

BEING FAMILIAR WITH THE NEW GUIDELINES IN PRACTICE: WHAT DOES ASTHMA MANAGEMENT LOOK LIKE IN 2021?

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ABSTRACT

In Singapore, 10.5 percent of adults aged between 18 and 69 years are affected by asthma. Suboptimal asthma control imposes a significant burden on healthcare systems and society. Short-acting beta-agonists (SABA) monotherapy had been the standard asthma treatment for many years in patients with mild asthma symptoms. However, according to current guidelines and new recommendations, SABAs are no longer recommended as the preferred reliever for patients when they are symptomatic and should not be used as monotherapy due to significant safety concerns and poor outcomes. In this article, we will review the current guideline recommendations and accompanying evidence for the treatment and management of asthma in clinical practice.

Keywords: asthma, inhaled corticosteroid, short-acting beta-2 agonist, asthma control

SFP2021; 47(7) : 6-8

THE BURDEN OF ASTHMA IN SINGAPORE

Asthma is a chronic inflammatory disorder of the airways characterised by inflammation and constriction of the air passages.¹ Globally, asthma affects 334 million patients of all age groups and is one of the most common chronic respiratory diseases seen in Singapore's primary care.^{2,3}

10.5 percent of Singaporean adults aged between 18 and 69 years are affected by asthma.³ Patients with asthma often require long-term medical treatment of their condition and may occasionally seek emergency rescue therapy at acute healthcare facilities or be hospitalised during exacerbations.³ Poor asthma control and high exacerbation rates result in a high percentage of patients missing work or school. The Asthma Insight and Management (AIM) survey reported 48 percent of patients aged 12 years and older in Singapore having missed work or school on an average of 7.7 days due to asthma in the past year.⁴

Poorly controlled asthma imposes a significant economic burden. A recent cross-sectional online survey was administered to Singapore residents to quantify the economic burden of asthma in Singapore by the level of symptom control. The total annual cost of adult and childhood asthma in Singapore was estimated to be SGD 1.74 billion (US\$1.25 billion) and SGD 0.35 billion (US\$0.25 billion), respectively. Combined, the annual economic burden of asthma in Singapore is SGD 2.09 billion (US\$1.50 billion) with 79 percent resulting from lost productivity.⁵ Therefore, better control of asthma is crucial to bring about not only health improvements but also healthcare expenditure savings and productivity gains.

UNMET NEEDS IN ASTHMA

According to guidelines, poorly controlled outcomes and exacerbations of asthma can be reduced with preventer (or controller) medications, particularly inhaled corticosteroid (ICS) – the mainstay of long-term asthma management.⁶⁻⁹ Singapore was the lowest among eight countries in the Asia-Pacific region with only one in four patients (26 percent) with asthma aged 12 years and older reporting controller medication use in the past month.⁴

A national audit conducted in Singapore identified one in three patients with a severe asthma exacerbation requiring mechanical ventilation or intensive care unit (ICU) admission was not on ICS before the exacerbation.¹⁰ The audit further reported the underuse of ICS and spirometry, inconsistent follow-up, and high smoking rates as gaps in care among severe asthma cases in Singapore.¹⁰ In the Asia-Pacific region, despite the proven efficacy of ICS medications, the majority of patients continue to rely on reliever medications to treat acute symptoms, resulting in suboptimal control.^{5,11} To reduce the impact of asthma in Singapore, more optimal ICS use as part of long-term management is needed.^{5,6}

RETHINKING ASTHMA TREATMENT: THE PROBLEM WITH SABA-ONLY TREATMENT

Short-acting beta-agonists (SABA) have been the mainstay treatment in patients with asthma. However, expert opinions, emerging evidence, and guidelines on the optimal use of beta-agonists have resulted in an evolution in our understanding of the impacts of this reliance of SABA use on patient outcomes.¹²

Higher use of SABA is associated with adverse clinical outcomes. Dispensing of three or more SABA inhalers (canisters) per year is associated with a higher risk of severe exacerbations and the use of one canister per month is associated with increased mortality.^{6,13} Regular use of SABA,

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even for one–two weeks, is associated with adverse effects.⁶ Conflicting perceptions and poor communication between patients and physicians about asthma status have been cited as a contributing factor to the over-reliance on SABA and the underuse of ICS.¹⁴ Over-reliance on SABA puts patients at an increased risk of asthma attacks, urgent hospitalisation, and even asthma-related death.^{6,12,13}

Patients with frequent exacerbations in asthma due to SABA monotherapy are routinely managed using oral corticosteroids (OCS), which then raises concerns associated with a high cumulative OCS dose and the adverse effects of these agents.¹⁵ Adverse effects of long-term OCS include obesity, diabetes, osteoporosis, cataracts, cardiovascular events, and hypertension.^{6,12} Treatment approaches to minimise the need for OCS are, therefore, a high priority.

