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The relation of sTRAIL levels and quality of life in severe persistent allergic asthma patients using omalizumab

Dear Editor,

In patients with allergic asthma, omalizumab inhibits both the early and late asthmatic response and several other markers of inflammation, including the requirement for inhaled or oral corticosteroids. These anti-inflammatory effects of omalizumab provide proof-of-concept of the key role played by immunoglobulin E in allergic respiratory disease. Omalizumab represents a novel approach to the treatment of asthma, inhibiting the inflammatory cascade before it starts. It blocks binding of free IgE on basophils and mast cells, thus inhibiting their activation by allergens [1]. As previously reported, the increase in eosinophil levels in allergic asthma was due to the increase in peripheral blood eosinophil survival promoted by TNF-related apoptosis-inducing ligand (TRAIL) [2]. And as an apoptotic molecule, TRAIL also present in cells that are involved in asthma, including eosinophils, mast cells, fibroblasts, and airway epithelial cells. It is expressed in airway remodeling and may be linked with the pathways of transforming growth factor beta1 (TGF- β 1), which is thought to damage the epithelium. The repair process of the epithelium is hindered as a result of increased apoptosis induced by TGF- β 1, which overlaps with the pathways of TRAIL. Moreover, analogs of TRAIL could have applications for asthma therapy [3].

In our previous report, we showed that sTRAIL levels of severe persistent allergic asthma patients were decreased after the anti-IgE treatment using omalizumab [4]. Thus, the paper suggested that TRAIL may act as a soluble effector, and the decrease after the omalizumab treatment might be an indicator of clinical improvement. However, those results were had a limitation of follow-up period (pre-treatment versus 4 months after treatment). The maximum effect of omalizumab occurred within 3 to 4 months [5–7]. However, all the patients in the study had been our clinical follow-up patients and the real success of the treatment modality was at the end of a year, at which time Omalizumab significantly improved asthma control test (ACT) and pulmonary function in patients with severe persistent asthma [8]. Quality of life increased in the patients due to control of asthma with omalizumab treatment at

the end of a year. It was previously reported that omalizumab treatment in severe allergic asthma influences systemic levels of oxidative stress markers, well-known inflammatory marker C-reactive protein, and ceruloplasmin oxidase activity involved in the interaction of oxidant and anti-oxidant balance [9,10].

Moreover, we evaluated the sTRAIL levels again and compared them to the pre-treatment period and at the fourth month of the treatment. At the time of diagnosis, the mean sTRAIL level in the severe persistent allergic asthma patients before the omalizumab started was 1663 ± 120.4 pg/mL (mean $\pm$ SD; n=14). At the fourth month, sTRAIL level decreased to 1443 ± 80.93 pg/mL (mean $\pm$ SD; n=14) [4]. Finally, after a year of omalizumab usage, when all patients maintained significant improvement by a decrease in clinical symptoms and an increase in ACT, we found that sTRAIL levels were also decreased to very low levels of 273 ± 62.80 pg/mL (mean $\pm$ SD; n=14).

In summary, omalizumab reduces symptoms and exacerbations in patients with persistent allergic asthma. Our findings reflect the different mechanism(s) in the pathogenesis of allergic diseases by the regulation of the inflammatory system and apoptosis.

In conclusion, we provide insight into novel mechanisms of asthma that could lead to speculative physiological functions of sTRAIL in allergic conditions, which will be of considerable interest to the scientific allergy community in the coming years.

Sincerely,

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