EP1_4

An Ultra-Low Dose of Tetrahydrocannabinol (THC) Protects the Heart From Ischemic Injury

Maayan Waldman[1], Yossef Sarne[2,3], Miriam Fishbein[2,3], Eitan Snir[1,3], Eyal Poret[1,3], Asher Shainberg[4], Edith Hochhauser[1,3]

[1]*Cardiac Research Laboratory, Felsenstein Medical Research Center, Rabin Medical Center, Israel*

[2]*Dept. of Physiology and Pharmacology, Tel Aviv University, Israel*

[3]*Sackler School of Medicine, Tel Aviv University, Israel*

[4]*Faculty of Life Sciences, Bar-Ilan University, Israel*

Tetrahydrocannabinol (THC), the major psychoactive component of marijuana,is acannabinoid agonist that exerts its effects by activating at least two specific receptors (CB1 and CB2) that belong to the seven transmembrane G-protein coupled receptor (GPCR) family. Both CB1 and CB2 mRNA and proteins are present in the heart**.**THC treatment was found to be beneficial against hypoxia in neonatal cardiomyocytes in vitro[1]. Furthermore, high doses of various cannabinoid drugs (1-50mg/kg) protect the heart against ischemia in vivo. Recently, we observed the neuroprotective effect of an ultra low dose of THC before brain insult[2].

This research was aimed to test and characterize the cardioprotective effects of a very low dose (0.002mg/kg) of THC which is 3-4 orders of magnitude lower than the conventional doses, administered before myocardial infarction in mice in vivo. Various parameters such as heart function, histology, biochemistry and intracellular signaling were analyzed. Three regimens of THC administration were tested: single THC application 2h or 48h before MI or 3 weeks continuous treatment before the induction of infarct.

All three protocols of THC administration were beneficial. In the case of THC treatment 2 hours before MI, fractional shortening was elevated (37±4% vs. 42±1%), troponin T leakage to the blood was reduced (14±3ng/ml vs. 10±4 ng/ml), infarct size was decreased (29±4% vs. 23±4%), and the accumulation of neutrophils to the infarct area declined (36±10 cells/field vs. 19±4 cells/field). ERK1/2 phosphorylation following infarct was inhibited by pre-treatment with THC.

Conclusion: A single low dose of THC before ischemia is a safe and effective treatment that reduces myocardial ischemic damage

References

[1]Shmist YA, THC protects cardiac cells from hypoxia via CB2 receptor activation and NO production. Mol Cell Biochem. 2006

[2]Fishbein M, Long-term behavioral and biochemical effects of an ultra-low dose of THC: neuroprotection and ERK signaling. Exp Brain Res, 2012