L. Deres[1], K. Szabadfi[2], K. Eros[3], M. Wilhelm[4], C.S. Cseko[5], J. Matuz[5], S. Farkas[5], R. Gabriel[2], K. Toth[1], R. Halmosi[1], **[1]University of Pecs, Medical School, 1st Department of Medicine - Pecs - Hungary**, [2]University of Pecs, Department of experimental zoology and neurobiology - Pecs - Hungary, [3]University of Pecs, Medical School, Department of Biochemistry and Medical Chemistry - Pecs - Hungary, [4]University of Pecs, Intitute of Sport Sciences and Physical Education - Pecs - Hungary, [5]Gedeon Richter Plc. - Budapest – Hungary:

Progression of vascular changing and hypertensive retinopathy during bradykinin B1 receptor antagonist treatment in SHR rats

Abstract: P6050

Progression of vascular changing and hypertensive retinopathy during bradykinin B1 receptor antagonist treatment in SHR rats

Authors:
L. Deres[1], K. Szabadfi[2], K. Eros[3], M. Wilhelm[4], C.S. Cseko[5], J. Matuz[5], S. Farkas[5], R. Gabriel[2], K. Toth[1], R. Halmosi[1], [1]University of Pecs, Medical School, 1st Department of Medicine - Pecs - Hungary, [2]University of Pecs, Department of experimental zoology and neurobiology - Pecs - Hungary, [3]University of Pecs, Medical School, Department of Biochemistry and Medical Chemistry - Pecs - Hungary, [4]University of Pecs, Intitute of Sport Sciences and Physical Education - Pecs - Hungary, [5]Gedeon Richter Plc. - Budapest - Hungary,

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Introduction: It is well known that currently used non-steroidal anti-inflammatory drugs have adverse effects on cardiovascular morbidity and mortality. NSAIDs are increasingly employed in ophthalmology to reduce miosis and inflammation, manage scleritis, and prevent and treat cystoid macular edema associated with cataract surgery. In addition, they may decrease postoperative pain and photophobia associated with refractive surgery and may reduce the itching associated with allergic conjunctivitis. NSAIDs also have therapeutic effects on diabetic retinopathy. In the present work we investigated the effects of a new analgesic compound, the bradykinin B1 receptor antagonist test substance, FGY-1153 on the progression of hypertensive retinopathy of spontaneously hypertensive rats (SHR) as a promising substituent of disadvantageous NSAIDs in cardiovascular regards.

Methods: The test substance was administered in rat chow test diet containing a concentration of 120 ppm or 400 ppm of FGY1153, or control diet containing no active ingredient. The treatment started at the age of 11 weeks and lasted for 26 weeks. We investigated the hypertensive organ damages on heart (previously reported), carotid artery, aortic segments and the retina with light microscopy, immunohistochemistry, electron microscopy and Western blot analysis.

Results: The intima-media thickness of great vessels and the amount of vascular wall collagen content did not decrease significantly in treated animals. The whole retina (OLM-ILM) and ONL was thicker in the FGY120 compared to the FGY400 and Control groups. However, no major alteration could be found in cell number of GCL/100 µm retina length in the examined groups. The number of cells in the GCL/100 µm in normal 3 months old animals is around 7, thus it can be supposed that the hypertensive condition per se reduces this number; aging may have an additional effect on this parameter. In the number of TUNEL-positive cells (n=1–2 section in each group) no differences could be observed in the Control and the FGY-1153-treated retinas. Increased GFAP immunoreactivity was observed in the entire width of the SHR retinas compared to WKY and FGY120 retinas. In the FGY400 group the GFAP-level was elevated compared to the FGY120 group, but was less strong than in the SHR group.

Summary: Both doses of FGY-1153 have been found retinoprotective; the lower dose seemed to be more effective. These effects were more prominent in the inner retina. The slight changes in the neurochemical makeup of retinal cells indicate that the alterations in the hypertensive retina may be due to a slowly developing excitotoxicity. The protective effect was manifested in retaining the integrity of the retinal tissue and ultrastructure, and decreasing apoptosis.