

## Rolipram: Eotaxin and phosphodiesterase IV inhibitor versus bronchial hyper-reactivity response

Sir,

I am writing this letter to comment on several previously published articles on the use of phosphodiesterase (PDE) 3 in combination with PDE 4 in patients with bronchial hyper-reactivity.<sup>[1,2]</sup> These articles suggest the superiority of this combination over conventional treatment; however, as discussed later, rolipram, an investigational PDE 4 inhibitor, may comparatively prove to be more beneficial when used in combination with a beta-agonist and corticosteroids.

Bronchial hyper-reactivity responses involve bronchial inflammation characterized by activation and accumulation of dendritic cells, eosinophils, mast cells, macrophages, T-lymphocytes, and tissue remodeling process.<sup>[3]</sup> Eotaxin, a chemo-attractant, causes up regulation of CD11b, eosinophil accumulation during an allergic response in lungs, and shedding of L-selectin in human eosinophils. Rolipram inhibits CD11b up regulations as well as eotaxin-induced trans-endothelial movement of eosinophils causing inhibition of eosinophil recruitment. In addition, rolipram also inhibit tumor necrosis factor (TNF)-alpha, at both mRNA and protein levels, thus enhancing its anti-inflammatory effects.<sup>[4]</sup> Moreover, Since PDE 4 enzymes are widely present in the respiratory tract that makes them susceptible to their inhibition by local application therefore inhaled administration of PDE 4 inhibitor has shown considerably more improvement.<sup>[5]</sup> On the other hand, beta-agonist cause bronchodilation therefore the synergistic effect of beta-agonist with PDE 4 inhibitor is indicated by inhibition of antigen-induced contraction and reduction of increase in vascular permeability which are key factors responsible for the patho-physiology of allergic diseases like asthma.<sup>[4]</sup> Furthermore, corticosteroids such as dexamethasone and fluticasone also partially reduce the release of eotaxin.

The combined use of  $\beta_2$ -agonists, rolipram, and steroids abolished TNF- $\alpha$ -induced eotaxin release and hence their combination has additive beneficial effects in the treatment of the eosinophilia associated with

asthma and other allergic diseases. Rolipram, being an investigational drug, should be combined with salbutamol and corticosteroids for the management of asthma. In addition, specific eotaxin inhibitors need to be identified that may not only help us to rectify asthmatic problems, but also leads to avoidance of asthmatic exacerbations and most other infections leading to eosinophilia.

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