Summary

Cataract (opacification of the lens in the eye) is now the leading cause of blindness worldwide. Epidemiological studies revealed up to a fivefold increased prevalence of cataract in diabetic subjects compared with the non-diabetic population. Growing evidence indicates that both duration of diabetes and quality of glycemic control are the most important risk factors for diabetic cataract formation. Cataract prevention in diabetics is of great importance because of a higher risk of cataract development in these patients. Diabetes is a risk factor for several complications during cataract surgery, which is currently the only known treatment for cataract.

The lens does not have its own blood supply, the supply of nutrients and the removal of metabolic products from the lens is the task of aqueous humor (AH). AH is secreted by the ciliary epithelium in the posterior chamber of the eye and flows around the lens and through the pupil to the anterior chamber. Analysis of endogenous components of aqueous humor is important for understanding its physiology and changes caused by the occurrence of eye disease (e.g. cataract).

Metabolomics is, nowadays, frequently implemented to understand pathophysiological processes responsible for disease occurrence and progression. The detailed identification of small molecule AH components and the indication of metabolites that differentiate aqueous humor in patients with cataract and diabetes type 2 from patients with non-diabetic cataracts may improve knowledge of the molecular mechanisms behind the increased risk of developing cataract in diabetic patients.

The aim of this study was to find differences in the composition of aqueous humor in patients with cataract and diabetes compared to patients in control group. For this purpose, a method for the preparation and analysis of the AH sample was developed using the LC-MS technique enabling the simultaneous determination of metabolites of different classes. The developed method was used to analyze the aqueous humor collected from patients undergoing cataract surgery. The analyses were performed using two types of chromatography, LC-RP-MS for the measurement of non-polar or low-polar metabolites and LC-HILIC-MS for measuring compounds with high polarity. The AH obtained from diabetic patients was compared to the fluid collected from the control group.

The study group included 35 patients (16 with type 2 diabetes and 19 control group). Patients in both groups were matched in terms of age, sex and BMI. The mean fasting glucose level was 152 ± 42 mg/dl for the T2DM group and 106 ± 15 mg/dl for the control patients. The average duration of diabetes in the study group was 11.6 ± 6 years, and the mean level of glycated hemoglobin was 7.2 ± 1.1%.

The final effect of the analyses was 29 statistically significant metabolites differentiating the studied groups. A decreased level of antioxidants, tryptophan derivatives or acylcarnitine has been observed. On the other hand, the level of glycosylated amino acids, which similarly to acylcarnitine was previously unrelated to cataract development, was significantly increased in patients with diabetes. Among other metabolites found, catechol sulfate, which can be related to intestinal microflora and dimethylbiguanide (metformin), which was found in the AH of patients using this oral antidiabetic drug, should also be mentioned.

The obtained results indicate increased oxidative stress and disturbances in the amino acid metabolism in AH of patients with type 2 diabetes, which may contribute to earlier cataract formation in this group of patients. Understanding the metabolic pathways associated with the accelerated development of cataracts may determine new therapeutic targets or inhibit the development of the disease.