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Modification of biochemical may prevent diabetic retinopathy

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Statement of the Problem: Modification of hyperglycemia induced different biochemical pathways and modulation of up regulated expression of angiogenic vascular endothelial growth factor (VEGF) and its receptor 2 (VEGF, VEGFR2) by peripheral retinal laser photocoagulation (PHC) may prevent vision loss owing to diabetic retinopathy (DR) in type 2 diabetes mellitus (DM). Unutilized enormous intracellular glucose in insulin nondependent tissues including retina, leads to increased formation of advanced glycation end products, activation of polyol pathway, anaerobic glycolysis and oxidative stress, resulting in glutamate toxicity and lipid peroxidation. Ultimately all these pathways converge to upregulation of proangiogenic VEGF and VEGFR2, the crucial player of the development of DR.

Purpose: The purpose of the present pilot study is to assess the effects of supplementation of B-vitamins (B1, B2, B3, B5 and B6), vitamin E and precedent peripheral laser PHC for pathological retinal degeneration and retinal breaks, on the development of DR.

Methodology: Two hundred patients of diagnosed type2 DM, who had been treated by oral antidiabetic medication along with B-vitamins and vitamin E since 2004, are included in this ongoing study. Baseline detailed fundus examinations excluded the presence of retinopathy. Twenty seven subjects of this group received peripheral retinal laser PHC for symptomatic retinal breaks. Baseline biochemical parameters like lactate/pyruvate ratio, advanced glycation end products (AGEs), malondialdehyde (MDA), VEGF and VEGFR2 were determined. Yearly fundus examinations were documented to detect the features of DR.

Findings: Twenty seven patients who received laser PHC and B-vitamins and vitamin E, do not show any feature of DR. Thirty two among 160 patients who received B-vitamins and vitamin E, developed very mild microangiopathy. Thirteen patients lost the follow-up.

Conclusion: Glycolysis and citric acid cycle should run uninterruptedly to prevent biochemical derangements which leads to increased expression of VEGF and VEGFR2. Previous peripheral retinal laser PHC probably create inhibitory signal for secretion of angiogenic VEGF and VEGFR2.

Flow chart \rightarrow

Anomalous glycolysis→altered L/P ratio and NAD+ /NADH→reductive stress in cellular level Increased lactate→lowering of cellular pH→reduced action of GLAST→glutamate toxicity→increased intracellular Ca++ →increased lipid peroxidation→diminished activity of G6PD→reduced function of deformed RBC→localized tissue hypoxia→upregulation of VEGF Unutilized glucose→increased AGEs→AGE+RAGE interaction→activation ofNADPH oxidase→increased endothelial and pericyte ROS production→upregulation of NF-kB→upregulation of VEGF Supplementation of B-vitamins→adequate supply of oxidized cofactors(NAD+ ,FAD,FMN,Pyridoxamine) →continuity of glycolysis and citric acid cycle→reduced biochemical derangements→less production of angiogenic VEGF and VEGFR2 Previous laser PHC→inhibitory signal on angiogenic VEGF→less chance of microangiopathy

Notes:

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Recent Publications

- 1. Mondal Lakshmi K, Baidya Krishna P, Bhattacharya Basudev et al. (2006) Relation between increased anaerobic glycolysis and visual acuity in long standing type 2 diabetes mellitus without retinopathy. Indian J Ophthalmol. 54(1):43-44.
- 2. Choudhuri Subhadip, Mandal Lakshmi K, Dutta Deep et al. (2013) Role of hyperglycemia-mediated erythrocyte redox state alteration in the development of diabetic retinopathy. Retina 33:207-2016.
- 3. Mondal Lakshmi K, Choudhuri Subhadip, Dutta Deep et al. (2013) Oxidative stress-associated neuroretinal dysfunction and nitrosative stress in diabetic retinopathy 37(6):401-407.
- 4. Choudhuri Subhadip, Dutta Deep, Sen Aditi, Chowdhury I H, Mitra Bhaskar et al. (2013). Role of N-epsilon- carboxy methyl lysine, advanced glycation end products and reactive oxygen species for the development of nonproliferative and proliferative retinopathy in type 2 diabetes mellitus. Molecular Vision. 19: 100-113.
- Paine Suman K, Basu Analava, Mondal Lakshmi K et al. (2012) Association of vascular endothelial growth factor, transforming growth factor beta, and interferon gamma gene polymorphisms with proliferative diabetic retinopathy. Mol Vis. 18:2749-2757.

Biography

Lakshmi Kanta Mondal has been acting as a Professor in the Department of Ophthalmology at the Regional Institute of Ophthalmology, Kolkata, West Bengal, India, since 2012. He has been teaching under-graduate and post-graduate students of Ophthalmology since 1998. He is an experienced Vitreo-Retinal Surgeon. His field of interest is biochemical derangements related to development of diabetic retinopathy. He obtained the degree of Doctor of Philosophy in Ophthalmology with major focus on Ophthalmology, Biochemistry and Molecular Biology in 2017.

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