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Autophagy inducer trehalose positive effect in db/db mice, genetic model of diabetes

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Autophagy suppression was shown in aging, diabetes [1]. Db/db mice is a model of diabetes, related to leptin receptor deficiency, was used in experiments. The aim – to evaluate effect of autophagy inducer trehalose on autophagic activity in db/db mice with significant lipid storage syndrome in liver and other organs. The study was carried out on a specific pathogen-free mice of db/db strain, 3 months old (SPF-vivarium of the Institute of Cytology and Genetics, SB RAS, Novosibirsk). Mice were subdivided into four groups: 1) WT mice + H_2O; 2) WT mice drinking 2 % trehalose (24 days); 3) db/db mice + H_2O; 4) db/db mice drinking 2 % trehalose (24 days). It was shown that treatment by trehalose reduced weight of db/db mice, improved glycemic profile and behavioral characteristics of db/db mice. Immunohistochemical analysis revealed significant decrease of LC3-II expression in hippocampal areas in db/db mice compared to the control WT mice, while trehalose treatment significantly increased this index. We have shown positive effect of trehalose in liver and heart of db/db mice, revealing activation of lipophagy by trehalose. According to electron microscopic study, trehalose significantly decreased volume density of lipid inclusions in cardiomyocytes of db/db mice. Trehalose can restore the suppressed autophagy induced by high glucose *in vivo* in db/db mice. Autophagy activation may be useful for treatment of diabetes, regulating the balance between apoptosis and autophagy by inhibiting mTOR signaling. Mechanism of protective effect of trehalose includes activation of hepatic transcription factor EB (TFEB), increasing TFEB nuclear translocation, elevating level of LC-3-II (marker of autophagosome) in mouse liver. These findings provide the basis for trehalose usage in pathology.

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