ABSTRACT

Keratoconus (KC) is a non-inflammatory disease of the cornea, in which ectasia and thinning occur probably due to defects in the collagen fibers binding. It is one of the most common indications for corneal transplantation. KC is a complex disorder with the involvement of both genetic and environmental factors; however the exact pathogenic mechanisms leading to the disease development have not been elucidated.

The main aim of our work was to compare the presence and enzyme activity of cross-linking enzymes lysyl oxidases (LOX and LOX-like enzymes), in control human cornea samples and explanted cornea gained from patients with KC. We also focused on diseases previously described to be associated with KC with the aim to identify common signs among them. Furthermore, we replicated association of single nucleotide polymorphisms (SNPs) in *LOX* and hepatocyte growth factor (*HGF*) with KC risk. We attempted to link all pathophysiological disturbances observed in KC into one common pathway. We have used a wide spectrum of methods (cell culturing, immunohisto- and immunocytochemistry, microscopy, fluorimetric enzyme activity measurement, genotyping and direct sequencing, statistical analysis).

We demonstrated the presence of entire family of LOX enzymes in control and in KC corneas, with decrease and the irregular pattern for LOX, LOX propeptide, LOXL2 and LOXL3. In average, 2.5-fold decrease in total LOX enzymes activity was detected. We found that mitral valve prolapse (MVP) and KC share structural alterations, indicating similar pathogenic mechanism(s) were involved in the development of both diseases. In our cohort of patients, we have excluded association of KC and macular corneal dystrophy (MCD). We demonstrated the association of rs2956540-C in *LOX* genomic area with protective effect and rs3735520-A in *HGF* genomic area as a risk factor for the development of KC. A theory about involvement of copper imbalance in KC development has been published. The contribution of SNPs and copper imbalance on KC development remains unclear.

In summary, we confirmed our hypothesis that impairment of cross-linking enzymes occurs in KC and that the same mechanism could be involved in MVP pathogenesis. We excluded association of MCD and KC in our group of patients.