Correspondence

LEPTIN, ADIPONECTIN, AND ASTHMA: FINDINGS FROM A POPULATION-BASED COHORT STUDY

To the Editor: We read with great interest the article by Sutherland et al[1] analyzing the cross-sectional associations between serum adipokines (ie, leptin and adiponectin) and asthma in approximately 1000 men and women aged 32 years in New Zealand. The investigators did not find any significant associations between serum adipokine levels and asthma other than an inverse association between adiponectin and fractional exhaled nitric oxide levels. Their article represents an important contribution to this nascent field of research.

We would like to emphasize, however, caution in interpreting their lack of significant findings. First, the use of nonfasting systemic adipokine concentrations may cause nondifferential information bias, in which case the bias may contribute to a lack of association due to increased variability. Second, insufficient power or type II error is a possible explanation for their results. The reported strength of the association in positive studies is usually modest, being stronger in girls and women.[2–4] A sample size of no more than 407 women may, therefore, be insufficient to detect significant results. Furthermore, several adipokine-asthma studies conducted in countries outside the United States do not show an obesity-asthma association, likely due to their lower prevalence and severity of obesity relative to studies in the United States. The prevalence of obesity (body mass index ≥30 [calculated as weight in kilograms divided by height in meters squared]) in the study population of Sutherland et al[1] (14% in men and 19% in women) is considerably lower than the reported prevalence in the United States. The authors do not provide details of the association between obesity (based on either body mass index or percentage of body fat) and asthma in their study.[1]

We would also like to point out the opposing direction of associations between adiponectin and most asthma outcome measures in men and women in Table 5 in the article by Sutherland et al.[1] We would like to request additional analysis of interactions between sex and adiponectin for the relevant asthma outcomes. If significant, this may suggest a sex-specific nature to the adiponectin-asthma association. Furthermore, the authors may consider a simultaneous analysis of the 2 opposing systemic adipokines with asthma. For example, Jartti et al[5] used the ratio between serum leptin and adiponectin as a predictor variable for this purpose.

Finally, the precise mechanism and significance of the associations between serum adipokines and human asthma at the current stage are confusing. This area of research needs additional study that may open up novel therapeutic strategies for asthma.

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Author Response: The potential problem with nonfasting adipokine levels has been raised before. Because of this concern, we are currently undertaking a validation of nonfasting adipokine levels. Preliminary data indicate that fasting and nonfasting values are highly correlated (adiponectin: n=30, rho=0.97, leptin: n=17, rho=0.98). Hence, it is unlikely that our negative findings are due to the use of nonfasting measurements.

The question of power and sample size is important and was discussed in the article. There was a nonsignificant trend toward an association between leptin and asthma in women. Despite the lower prevalence of obesity in this cohort (compared with the United States), we have previously demonstrated significant associations between obesity and asthma in women in this cohort.[1,2] Since leptin is effectively a surrogate marker for body fat (rho=0.86 in women), it is not surprising that there is a trend toward an association between leptin and asthma. However, the hypothesis being tested was whether the asthma-obesity association was mediated by the proinflammatory effect of leptin. We did not find evidence to support this.

As noted in the article, there were several sex-adipokine interactions and we therefore analyzed the sexes separately. For adiponectin, the significant interactions were for asthma diagnosis (P=.04) and for log nitric oxide (P=.02). The other interaction terms were not significant (P>.1). These interaction terms were similar if the analyses adjusted for body fat and smoking.

The leptin to adiponectin ratio is also highly correlated with body fat (rho=0.80 in women). Reanalyzing the data using the ratio provides results similar to those using adipokines independently

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