( ) R1 ( ) R2 (X) R3 ( ) PG0 ( ) PG1 ( ) Estagiário ( ) Tecnólogo ( ) PIBIC

Last Name - Bottós
First Name - Juliana
Middle - Mantovani

Service (sector)
Retina and Vitreous

Nº CEP
1937/06

EFFECTS OF ANGIOTENSIN-CONVERTING ENZYME INHIBITOR AND ANGIOTENSIN II RECEPTOR ANTAGONIST IN DIABETIC RABBIT RETINA

Juliana Bottós, Tatiana Helfenstein, Silvia Ihara, Francisco Fonseca, Verônica Lima, Thatiana Orsi, Maurício Maia, Eduardo Rodrigues, Michel Farah

Purpose: 1. To verify the effects of the angiotensin converting enzyme inhibitor (ACEI) quinapril and the angiotensin II receptor antagonist (ARA) olmesartan on retina of hypercholesterolemic and diet-induced diabetic rabbits. 2. To present a new animal model for diabetic retinopathy in rabbit eyes. Methods: The study was conducted in compliance with the UNIFESP Ethical Committee. Diabetes and hypercholesterolemia were induced in New Zealand white male rabbits by with high-fat/high-sucrose diet (contained 10% lard and 37% sucrose). Water and chow were given ad libitum. The high-fat/high-sucrose diet feeding was maintained for 6 months. After 12 and 24 week period, the efficacy of the diet in inducing diabetes and hypercholesterolemia was examined by plasma glucose levels, plasma total cholesterol, high-density lipoprotein (HDL) cholesterol and triglyceride. The rabbits were divided into four groups. Groups II, III and IV received the high-fat/high-sucrose diet. Animals belonging to group I (n=10) formed the control group, and group II (n=10) formed the untreated group. Animals from group III (n=10) received the quinapril 30/mg/day orally, added to the chow. Animals from group IV (n=10) received the olmesartan 5mg/kg/day orally added to the chow. Clinical Analyses – Fundus photographs and fluorescein angiography were performed at the third and sixth month. The prevalence of microaneurysms in each retina was determined based on standard photographs, with radius equivalent to the diameter of the average optic disc (1500 microns), considering the area within 1500microns of the border of the optic disc. The number of microaneurysms was analyzed and the animals were graduated into 4 levels: I – < 10; II – 11-30; III– 31-40; IV - > 40 microaneurysms. All evaluations were performed in a masked fashion. Biochemical Parameters - All blood samples were obtained after a 12-hour fast. Serum glucose and lipid profile were determined at baseline, after 3 and 6 months by standard techniques using an enzymatic assay. Results: All the animals induced by the diabetogenic and cholesterol-rich diet were diabetics at 6 months after induction (glycemia 316.3 ± 127.21 mg/dl). No differences between groups II, III and IV were observed regarding glucose levels. The control group (I) had a mean glycemia of 104.60 ± 5.3 mg/dl. Clinical study of all diabetic groups (II, III and IV) by 12 weeks revealed the early clinical features of

diabetic retinopathy included hyperfluorescent dots consistent with microaneurysms. Group II developed microaneurysms at level IV, while groups III and IV presented microaneurysms at level III. Clinical findings did not change appreciably by 24 weeks and there were no differences among the groups. Conclusion: 1. No significant clinical benefit was observed regarding retinal protection with the use of ACEI or ARA for the treatment of diabetic retinopathy. 2. New Zealand White rabbits fed with high-fat/high-sucrose diet seem to provide a convenient animal model for studying diabetic retinopathy.