Evaluation of angiotensin-converting enzyme and adenosine deaminase polymorphisms in patients with type 2 diabetes mellitus

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Diabetes mellitus (DM) is a heterogeneous group of metabolic disorders characterized by chronic hyperglycemia, with changes in carbohydrate, fatty acid and protein metabolism. Type 2 diabetes mellitus (DMT2) is the most common form of this disease, which affects approximately 90% of people who have DM. It is characterized mainly by changes in the action and secretion of insulin, although the etiology, genetics and specific pathophysiology of the disease are not yet completely determined. DMT2 patients have a higher risk of developing macro- and microvascular complications. Studies have shown that angiotensin-converting enzyme (ACE) and adenosine deaminase (ADA) may be related to the development of DMT2 or its complications. Based on these data, we studied the I/D polymorphism of the ACE gene and the TaqI polymorphism in the ADA gene in 162 patients with DMT2 and 160 blood donors. According to the American Diabetes Association, people with diabetes who have HDL-C below 40 mg/dL or LDL-C above 100 mg/dL or triglycerides above 150 mg/dL are at increased risk of developing cardiovascular disease. Therefore, we selected 81 individuals with these characteristics to compose the study group of diabetic patients designated “risk of cardiovascular disease”. The polymorphisms were evaluated by PCR for the ACE gene and PCR-RFLP for the ADA gene. The frequencies obtained for the ACE gene polymorphism were: in diabetic patients: I/I (19.1%), I/D (52.5%) and D/D (28.4%); in control group: I/I (12.5%), I/D (55.6%) and D/D (31.9%), and in the group of patients with cardiovascular disease risk: I/I (16%), I/D (59.3%) and D/D (24.7%). The frequencies for the ADA gene polymorphism were: in diabetic patients: ADA * 1/* 1 (89.31%), ADA * 1/* 2 (10.06%) and ADA * 2/* 2 (0.63%); in control group: ADA * 1/* 1 (91.25%), ADA * 1/* 2 (7.50%) and ADA * 2/* 2 (1.25%), and in patients with cardiovascular risk: ADA * 1/* 1 (91.20%), ADA * 1/* 2 (7.50%) and ADA *2/* 2 (0.0%). There were no significant differences in any of the groups and genes analyzed, although the genotypic and allelic frequencies are similar to those in other studies in different populations, especially those who participated in the Brazilian population formation. Our results support those of other authors who found, in admixed populations, no correlation between I/D polymorphism of the ACE gene and DMT2 and cardiovascular diseases. For the TaqI polymorphism of
the ADA gene, there are reports that enzyme activity is elevated in patients with DM, but the authors are not sure about the true mechanisms involved in this process. Although no relationship was found between these polymorphisms and DMT2, we believe that further studies are needed in the Brazilian population, as well as the study of haplotypes of the ACE gene and of correlations between activities of these enzymes and their genetic polymorphisms in DMT2 patients and healthy subjects of the Brazilian population.

**Key words:** Type 2 diabetes mellitus; Angiotensin-converting enzyme; Adenosine deaminase; Cardiovascular risk; Genetic polymorphisms