Summary

Introduction: Relation of diabetes mellitus (DM) to the diabetic keratopathy and various stages of corneal nerve fiber damage has been well accepted. A possible association between changes in the cornea of diabetic patients and diabetic retinopathy (DR), DM duration, and age at the time of DM diagnosis were evaluated. Neuropathies are among the most common long-term complications of diabetes mellitus. Good glycemic control is essential in prevention of this complication. DM patients with similar mean glucose levels or glycated hemoglobin (HbA1c) levels often exhibit differences in evaluation of diabetic complications. One reason for these differences may be the differences in glucose variability.
DM patients with similar mean glucose levels or HbA1c levels often exhibit differences in glucose variability

Hypothesis: Diabetes mellitus damages the subbasal nerve fibers of the corneal and affects the density of epithelial, endothelial and stromal cells. Corneal changes in patients with DM are dependent on the degree of diabetic retinopathy (DR), age at diagnosis, duration of DM, and compensation parameters.

Purpose: To compare changes in cell density in individual layers of cornea and status of subbasal nerve fibers in patients with type 1 DM (DM 1) and in healthy subjects. To evaluate the dependence of corneal changes in diabetic patients and the degree of DR, duration of DM 1, age at the time of diagnosis of DM 1 and parameters of glycemic compensation.

Methods: The study included 60 patients with DM 1 and 20 healthy control subjects. The subjects were examined using in vivo corneal confocal microscopy (IVCM). The density of basal epithelial cells, keratocytes and endothelial cells, and the status of the subbasal nerve fibers [corneal nerve fiber density (NFD), nerve fiber length (NFL), and nerve branch density (NBD)] were evaluated using IVCM. We evaluated the dependence of corneal changes in diabetic patients and the degree of DR, duration of DM 1, age at the time of diagnosis of DM 1 and parameters of glycemic compensation.
Among 20 patients with DM 1 treated with an intensified insulin regimen, possible associations between the status of the subbasal nerve fibers and parameters of glycemic

compensation (HbA1c, glycemia SD, and insulin dose), and other clinical factors were evaluated.

Results: Basal epithelial cell density increased with age (p=0.026), while stromal and endothelial cell density decreased with age (p=0.003, p=0.0005, p<0.0001). After the DM 1 diagnosis was established, this association with age weakens. We proved nerve fiber damage in DM 1 patients (p<0.0001). The damage correlated with the degree of DR. DM 1 patients with higher age at DM 1 diagnosis had a higher nerve fiber density (p=0.0021). HbA1c had a negligible effect on corneal nerve parameters. Also, NBD was the highest in those with higher glycemic variability (p = 0.023). NFD, NFL, and NBD were statistically significantly higher in those with higher total insulin per kilogram (p = 0.02, p = 0.01, and p = 0.012, respectively).

Conclusion: These results indicate that age at DM 1 diagnosis has an important effect on final nerve fiber and corneal cell density. Total insulin dose per kilogram may be an important factor influencing nerve fiber status and needs to be considered in future studies of diabetic neuropathy and its progression. Also, more attention must be paid to other possible factors when elucidating the development of diabetic complications.

Key words: Corneal confocal microscopy, Diabetes mellitus type 1, Diabetic keratopathy, Corneal nerve fiber, Diabetic retinopathy, Diabetic neuropathy, Glucose variability