COMMENTS AND RESPONSES

Comment on: Leeds et al. High Prevalence of Microvascular Complications in Adults With Type 1 Diabetes and Newly Diagnosed Celiac Disease. Diabetes Care 2011;34:2158–2163

We read with great interest the article by Leeds et al. (1), which reported an increased prevalence of diabetic nephropathy (DN) and diabetic retinopathy (DR) in adults with type 1 diabetes and newly diagnosed celiac disease (CD). After patients were on a gluten-free diet (GFD) for 1 year, Leeds et al. (1) observed a significant improvement in the prevalence of advanced DN; by contrast, there was still a higher prevalence of advanced DR. Several factors were analyzed to understand the underlying mechanisms of these findings. In particular, Leeds et al. discuss the influence of higher glycosylated hemoglobin (HbA_{1c}) and lower HDL cholesterol in the study population before GFD compared with subjects affected only by type 1 diabetes.

We agree with the authors that higher HbA_{1c} and lower HDL cholesterol are possible explanations of their findings. Furthermore, we would also like to highlight the potential role of altered apolipoprotein A-I (Apo A-I) secretion in newly diagnosed CD patients as an explanation for the different results observed between DN and DR. Apo A-I is the major HDL structural protein, essential for reverse transport of cholesterol from peripheral tissue to the liver (2). It is also characterized by antioxidant and anti-inflammatory effects (2). Apo A-I has been reported as being synthesized by the liver and the intestine and, more recently, by the vitreous fluid and retinal pigment epithelium (3). Our group previously reported that serum levels of HDL and Apo A-I are decreased in individuals with CD, and subsequent restoration of blood lipid profile is observed after GFD (4). Alterations of the small bowel mucosa could be responsible for decreased intestinal Apo A-I secretion and, consequently, for reduced HDL synthesis (4). The reduced intestinal secretion of Apo A-I in individuals with type 1 diabetes affected by CD could contribute to the increased prevalence of DN in these subjects compared with individuals with type 1 diabetes alone and would also be of relevance in the assessment of macrovascular complications in these patients. Also, the restoration of Apo A-I and HDL levels due to the normalization of the intestinal villi after GFD could be responsible, at least partially, for the improvement of DN.

As regards DR, the discovery of increased Apo A-I mRNA levels and protein content in the vitreous fluid and retina of patients with DR as compared with healthy subjects (5) has lead to the hypothesis that intraocularly produced lipoproteins rather than serum lipids may be more important in the pathogenesis of DR (3). This could explain why DR did not improve after GFD in subjects with CD.

In conclusion, the findings of Leeds et al. (1) may also support a key role of Apo A-I intestinal secretion in the pathogenesis of DN in subjects with type 1 diabetes and CD. Consistent with the increased need for personalized medicine in diabetes (5), all together, these findings (1,4) may contribute to a better understanding of type 1 diabetes and its complications and better care of our diabetic patients.

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