

Budesonide/Formoterol *new combination for both maintenance and reliever therapy*

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Pediatric asthma has several particular characteristics, which makes it difficult to treat. There is episodic increase in symptoms associated with symptoms-free periods and near-normal lung function. The old strategies used fixed-dose combination of long acting β_2 -agonists (LAB2-A) plus inhaled corticosteroids (ICS) or fixed-dose of ICS alone for moderate-to-severe persistent asthma in pediatrics. These schemes tend to undertreat or overtreat the children, because of the high variability in the disease activity.

The purpose of this study was to adjust the treatment strategy, based on the symptoms-free periods associated with worsening periods. 341 children aged 4 to 11 years were enrolled in a 12 month study; they had asthma history for over 6 months, uncontrolled on ICS. The efficacy and safety of a novel regimen was investigated: budesonid/formoterol 80/4,5 μg maintenance plus additional inhalations for symptoms relief (Symbicort maintenance and relief therapy-SMART); This was called the SMART regimen and was compared with budesonide/formoterol 80/4,5 μg (fixed combination) plus blinded terbutaline for rescue medication, or with a fourfold-higher maintenance dose of budesonide 320 μg (fixed dose), plus blinded terbutaline for rescue medication. The patient was allowed to use reliever medication whenever needed, but no more than 7 times per day, besides their daily maintenance treatment.

The efficacy was studied based on the time to the first exacerbation. The SMART regimen

significantly prolonged the time to the first exacerbation vs fixed-dose combination ($p < 0.001$) and fixed-dose budesonid ($p = 0.02$), reduced their number: 14% vs 38% ($p = 0.01$) and 26% ($p = 0.022$) respectively. Also, in the SMART group the morning and the evening peak expiratory flow (PEF) was higher: 255 l/min vs 242 l/min ($p = 0.22$) and 238 l/min ($p = 0.0019$) respectively, the number of as-needed inhalations was smaller: 0.58 vs 0.76 ($p = 0.038$) and 0.74 ($p = 0.1$) respectively, and children grew significantly more: there was an adjusted mean difference in growth of 1 cm between patients receiving SMART vs those receiving fixed-dose budesonide (0.3 to 1.7, $p = 0.0054$) and a difference of 0.9 cm was seen between the fixed-dose combination and fixed-dose budesonide group (0.2 to 1.6, $p = 0.0099$).

This study was the first to use a new protocol for both the maintenance and the relief of asthma symptoms in children: the SMART regimen. Compared to other fixed-dose combination ICS plus LAB2-A or ICS alone, the SMART regimen greatly reduced the number of exacerbations, improved the lung function and growth rate; this has been accomplished using a single inhaler, maintaining a low overall dose of ICS and avoiding excessive use of β_2 -agonist rescue medication (which does not reduce underlying inflammation). SMART regimen proved to be a simple effective approach and a well-tolerated treatment strategy in pediatric asthma.

Comment on the paper:

Bisgaard H, Sci DM, Le Roux P et al – **Budesonide/Formoterol Maintenance Plus Reliever Therapy. A New Strategy in Pediatric Asthma.** *Chest* 2006; 130:1733-1743