



The application of budesonide/formoterol (Symbicort®) adjustable maintenance dosing to real-life clinical practice

J. HAUGHNEY¹, M.R. SEARS²

Department of General Practice and Primary Care,¹ University of Aberdeen, Aberdeen, Scotland; UK, Department of Medicine,² Firestone Institute for Respiratory Health, McMaster University, Hamilton, Ontario, Canada

SUMMARY

Despite effective drugs and devices, optimal asthma control is rarely achieved long term. Clinicians should consider both the therapies and management strategies employed. Adjustable maintenance dosing, where patients step-up or step-down their medication depending on symptom level, has been proposed to improve asthma control in a real-life setting. To implement adjustable maintenance dosing, patients require a Personalised Asthma Action Plan, detailing instructions agreed between patient and clinician on how they should adjust their dose in line with asthma variations to prevent deterioration in control.

Several factors are necessary to achieve a clinician-agreed and supported patient-adjusted management strategy: effective therapy; patient willingness to participate in their action plan, which should not be over-complicated to follow; adequate physician time for patient education about their disease and action plan. Results from eight studies have shown that adjustable maintenance dosing is practical and results in equal or better control with less medication use and lower costs than fixed dosing.

Keywords: Real-life; budesonide/formoterol; asthma; adjustable maintenance dosing

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INTRODUCTION

Adjustable maintenance dosing, where patients step their medication up or down depending on their level of symptoms, with budesonide/formoterol in a single inhaler has been studied in over 10,000 asthma patients in eight studies as part of the Symbicort® adjustable maintenance dosing (SAMD) programme. Several advantages over fixed dosing, an established therapy in the management of asthma, have been observed namely, improved asthma control, maintenance of a high health-related quality of life (HRQL) with a lower drug load and reduced costs associated with a lower effective dose of medication (1–3).

Adding a long-acting β_2 -agonist to inhaled corticosteroids, e.g. formoterol to budesonide, is well recognised as an effective and well-tolerated treatment for persistent asthma (4–7). Convenience is improved when a single inhaler containing both drugs is used (8). The use of budesonide/formoterol in a single inhaler (Symbicort) allows patients to adjust both their inhaled corticosteroids and long-acting β_2 -agonist in

accordance with their symptoms, which in conjunction with a Personalised Asthma Action Plan (PAAP) – written instructions about treatment adjustments for patients to follow when their asthma symptoms vary – may help improve overall asthma management. As discussed in detail elsewhere in the supplement (9), it is the unique pharmacological profile of formoterol that makes budesonide/formoterol in a single inhaler the only currently available medication able to be considered for an adjustable maintenance dosing regimen for patients requiring both an inhaled corticosteroid and long-acting β_2 -agonist. The severity of asthma is known to vary and the aim of this approach to treating asthma is to maximise control, while minimising medication use, by adjusting the dose quickly in response to variations in symptoms.

The objective of this supplement is to explore why adjustable maintenance dosing may be more appropriate for some patients in a real-life setting than traditional fixed-dosing regimens.

ACHIEVING GUIDED SELF-MANAGEMENT

The principal objective in the management of asthma is to gain and maintain control. Guidelines (6,7) assist physicians in making choices when treating an asthma patient. However, even with asthma guidelines available, current levels of asthma control are unsatisfactory and improvements are necessary (10).

Correspondence to:

J. Haughney, Department of General Practice and Primary Care, Foresterhill Health Centre, University of Aberdeen, Westburn Road, Aberdeen AB25 2AY, UK
Tel.: +44-1224-553972
Fax: +44-1224-550683
Email: j.haughney@abdn.ac.uk

Effective asthma treatments alone may not be sufficient to achieve optimal control. Guidelines advocate the use of written management plans to facilitate the treatment of asthma (6,7). With appropriate treatments, selected on review of patients' severity of asthma, each patient is offered a written PAAP that gives instructions on appropriate action to take when their symptoms change as a result of the variability of their asthma. For a symptom-driven PAAP to facilitate asthma management, patients must be able to recognise a deterioration in their asthma control. Education about patients' interpretation of key symptoms is often useful. However, some patients with asthma are poor perceivers of control (11) and would not benefit from a symptom-driven PAAP, a strategy that may even be detrimental to the health of these patients. In such cases, objective measurements, such as changes in peak expiratory flow (PEF), would be beneficial. Physicians play a major role in the success of these management plans by educating the patient as to the best approach in treating their asthma. Table 1 (12) illustrates key skills that patients need to learn from their physician or from another healthcare professional. Physician-led patient education and the use of written action plans are known to improve asthma control (13–17). Furthermore, the implementation of written action plans with appropriate medication has been shown to reduce the risk of death from asthma (18).

