

SHORT REPORT

Does use of a corticosteroid/long-acting beta-agonist combination inhaler increase adherence to inhaled corticosteroids?

Jay Foden^a, *Christopher H Hand^b

^a Final year medical student, School of Medicine, Health Policy and Practice, University of East Anglia, Norwich, UK

^b Honorary Professor, School of Medicine, Health Policy and Practice, University of East Anglia, Norwich, UK

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Summary

This 12-month retrospective pilot study analysed prescription data of 82 patients with asthma from six practices in Norfolk. Patients on an inhaled corticosteroid/long-acting beta-agonist combination inhaler had significantly greater adherence to inhaled corticosteroids compared to those on a corticosteroid inhaler alone (72.2% versus 40.5%, $p=0.001$).

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Introduction

Patients who adhere to treatment with inhaled corticosteroids (ICS) have reduced rates of asthma-related morbidity and mortality.¹ There is evidence to suggest that when taken together, a long-acting beta-agonist (LABA) improves the penetration of ICS into the lung cell.² Guideline-defined asthma control can be achieved using a combination inhaler containing fluticasone and salmeterol, and this is more effective than using fluticasone alone.³ However, the literature comparing patient adherence with combination ICS/LABA inhalers versus separate ICS inhalers is limited.

This pilot study set out to explore whether use of combination ICS/LABA inhalers is associated with increased adherence to ICS treatment compared to treatment with ICS inhalers alone.

Methods

The patients were from six general practices in Norfolk, aged from 18 to 45, and had used either an ICS/LABA combination inhaler or an ICS inhaler for the whole of the study period. The patients were told that the study was retrospective and that the number of inhalers prescribed over the last 12 months would be extracted from their medical record. They

were also told that their prescription data would not be discussed with either their general practitioner (GP) or the practice nurse. Patients were excluded if: they were in long-stay residential homes or hospitals during the time period being studied; they had a diagnosis of chronic obstructive pulmonary disease, bronchiectasis or cystic fibrosis; they were taking oral steroids (except rescue courses of which they should have required less than six); or if they had required a change in the type of medications required in the study period (though patients or stepping up stepping down their treatment were included).

The numbers of each inhaler ordered multiplied by the number of inhalations per inhaler was taken as the number of inhalations taken per year. Adherence was calculated by dividing the number of inhalations taken per year by the number of inhalations prescribed per year and expressed as a percentage. Where patients had been prescribed both types of inhaler, they were allocated to the ICS/LABA group.

Nonparametric data were compared with the Mann Whitney test. Univariable and multivariable regression were used to explore potentially confounding variables relating to adherence. StatsDirect was used for the statistical analyses.

* Corresponding author: Professor Christopher Hand, School of Medicine, Health Policy and Practice, University of East Anglia, Norwich, NR4 7TJ, UK. Tel: +44 (0)1603 591226 Fax: +44 (0)1603 593752 E-mail: c.hand@uea.ac.uk

Table 1. Characteristics of subjects.

	ICS/LABA	ICS
N	25	57
Median age (IQR)	40 (36 to 42)	33 (26 to 40)
Gender, % female	62.5	63.8
Inhalers		
Seretide	21	
Symbicort	4	
Beclomethasone		51
Fluticasone		5
Budesonide		1
Adherence % (IQR)	72.2 (54.8 to 98.6)	40.5 (27.4 to 82.2)
Median SABA use (IQR)	3 (2 to 7)	4 (2 to 6)

ICS/LABA = Inhaled corticosteroid/long-acting beta-agonist combined inhaler; ICS = Inhaled corticosteroid inhaler; IQR = Interquartile range; SABA = Short-acting beta-agonist inhaler

The study was approved by the Norfolk Research Ethics Committee.

Results

There were 664 eligible patients of whom 110 (16.6%) consented. Ten sets of data were incomplete, seven patients had changed the type of medication during the study period, in 10 patients the prescribed ICS dose was not clear, and one patient did not collect any inhalers in the study period. This left 82 participants (52 female and 30 male, median age 36.5) of whom 25 (30.5%) were on ICS/LABA inhalers and 57 (69.5%) on ICS inhalers alone (Table 1).

Patients on ICS/LABA inhalers had significantly greater adherence compared to those on ICS inhalers (72.2% versus 40.5%, $p=0.001$). This is equivalent to 2.3 inhalations/day and 1.1 inhalation/day respectively. Older patients were more likely to be on an ICS/LABA inhaler (median age 40 versus 33, $p=0.006$); they also had greater adherence but this was not statistically significant (65.8% versus 41.1%, $p=0.17$). There were no significant gender differences.

Although patients using ICS inhalers ordered more short-acting beta-agonist (SABA) inhalers (4 versus 3), this was not statistically significant. There were no age or gender differences in the collection of SABA inhalers.

Univariable and multivariable regression analysis showed that both the use of ICS/LABA inhalers and the number of SABA inhalers predicted adherence to ICS but that age and gender did not. Use of an ICS/LABA inhaler increased adherence by 30.83% (95% CI 22.98 to 50.37, $p=0.001$). For each additional SABA inhaler used adherence increased by 3.05% (1.35 to 4.75, $p=0.0006$).

Discussion

Although there is some evidence on adherence in relation to

ICS/LABA inhalers from north America,⁴ this is the first UK primary care study. The low response rate (one in six) clearly limits the generalisability of this study. However, the results are highly significant both statistically and clinically. Patients taking one inhalation/day of their ICS inhaler are very unlikely to achieve adequate symptom control.

Using prescription collection as a proxy for adherence – given the very low response rate – is likely to overestimate adherence. The ICS/LABA combination inhalers were mostly Accuhalers or Turbohalers, and the ICS inhalers were mostly pressurised metered-dose inhalers (MDIs). It is likely that any bias is likely to apply to both types of inhaler but this cannot be assumed. However, those patients prescribed both ICS and ICS/LABA inhalers were allocated to the ICS/LABA group, which would reduce any difference that was found. Although some possible confounders were explored, others such as steroid dose, severity, number of exacerbations, and duration of asthma therapy, were not.

Why should there be a difference? Patients experience some symptomatic relief taking a LABA, and this is partly supported by patients on ICS/LABA inhalers ordering fewer SABA inhalers. A larger study with a higher response rate is needed to confirm this. Better immediate symptom control may reinforce the need to take this inhaler, whereas for ICS inhalers no relief is experienced, any beneficial effect takes time to appear, and when the inhaler is stopped it takes time to wear off. The strong independent relationship of SABA inhaler use with adherence is worth exploring further.

What are the implications of this study? ICS/LABA inhalers may be considered for patients with poor asthma control whose adherence to ICS inhalers is poor (i.e. less than 2 inhalations/day). Whether such an approach is more cost-effective than using ICS and LABA inhalers separately remains to be seen.

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Conflict of interest

None declared.

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