EFFECT OF COMBINED TREATMENT WITH MELATONIN AND INSULIN ON EXPRESSION OF GENES RELATED TO MITOCHONDRIAL FUNCTION ON LIVER FROM DIABETIC RATS.

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Diabetes mellitus is characterized by hyperglycemia caused by reduced insulin sensitivity and/or lack of insulin secretion. Researches shows presence of mitochondrial dysfunction in skeletal muscle and adipose tissue of diabetic animals while the liver is less studied. The aim of the study was to investigate the effect of long-term combined treatment with melatonin and insulin on expression of genes related to mitochondrial function in the liver from diabetic animals. Diabetes was induced by streptozotocin administration (120mg/kg, i.p.) on five days-old male rats. After weaning (3 weeks old), the animals were divided into the following groups: control (C) - control group; diabetic (D) - diabetic animals without treatment; melatonin (M) - diabetic rats treated with melatonin (0.2 mg/kg); melatonin with insulin (MI) - diabetic rats treated with melatonin (0.2 mg/kg) and insulin and the insulin group (I) - diabetic rats treated with insulin only. With 12 week of life the animals were euthanized and the liver was removed and homogenized in Trizol for gene expression analysis by qPCR. The genes evaluated were for Peroxisome proliferator-activated receptor gamma coactivator 1-alpha (PGC-1α) and its isoforms α1-α4, Peroxisome proliferator-activated receptor alpha (PPARα) and Mitochondrial uncoupling protein 2 (UCP2). One Way ANOVA with p<0.05 was used in the statistical analysis. Although diabetic animals have not shown a reduction in gene expression of the total PGC1α, treatment with melatonin, with or without insulin, significantly increased the expression of the total PGC1α and isoform PGC1α.1, but did not alter the gene expression of isoform PGC1α.4. There was no amplification of mRNA for PGC-1α.2 and PGC-1α.3 isoforms in the liver of animals. There was no change in gene expression of UCP2 and PPARα between groups. In conclusion, treatment with melatonin associated with insulin can increase PGC1α expression in liver tissue of diabetic animals.

Key Words
Melatonin, Diabetes, Mitochondria

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