While action plans are a critical component of guidelines, with strong advocacy for their use and clinical benefit in asthma treatment (13), many patients are not provided with them and their use continues to be limited (19,20). Perceived lack of clinician time for education, fear of loss of control by clinicians, fear of abandonment by patients, poor patient understanding or perception of symptoms and lack of education about asthma are likely factors. The complexity of treatment and PAAPs may also be responsible. Adding complexity to treatment regimens is known to adversely affect adherence (21,22). Simplification of treatment regimens and clearly constructed PAAPs, which are easy to follow and understand, are key to assisting patients in controlling

their asthma. Measures that reduce the complexity of asthma management should make it easier for physicians to communicate the instructions for asthma management to their patients.

The physician–patient partnership, based on mutual trust and respect including regular review and reinforcement (23), is likely to improve adherence and may be as important in long-term management as drug selection. Each asthma consultation is an opportunity for physicians to build on this partnership and further enhance the knowledge and skills of patients. Clear communication between physicians and patients is crucial to meet patients' information needs, which should facilitate adherence. However, individual personalities impact on adherence and the success of asthma management (24) as patients may amend their own treatment plans to suit their needs, often as a consequence of their own experiences with asthma (25). Although it is difficult to control patient adherence, physicians need to be aware of factors that may influence patient decisions towards treatment and adapt individual patient's PAAPs and aspects of education accordingly. As the aim of asthma management is to give patients the ability to control their own condition under the guidance of their physician, it is clear that the patient–physician relationship is extremely important in sustaining long-term adherence.

We need to be realistic in our approach to asthma management using currently available medications to their full potential. Successful guided self-management can only be achieved if: patients are willing to participate in their own PAAP, PAAPs are not too complicated for the patient to follow, physicians provide enough time to educate the patient about their disease and PAAP. The variable nature of asthma means that symptoms, lung function and other characteristics are often changing, requiring adjustments to treatment. Changing medication dose as part of a PAAP is potentially a complicated process if patients need to change or increase a number of inhalers to regain control of their asthma. In patients requiring both an inhaled corticosteroid and long-acting β_2 -agonist, a novel approach to overcome

Table 1 Self-management skills required for successful treatment (12). Reproduced with kind permission from the BMJ Publishing Group

Patients should:

Accept that asthma is long-term and treatable disease
Be able to accurately describe asthma and its treatment
Actively participate in the control and management of their asthma
Identify factors that make their asthma worse
Be able to describe strategies for avoidance or reduction of exacerbating factors
Recognise the signs and symptoms of worsening asthma
Follow a personalised written treatment plan
Use correct technique for taking drugs, including inhalants by metered-dose inhalers, dry-powder inhalers, diskhalers, spacers or nebulisers
Take appropriate action to prevent and treat symptoms in different situations
Use medical resources appropriately for routine and acute care
Monitor symptoms and objective measures of asthma control
Identify barriers to compliance (adherence) to the treatment plan
Address specific problems that have an impact on their individual condition

this problem is adjustable maintenance therapy using a single inhaler. The only currently available treatment suitable for such a flexible approach, where the patient can adjust their treatment in line with changing symptoms from a single inhaler, is budesonide/formoterol.

THE SAMD STUDIES – DESIGNED TO REFLECT REAL LIFE

Adjustable maintenance dosing with budesonide/formoterol in a single inhaler (Symbicort) has been studied in over 10,000 adult patients with asthma, recruited into eight studies in Europe and Canada as part of the SAMD clinical study programme (9). The results from SAMD indicate that adjustable maintenance dosing with budesonide/formoterol in a single inhaler is effective and well tolerated, maintains HRQL and is cost-effective for treating asthma compared with fixed dosing (1–3). The SAMD programme is the first to examine the use of budesonide/formoterol in a single inhaler as part of a PAAP.

All studies in the SAMD programme were conducted in a real-life setting with broad entry criteria and relatively few practice visits to emulate as natural a setting as possible. The studies were open label, and as physicians and patients were aware of patients' dose, they could effectively manage step-ups or step-downs in dose. A criticism of open design is that it may influence perception of treatment efficacy. However, the alternative, i.e. a controlled, double-blinded, clinical trial, could not have reflected real-life practice, as it would have introduced unnecessary complexity (several blinded inhalers rather than a single inhaler) with the potential of compromising patient outcomes and adherence. In addition, the main focus of these studies was not to determine the efficacy of budesonide/formoterol in a single inhaler, as this has already been established. The principal aim was to investigate both the pharmacological impact of short-term dose adjustment and the concept of patient-instigated adjustable maintenance dosing, using a long-acting β_2 -agonist and a corticosteroid in a single inhaler, in a variety of patient groups and healthcare models. A double-blind, double-dummy approach would have been inappropriate.

