severity or indication.^{2,3} The authors used a pharmacoepidemiologic technique of selecting cohorts by matching on baseline characteristics that included oral corticosteroid prescriptions, average short-acting β -agonist daily dose, and for the step-up population, average daily inhaled corticosteroid (ICS) dose. Although the groups were well matched at baseline, approximately 85% of subjects had no oral corticosteroid use, almost 50% of initial ICS users had no short-acting β -agonist use, and 75% of the step-up patients were on 0 to 99 $\mu\text{g}/\text{d}$ ICS, which does not appear consistent with justification of changes in maintenance treatment according to asthma treatment guidelines.⁴ The decision to start patients on ICS or increase the ICS dose may have occurred because of additional clinical data of which the physician was aware but which may not have been coded from text notes in the General Practice Research Database or included in this analysis. Information such as the short-acting β -agonist to ICS prescriptions ratio, changes in patterns of short-acting β -agonist prescriptions, lung function, and unscheduled general practitioner visits or emergency department encounters are often used to further describe asthma control but were not included in this study.

These data illustrate that confounding by severity appears likely, and disease severity differed at baseline in that an ICS dose ≥ 400 $\mu\text{g}/\text{d}$ was noted for 41% of FP subjects versus only 16% for BDP (Fig 1, A) and 77% versus 62% in the step-up group (Fig 1, B). Unfortunately, this difference in severity was not accounted for in the analysis. If the patients were, in fact, well matched for disease severity, one would have expected similar baseline ICS doses and not the variance observed between FP and BDP. Despite these differences in baseline ICS use, the authors claim

that the treatment groups were similar in observable variables and thus had similar asthma severity. Physicians may prescribe higher ICS doses to more severe patients per guidelines,⁴ so the outcomes of interest may have been more related to differences in asthma severity and not treatment.

To mitigate potential bias, the authors could have either matched cohorts on an equal baseline ICS dose or conducted a stratified analysis by baseline ICS dose to see whether an effect was observed when comparisons were made within more homogeneous subgroups. These additional analyses would have provided more information about the robustness of any overall association observed. Considering these results are not consistent with clinical trials comparing equivalent doses of BDP with FP that have shown similar asthma control and FEV₁ improvements, we cannot rule out confounding by severity as a possible explanation for the association reported in this retrospective analysis.⁵⁻⁷

Richard H. Stanford, PharmD, MS

Steven W. Yancey, MS

David A. Stempel, MD

From GlaxoSmithKline, Research Triangle Park, NC. E-mail: richard.h.stanford@gsk.com.

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