EDITORIAL

Retinal Neurodegeneration in the Course of Diabetes: Neuroprotection as a Potential Treatment Target

Diabetic retinopathy (DR) is a major complication of diabetes and is considered one of the main causes of blindness both in moderate- and high-income countries. Epidemiological studies have shown that about 1/3 of diabetics show signs of DR and about 1/10 faces the gloomy vision of DR progression, including macular oedema and proliferative diabetic retinopathy [1-3]. For many years DR has been perceived as a vascular disorder only. Currently we know that chronically increased blood glucose levels can damage retinal ganglion cells, amacrine cells and photoreceptors [4-6]. However the exact mechanisms and contribution of different factors involved in the development and progression of DR remain unclear. The aim of this special issue "*Retinal neurodegeneration in the course of diabetes. Neuroprotection as a potential treatment target*" is to provide a deeper insight into the new molecular mechanisms that control survival and apoptosis of retinal cells. Moreover a range of neuroprotective agents that are likely to lead to a new therapeutic strategy in the early stages of DR are discussed. Prospect of incorporating the concept of *"neurodegeneration*" in ophthalmology is based on anatomical implications.

The optic nerve anatomy, closely related to that of the central nervous system (CNS), has encouraged Szmygel Ł. *et al*. to present their conception of studies of the optic nerve assessment in diabetic ketoacidosis (DKA) in children with type 1 diabetes mellitus (T1DM) [7]. In the article "*Optic nerve and cerebral edema in the course of diabetic ketoacidosis*" the authors present comprehensive evidence supporting the need for ultrasound examination of the optic nerve sheath diameter as an additional tool to estimate the risk of brain edema in T1DM children in the course of DKA treatment. This novel technique seems to be a promising, non-invasive bedside tool. Currently the use of ultrasound is gaining popularity, particularly in the Emergency Room and Critical Care settings [7]. What Furthermore, long-term consequences of brain edema can be seen in the group of patients previously treated for diabetic ketoacidosis? Is this a process concomitant to long-term vascular complications, such as diabetic retinopathy? We don't know. Although the role of hyperglycaemia in diabetic retinopathy has been well documented, acute effects of hyperglycaemia on human retinal cells are much less known. In the manuscript Martin *et al*. have demonstrated that there was a significant difference in the presence of brain edema based on location brain vessels vs. retinal capillary bed, indicating that the location of the capillary bed is the factor influencing the occurrence of edema in patients with DKA [6]. Interestingly, during the insult of DKA and its treatment the blood–retinal barrier (BRB) does not experience the same degree of perturbation as the blood–brain barrier (BBB). The greater stability of the retinal microvasculature may be due to the increased number of pericytes in the BRB in comparison with the BBB [6]. Further research is needed in this field.

Diabetes increases oxidative stress in the retina, and overwhelming evidence suggests a two-way relationship between oxidative stress and other metabolic abnormalities. Mrugacz M, *et al*. in their manuscript *"Neuroretinal apoptosis as a vascular dysfunction in diabetic patients"* provide a comprehensive overview of the outcomes of metabolic and non-metabolic pathways in the development of diabetic retinopathy, emphasizing the role of neuronal apoptosis [8].

The review "*Retinal neurodegeneration in the course of diabetes-pathogenesis and clinical perspective*" by Araszkiewicz A and Zozulinska-Ziolkiewicz D discuss in details the main features of retinal degeneration and its clinical relevance in diabetic patients. Moreover, they describe possibilities of early detection of neurodegeneration in diabetic patients by the use of non-invasive methods assessing the Retinal Nerve Fiber Layer (RNFL) and the Ganglion Cell Layer (GCL) [9].

The latest achievements in the field of potential molecular mechanisms in autophagy involved in DR pathophysiology presented in "*Authophagy in diabetic retinopathy*" by Di Rosa M, *et al*. A complex interplay between autophagy and apoptosis mechanisms determines the degree of cellular apoptosis and the progression of diabetic retinopathy. Both redox signaling and autophagy are double-edged processes; they can be detrimental or beneficial, depending on the delicate balance [10].

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The review *"Neurodegeneration and neuroinflammation in diabetic retinopathy: potential approaches to delay neuronal loss"* by Kadłubowska J, *et al*. indicates that retinal neurodegeneration and inflammation may be linked to chronic vascular complications in the course of diabetes. Inflammatory lesions may occur first and precede vascular damage [11].

Promising potential therapies based on these particular aspects of DR pathophysiology are also discussed.

The last review article in this special issue presents the most recent studies of the role of neurodegenerative and neuroprotective factors in the course of diabetes. Beń-Skowronek I. in his article "*Growth factors in pathogenesis of retinal neurodegeneration in diabetes mellitus*" emphasizes the role of neurodegenerative factors as important mediators in the pathogenesis of DR [12]. From a clinical point of view, identification of patients who is at risk to develop retinal degeneration will be of key importance for therapies based on neuroprotections. Further research in this field may help us find novel treatments that could delay or even stop the progression of DR at early stages.

All up-to-date and cross-checked opinions presented in this special issue should help both clinicians and researchers increase their awareness of retinal neurodegeneration and possibilities of neuroprotection against this devastating complication of diabetes.

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