Based on significant evidence on safety issues (severe exacerbations and death) with SABA-only treatment^{12–14} for asthma and the supporting data that adding ICSs significantly reduces the risk of asthma deaths, hospitalisation, and exacerbations requiring OCS,^{16–18} the Global Initiative for Asthma (GINA) now no longer recommends treatment of asthma in adults and adolescents with SABA alone.⁶

OPTIMAL ICS USE AS PART OF LONG-TERM MANAGEMENT: TREATMENT GUIDELINES

The Global Initiative for Asthma (GINA) recommends that all patients with asthma aged 12 years and above receive ICS-containing controller treatment to reduce their risk of serious exacerbations and to control symptoms. For reliever recommendation, the current GINA report consists of two “tracks” or reliever options.⁶

The first track utilises low-dose ICS- formoterol as the reliever. Track two, using SABA as the reliever, is suggested only as an alternative approach if track one is not possible or not preferred by a patient with no exacerbations on their current therapy. Track one is the preferred GINA approach based on the evidence of a reduction in risk of severe exacerbations compared with using SABA reliever, with similar symptom control and similar lung function.

Evidence for these recommendations was prompted by large randomised controlled trials and real-world studies.^{19–22} The Symbicort Given as-needed in Mild Asthma (SYGMA) trial programme consisting of SYGMA 1 and 2 Phase III trials in more than 8000 patients showed the efficacy and safety of budesonide–formoterol as a reliever therapy in the absence of regular maintenance treatment in patients with mild asthma.^{19,20} The SYGMA 1 trial¹⁹ showed the superiority of budesonide–formoterol over as-needed SABA as a reliever agent, both for symptom control and the prevention of exacerbations, with no evidence of budesonide–formoterol overuse. The SYGMA 2 trial²⁰ confirmed noninferiority in exacerbation reduction of the as-needed budesonide–formoterol combination compared to the maintenance ICS plus as-needed SABA regimen.

Starting with SABA alone trains the patient to regard it as their primary asthma treatment.^{6,14} Physicians would, therefore, need to review SABA use with patients, particularly to identify those using three or more SABA inhalers per year and educate them on the new GINA strategy of using ICS-containing controller treatment for relief of symptoms in place of SABA therapy.^{6,12}

The Singapore ACE Clinical Guidance (ACG)^{2,3} had also outlined recommendations on ICS as the mainstay treatment. ICS–formoterol has been approved in Singapore for the treatment of asthma to achieve overall asthma control, including the prevention and relief of symptoms as well as the reduction of the risk of exacerbations.^{2,3}

ACE Clinical Guidance (ACG) guidelines recommend maintaining ICS as the mainstay of long-term asthma management as it addresses airway inflammation, reduces poor asthma outcomes,^{6,16–18,23} and represents the most effective preventer option across the asthma treatment steps.^{2,3} In line with the recent update with GINA, ACG does not recommend the use of SABA alone (without a preventer) for the long-term treatment of patients aged six years and older, even in those with infrequent or minor symptoms. As demonstrated in the SYGMA trials^{20,21}, patients relying on SABA alone (without a preventer) are more likely to experience poor asthma outcomes, such as the need for OCS or hospitalisations compared to patients using an ICS containing treatment as the preventer and with SABA as the reliever. Nonetheless, SABA is still recommended for short-term relief of symptoms, but only with ICS use.

Across the asthma treatment steps highlighted in the guideline, daily ICS-containing treatment is the most effective preventer option and is important for patients at a higher risk of poor asthma outcomes. The decision regarding the choice or adjustment of preventer treatment should be guided by asthma symptoms, risk of poor asthma outcomes, and influencing factors described in the guideline.^{2,3} If asthma symptoms remain consistently managed for more than three–six months, clinicians can consider stepping down the preventer treatment gradually, to the lowest effective ICS dose. However, ACG does not recommend stopping ICS altogether in patients with asthma aged five years or older as this is associated with an increased risk of exacerbations.

CONCLUSION

Optimised control of asthma is crucial as it has the potential to generate not only health improvements but also improve productivity and reduce the economic burden of the country. While the negative effect of SABA monotherapy and overuse is clearly understood, physicians should continue to review SABA use in their patients and educate patients with asthma on new guidelines on the recommended treatment strategy – ICS-containing controller treatment in place of SABA therapy to reduce patient’s risk of serious exacerbations and improve asthma control.

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LEARNING POINTS

- Recent guidelines recommend preventer (or controller) medications, particularly inhaled corticosteroid (ICS) as the mainstay of long-term asthma management to reduce poorly controlled outcomes and exacerbations of asthma.
- The Global Initiative for Asthma (GINA) and ACE Clinical Guidance (ACG) guidelines no longer recommends the treatment of asthma in adults and adolescents with SABA monotherapy due to safety concerns.
- Budesonide-formoterol has been approved in Singapore for the treatment of mild asthma to achieve overall asthma control, including the prevention and relief of symptoms as well as the reduction of the risk of exacerbations