Respiratory Medicine 111 (2016) 1–7

Contents lists available at ScienceDirect

Respiratory Medicine

journal homepage: www.elsevier.com/locate/rmed

Review article

Achieving asthma control with ICS/LABA: A review of strategies for asthma management and prevention

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ARTICLE INFO

Article history:
Received 22 June 2015
Accepted 2 November 2015
Available online 6 November 2015

Keywords:
Asthma
Beclometasone
Budesonide
Formoterol
ICS/LABA
Maintenance and reliever therapy

ABSTRACT

Maintenance treatment with an inhaled corticosteroid (ICS) and a long-acting β_2-agonist (LABA) is recommended for patients whose asthma is not controlled with a low-to-moderate dose of ICS alone; a separate reliever medication is used on an as-needed basis. The Gaining Optimal Asthma ControL (GOAL) study demonstrated that salmeterol/fluticasone maintenance treatment can improve asthma control and reduce future risk compared with fluticasone alone, although the dose escalation design of this study meant that most patients treated with salmeterol/fluticasone were receiving the highest dose of ICS at the end of the study. Similarly, budesonide/formoterol maintenance therapy improved asthma control and reduced future risk compared with budesonide alone in the Formoterol and Corticosteroids Establishing Therapy (FACET) study. An alternative approach to asthma management is to use an ICS/LABA for both maintenance and reliever therapy. A large body of clinical evidence has shown that the use of budesonide/formoterol in this way improves both current control and reduces future risk compared with ICS/LABA plus as-needed short-acting β_2-agonist (SABA), even when patients receive lower maintenance doses of ICS as part of the maintenance and reliever therapy regimen. In addition, one study has shown that beclometasone/formoterol maintenance and reliever therapy reduces exacerbations more effectively than beclometasone/formoterol plus as-needed SABA. The use of ICS/LABA as both maintenance and reliever therapy ensures that an increase in reliever use in response to worsening symptoms is automatically matched by an increase in ICS.

Contents

Abbreviations: ACQ, Asthma Control Questionnaire; bd, twice-daily; CI, confidence interval; FACET, Formoterol and Corticosteroids Establishing Therapy; GINA, Global Initiative for Asthma; GOAL, Gaining Optimal Asthma ControL; HR, hazard ratio; ICS, inhaled corticosteroid; LABA, long-acting β_2-agonist; SABA, short-acting β_2-agonist.

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http://dx.doi.org/10.1016/j.rmed.2015.11.002

1. Introduction

Asthma is a major public health problem worldwide, which, when uncontrolled, can severely limit the patient's daily life [1]. The primary aim of treatment is to achieve and maintain overall asthma control by reducing the severity of current symptoms and minimising future risk [1,2]. Current control is characterised by the frequency of symptoms, use of reliever medication, lung function and physical activity limitation. Future risk includes longer-term factors such as the frequency of exacerbations, decline in lung function over time and adverse effects of treatment [1,2].

Maintenance treatment with an ICS and a LABA, either separately or as a fixed-dose formulation, is recommended for patients whose asthma is not adequately controlled when treated with a low-to-moderate dose of ICS alone; a separate reliever inhaler is used on an as-needed basis [1]. Many different ICS/LABA fixed-dose combinations are available for use in patients with asthma. For example, budesonide/formoterol and salmeterol/fluticasone propionate (from herein referred to as fluticasone) have been available for many years and their efficacy in patients with asthma has been demonstrated in several large-scale randomised trials [3,4]. More recently, beclometasone/formoterol, fluticasone/formoterol and vilanterol/fluticasone furoate have been approved for use in adult patients with asthma [5–9]. Mometasone/formoterol is also available in the USA [10].

An alternative approach to the management of asthma is to use budesonide/formoterol or beclometasone/formoterol as both maintenance and reliever therapy, providing patients with a simplified treatment regimen that requires only a single inhaler. By employing this treatment strategy, patients receive ICS in addition to a fast-acting bronchodilator whenever they require reliever medication, meaning that inflammation can be targeted when symptoms increase [11]. This approach has shown utility in the management of asthma [12–19], and is recommended by GINA and approved for use in Europe and a number of other countries around the world [1].

In this article, the role of ICS/LABA in the management of asthma will be reviewed, considering both current control and future risk. We will summarise results from the landmark GOAL and FACET studies, which demonstrated the advantages of adding a LABA to an ICS by comparing salmeterol/fluticasone or budesonide/formoterol with ICS alone [3,4]. We will then explain how data from the budesonide/formoterol and beclometasone/formoterol maintenance and reliever therapy studies [12–17,19], in particular, expand upon the findings of both GOAL and FACET.

2. Achieving current control and reducing future risk: the ICS/LABA approach

In patients whose asthma is not well controlled with a low dose of ICS, there are two possible strategies that can be used to improve control: increasing the dose of ICS or adding a LABA [1]. However, concern has been expressed that the addition of a LABA to a low dose of ICS may enhance current control but mask inflammation, therefore increasing future risk [20,21].

In the FACET study, patients who had stable asthma after a run-in period were randomised to receive budesonide (at a low or high dose) in combination with either formoterol or placebo (Table 1) [3]. Patients were eligible for inclusion if they had been diagnosed with asthma for at least six months and had been treated with an ICS for at least three months, although patients receiving high doses of ICS at baseline were excluded. The addition of formoterol to budesonide enhanced current control compared with an increased dose of budesonide. Indeed, the addition of formoterol to budesonide was associated with a significantly higher number of episode-free days and greater improvements in day and night-time symptom scores compared with the same dose of budesonide alone ($p = 0.001$). While the mean number of episode-free days was significantly increased with the addition of formoterol 12 μg to twice-daily budesonide 100 μg (metered dose), there was no significant increase with twice-daily budesonide 400 μg alone (Fig. 1A). In contrast, although the addition of formoterol to a low dose of budesonide decreased future risk by reducing the rate of severe exacerbations by 26%, a greater reduction was achieved

Table 1
Overview of study design and patient numbers in the FACET [3] and GOAL [4] studies.

Parameter	FACET [3]	GOAL [4]
Patients, n	852	3039[a]/2890[b]
Run-in period		
Treatment received	BUD 800 μg	Usual dose (if any) of ICS
Duration, weeks	4	4
Study duration, months	12	12
Study interventions[c]	1. BUD 100 μg + placebo 2. BUD 100 μg + FORM 12 μg 3. BUD 400 μg + placebo 4. BUD 400 μg + FORM 12 μg	1. FLU (100, 250 or 500 μg) 2. SAL/FLU (50/100, 50/250 or 50/500 μg)
Dosing frequency	Twice daily	Twice daily

All BUD and FORM doses are shown as metered dose.
BUD, budesonide; FACET, Formoterol and Corticosteroids Establishing Therapy; FLU, fluticasone; FORM, formoterol; GOAL, Gaining Optimal Asthma ControL; ICS, inhaled corticosteroid; SAL, salmeterol.
[a] Completed phase 1: dose escalation phase in which treatment was stepped up every 12 weeks until total asthma control was achieved or highest dose of study drug reached (SAL/FLU 50/500 μg or FLU 500 μg bd).
[b] Completed phase 2: remained on dose at which they achieved total asthma control or the maximum dose of study medication until the end of the 12-month double-blind treatment period.
[c] Patients were randomised to one of the treatment arms.