Each study in the programme had broad inclusion criteria in an attempt to mirror the real-life consulting room situation. Flexibility in the SAMD programme, in terms of the components of the PAAP (symptoms and lung-function measurements used) and study design, acknowledged country-specific differences in healthcare systems, which aimed to reflect real-life practice in each country. As these were clinical studies, instructions for dose adjustments were rigid (rather than individualised for each patient) to enable comparisons to be drawn from the results from each of the studies. By definition, PAAPs are personalised and, in real-life, instructions should not only be clear and easy to follow but also tailored to the individual patient.

In the SAMD studies, variables such as exacerbations, asthma severity, HRQL, and asthma-free days were examined. Adjustable maintenance dosing with budesonide/formoterol, as part of a PAAP, was found to be as effective as or better than fixed dosing with an overall lower drug usage at a lower cost (1–3). These positive results for adjustable maintenance dosing suggest that a flexible approach to therapy may become the preferred option in asthma management in a real-life situation.

SAMD AND PAAP – A GOOD PARTNERSHIP?

Budesonide/formoterol adjustable maintenance dosing allows patients to increase the dose of medication at the onset of symptom worsening as a strategy to prevent exacerbations. Budesonide/formoterol in a single inhaler is the only current treatment suitable for adjustable maintenance dosing in patients requiring both an inhaled corticosteroid and long-acting β_2 -agonist, as the dose–response profiles of the monocomponents are favourable for this flexible approach (9).

Increasing the dose of inhaled corticosteroids 5-fold at times of asthma worsening is effective in preventing exacerbations (26). In a comparison of physician-managed and guided self-managed treatment, patients prescribed variable doses of budesonide, based on PEF measurements, showed improvements in asthma control, including reduced sleep disturbance and improved symptoms and activity scores, compared with baseline (27). These two studies and the SAMD studies support a flexible approach to asthma management, allowing patients to take less medication overall, but with equal or improved efficacy by adjusting their medication dose depending on symptoms.

Adjustable maintenance dosing with a PAAP is a pragmatic approach that provides a simple and practical way for patients to take their medication in a tailored fashion with the benefit of improving asthma control at an overall lower drug load and reducing costs. With patients following their symptom-guided PAAP and adjusting their dose appropriately, it would be no surprise to see a reduction in the number of additional clinic visits, further reducing costs. Adjustable maintenance dosing with a PAAP seems a logical step towards optimising therapy with an established, effective treatment and ensures that each patient receives structured treatment according to individual need. Indeed, this approach offers additional choice in asthma management, and many patients may opt for greater involvement and contribution to their medical care, particularly as SAMD may offer greater patient enablement over fixed-dosing strategies (28). Furthermore, the physician guiding the patient through their management plan should help build a strong patient–physician relationships, leading to better adherence to treatment.

CONCLUSIONS

Used together for maintenance therapy, inhaled corticosteroids and long-acting β_2 -agonists, such as budesonide/formoterol, provide a preferable alternative to increasing corticosteroid dose in patients who are uncontrolled with standard doses of corticosteroids alone (6,7). The use of adjustable doses of an inhaled corticosteroid and a long-acting β_2 -agonist in a single inhaler can assist self-management by providing a simple and convenient means for patients to modify their dose of maintenance medication.

Adjustable maintenance dosing with budesonide/formoterol in a single inhaler, using a PAAP, provides equally effective asthma control and maintains HRQL compared with fixed dosing. All these benefits were achieved at a lower overall drug load and reduced costs. The robustness of these SAMD studies is emphasised as the programme involved over 10,000 patients from several different countries and included variations in action plans and study design to reflect usual clinical practice in those countries. Furthermore, the majority of SAMD study centres were not research aware, indicating that adjustable maintenance dosing with budesonide/formoterol is applicable in real-life practices. To lend additional support to these naturalistic studies, further long-term research is required to explore the role and dosing of adjustable maintenance treatment with budesonide/formoterol and effects on airway inflammation, remodelling and other long-term asthma outcomes.

Adjustable maintenance dosing with budesonide/formoterol offers a simple, yet effective, approach to the treatment of asthma that may have substantial benefits for disease control if implemented correctly. Furthermore, it reflects the real-life consulting room situation with adjustments made in patients' medication levels depending on the current status of their asthma. This strategy has many benefits; namely, improving patient knowledge of their disease, patient involvement in the day-to-day management of their disease, maximising control of asthma in a flexible manner and minimising daily medications. Co-operation between patients and physicians is crucial if such programmes are to have a significant impact on the overall control of asthma.

In summary, the SAMD studies showed that adjustable maintenance dosing is practical and results in equal or better asthma control with less medication use. This is achieved at a lower overall cost than fixed dosing, suggesting that adjustable maintenance dosing is the preferred option in asthma management.

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