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Impact of combined inhalation of roflumilast or formoterol plus fluticasone on matrix metalloproteinase-9 and its inhibitor in ovalbumin-asthmatic mice

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Statement of the Problem: In a recently-published work, we concluded that co-inhalation of roflumilast+fluticasone more significantly improved inflammatory and histopathological changes than co-inhalation of formoterol+fluticasone in ovalbumin-asthmatic mice. The matrix metalloproteinase-9 (MMP-9) is the principal MMP involved in pathogenesis of asthma, and thus its inhibition could be beneficial to protect against airway inflammation and remodeling. This study was designed in ovalbumin-asthmatic mice to investigate effects of inhaled roflumilast and formoterol alone or combined with fluticasone on levels of matrix metalloproteinase-9 (MMP-9) and its tissue inhibitor-1 (TIMP-1) in the bronchoalveolar lavage fluid (BALF).

Methodology & Theoretical Orientation: Asthma was induced in female BALB/c mice by ovalbumin sensitization and challenge. In addition to the normal control (NC) group, the ovalbumin-asthmatic mice were randomly divided into seven groups (n=8): positive control (PC), vehicle-treated, and five drug-treated groups. Treatments (μg/kg) were given as 15 min-inhalation once/day for seven days as follows: roflumilast (R, 500), formoterol (Fo, 50), fluticasone (F, 1000), roflumilast+fluticasone (R+F, 500+1000), and formoterol+fluticasone (Fo+F, 50+1000).

Findings: The PC mice showed significant increases of the levels of MMP-9 and TIMP-1 in the BALF compared to the NC group. All treatments (except formoterol) significantly decreased these ovalbumin-induced changes mainly with the R+F group which showed a non-significant difference from the NC group. The combinations were significantly different from monotherapies and the R+F group was significantly different from the Fo+F group.

Conclusion & Significance: Co-inhalation of roflumilast+fluticasone more significantly improved the BALF levels of MMP-9 and TIMP-1 than co-inhalation of formoterol+fluticasone in the ovalbumin-asthmatic mice. Recommendations of adding inhaled roflumilast to inhaled corticosteroids could be beneficial in treatment of asthma due to its antiinflammatory and antifibrotic effects.

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Biography

Hussam Murad worked as a Professor at Pharmacology and Clinical Pharmacy Departments in a number of universities in Egypt and Saudi Arabia. He has an experience of about 25 years in teaching and research. He has worked in 10 research projects as a Principal Investigator and as a first Co-investigator in another four. He has got funds from King Abdulaziz City for Science and Technology (KACST), Riyad, SA, and Deanship of Scientific Research, King Abdulaziz University (KAU), Jeddah, SA. He received the award of scientific publication from KAU, in 2015 and in 2017.

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