

The potential anti-inflammatory role of adiponectin in developing allergic asthma

Milena Spasovska^{1*}, Tatjana Kadifkova Panovska²

¹Diagnostic clinical laboratory P.H.I. General Hospital, Sirma Vojvoda 1, 6000 Ohrid, Republic of North Macedonia

²Faculty of Pharmacy, Ss. Cyril and Methodius University in Skopje, Mother Theresa 47, 1000 Skopje, Republic of North Macedonia

Introduction

The incidence of asthma and obesity is increasing worldwide. There is a lot of research focused on connection between these two inflammatory conditions leading to the study of adiponectin, hormone secreted by the adipose tissue, due to its anti-inflammatory action. Systemic inflammation in obesity could up-regulate the asthmatic pathway, and this is modified by the adipokines and other systemic inflammatory markers like: C-reactive protein (CRP) and interleukin 6 (IL-6) (Ali and Ulrik, 2013). This study summarizes the role of adiponectin, as biomarker for pathological obesity, in the processes of developing allergic asthma. Correlation of adiponectin with inflammatory marker protein CRP, IL-6, is assessed in order to determine the relation of pathologic obesity with allergic asthma.

Materials and methods

Materials

The study involved 90 people, of which 50 patients with asthma and 40 healthy controls subjects.

Patients were selected from the department of Allergology in Ohrid. Informed consents for all patients were obtained. The study was performed in accordance with the ethical principles of the Helsinki Declaration on Medical Research on Humans.

All patients were subjected to full clinical examination:

1. BMI was calculated according to weight which was measured in kg and height which was measured in meters (weight and height were self-reported).

2. Laboratory analysis included: specific IgE (sIgE), inflammatory marker adiponectin, CRP, and IL-6.

Method

Serum sIgE was detected with immunoblotting test on nitrocellulose membrane coated with 20 selected allergens using RIDA qline allergy kit. Measurement of adiponectin serum level was done for all cases and control group by enzyme-linked immunosorbent assay technique (ELISA). Serum levels of hsCRP were determined with immunoturbidimetric method. Serum levels of IL-6 were determined with electrochemiluminescence immunoassay (ECLIA).

Statistical analysis was performed with IBM SPSS Statistics. Normality tests were done using the Shapiro test. The data were presented as mean \pm standard deviation (SD). ANOVA test was used to compare the four groups followed by pairwise comparisons using least significant difference (LSD) test. P value < 0.05 was considered significant.

Results and discussion

The patient and control group were divided into two subgroups using BMI classification in order to see if adiponectin as marker for obesity is involved in allergic asthma.

In our study, serum level of IL-6 was found to be significantly elevated in obese versus normal-weight individuals whether asthmatic or control. Chronic inflammation in adipose tissue, that produces inflammatory markers like IL-6, is considered a crucial

risk factor that contributes to low grade systemic inflammation (Cheng et al., 2012). IL-6 contributes to inflammation in obesity, suppress adiponectin production, enhance airway remodeling and worse pulmonary function.

hsCRP was found to be significantly higher in asthmatic obese group than the other 3 groups (asthmatic lean, control lean and control obese) and it was found to be significantly higher in the asthmatic lean when compared with the lean controls. Thus, hsCRP could be considered surrogate marker for inflammation for developing asthma and pathological obesity (Park et al., 2004).

Serum level of adiponectin was significantly elevated in normal-weight individuals versus asthmatic obese group and control obese, the differences compared with asthmatic lean were not significant. Thus, obesity may be a contributor to inflammation, because adiponectin as anti-inflammatory protein is decreased (Sood et al., 2011).

There were significantly positive correlations between circulating levels of IL-6 and CRP with BMI, while serum adiponectin level showed negative correlation. There is interaction between asthma and obesity, with regards to inflammation. Because of increased levels of obesity biomarkers (IL-6, CRP), intensity of airway inflammation could be greater in obese asthmatic patients (Magdy et al., 2015).

The clinical importance is that low level of anti-inflammatory protein, adiponectin that occur in obese state, contributes to increasing prevalence in patients with asthma. Asthma and obesity as inflammatory processes, trigger the immune response through the activation of Th2 cells, which leads to a reduction release of adiponectin as an anti-inflammatory protein (Otelea et al., 2021)

In these patients, adiponectin levels negatively correlated with inflammatory marker IL-6, although IL-6 positively correlated with CRP. IL-6 as pro-inflammatory cytokine induces production of CRP, leading to increase systemic inflammation (Bacheci et al., 2007). These findings suggest that IL-6 may be response for metabolic disorders in obesity and dysregulated production of adipokines and suppression of adiponectin.

Conclusion

Adiponectin as anti-inflammatory adipocytokine, inhibits inflammation in allergic asthma, which can arise in pathological obesity.

Adiponectin expression is negatively regulated by pro-inflammatory cytokines IL-6.

Adiponectin and adipose tissue-derived cytokine IL-6, could lead to synergistic effect between obesity and progression on airway inflammation.

hsCRP can be used as a surrogate marker for evaluation of obesity and asthma, while adiponectin and IL-6 could be considered surrogate markers for obesity.

References

- Ali, Z., Ulrik, C.S., 2013. Obesity and asthma: a coincidence or a causal relationship? A systematic review. *Respir. Med.* 107, 1287-1300. <https://doi.org/10.1016/j.rmed.2013.03.019>
- Bahceci, M., Gokalp, D., Bahceci, S., Tuzcu, A., Atmaca, S., Arıkan, S., 2007. The correlation between adiposity and adiponectin, tumor necrosis factor alpha, interleukin-6 and high sensitivity C-reactive protein levels. Is adipocyte size associated with inflammation in adults? *J. Endocrinol. Invest.* 30, 210-214. <https://doi.org/10.1007/BF03347427>
- Cheng, X., Folco, E.J., Shimizu, K., Libby, P., 2012. Adiponectin induces pro-inflammatory programs in human macrophages and CD4+ T cells. *J. Biol. Chem.* 287, 36896-36904. <https://doi.org/10.1074/jbc.M112.409516>
- Magdy, Z., Hafez, A-H., Mohammed, H., Mahmoud, H., Mohammad, A., Rabie, A., Engy, O., Amal, O., Mohamed, Z., 2015. Cytokine profile of obese asthma phenotype. *Egypt J. P. Allergy Immunol.* 13, 21-28.
- Otelea, M.R., Arghil, O.C, Zugravu, C., Rascu, A., 2021. Adiponectin and asthma: knowns, unknowns and controversies. *Int. J. Mol. Sci.* 22, 8971. <https://doi.org/10.3390/ijms22168971>
- Park, H.S., Park, J.Y., Yu, R., 2004. Relationship of obesity and visceral adiposity with serum concentrations of CRP, TNF-alpha and IL-6. *Diabetes Res. Clin. Pract.* 69, 29-35. <https://doi.org/10.1016/j.diabres.2004.11.007>
- Sood, A., Dominic, E., Qualls, C., Steffes, M.W., Thyagarajan, B., Smith, L.J, Lewis, C.E, Jacobs, D.R. Jr., 2011. Serum adiponectin is associated with adverse outcomes of asthma in men but not in women. *Front. Pharmacol.* 2, 55. <https://doi.org/10.3389/fphar.2011.00055>