**BREATHOMICS FOR ASSESSING PHARMACOLOGICALTREATMENT IN COPD**

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**Background**

Prospective pharmacological studies on breathomics in patients with chronic obstructive pulmonary disease (COPD) are not available. We aimed to assess the effects of steroid treatment and withdrawal of an extrafine inhaled corticosteroid (ICS)-long-acting β2-agonist (LABA) fixed dose combination (FDC) in a multidimensional classification model including breathomics.

**Methods**

A pilot, proof-of-concept, pharmacological study was undertaken in 14 patients with COPD on maintenance treatment with inhaled fluticasone propionate/salmeterol (500/50 µg b.i.d.) for at least 8 weeks (visit 1). Patients received 2-week treatment with inhaled beclomethasone dipropionate/formoterol (100/6 µg b.i.d.) (visit 2), 4-week treatment with formoterol alone (6 µg b.i.d.) (visit 3), and 4-week treatment with beclomethasone/formoterol (100/6 µg b.i.d.) (visit 4). Exhaled breath analysis with two e-noses, based on different technologies, and exhaled breath condensate (EBC) NMR-based metabolomics were performed. Sputum cell counts, sputum supernatant and EBC prostaglandin E2 and 15-F2t-isoprostane, fraction of exhaled nitric oxide, and spirometry were also measured.

**Results**

Three independent breathomic techniques showed that extrafine beclomethasone/formoterol short-term treatment was associated with different breathprints compared with regular fluticasone propionate/salmeterol. Differences in EBC formate and acetate levels were observed across visits. Either ICS/LABA FDC treatment versus formoterol alone was associated with increased pre-bronchodilator forced expiratory flow at 25%-75% of forced vital capacity (FEF25%-75%) and forced expiratory volume in one second (FEV1)/forced vital capacity (FVC) ($P = 0.008$-$0.029$). The multidimensional model distinguished fluticasone propionate/salmeterol (visit 1) versus beclomethasone/formoterol (visit 4) (accuracy = 85.7%, odds ratio (OR) = 22.2, $P < 0.01$), fluticasone propionate/salmeterol (visit 1) versus formoterol alone (visit 3) (accuracy = 70.4%, OR = 6.29, $P < 0.01$), and formoterol alone (visit 3) versus beclomethasone/formoterol (visit 4) (accuracy = 76.0%, OR 8.63, $P < 0.01$).

**Conclusions**

Breathomics could be used for assessing the effects of ICS treatment and withdrawal in COPD patients. Large, controlled, prospective pharmacological trials are required to clarify the biological implications of breathomics changes.

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