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Asenapine Effects On Peroxidation and Calcium Movements in HL-1 Cells

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Introduction Bipolar patients are at higher risk for cardiovascular morbidity and mortality than their counterparts in the general population. In a recent *in vitro* study, Asenapine, a new antipsychotic for the treatment of mania/mixed mania, was found to keep physiological endothelial function by activation of eNOS-related NO release and to protect endothelial cells against peroxidation by interference with mitochondria, apoptosis and cell survival.

Objectives To examine the cardiac protective effects elicited by Asenapine against peroxidation and on the Ca2+ movements.

Methods In HL-1 that had undergone oxidative stress by 20 min hydrogen peroxide the effects of 30 min pre-treatment with Asenapine on survival and proliferation will be examined. In Fura-2AM loaded HL-1 we will next analyze the effects of Asenapine on Ca2+ movements and the related involvement of cAMP/PKA and PLC pathways, CaMKII, L and T type Ca2+ channels and 5HT1A receptors. The role of 'capacitative" Ca2+ entry, plasma-membrane Ca2+ pump inhibitor (PMCA) and Na+/Ca2+ exchanger will be analyzed. Changes of membrane potential caused by interference with K+ channels will be examined, as well.

Results We expect to find a proliferative and anti-peroxidative effect of Asenapine in HL-1 cells. Asenapine could also affect Ca2+ movements through cAMP/PKA and PLC-dependent signalling and the involvement of 5HT1A receptors. The effects of Asenapine could also be related to changes of plasma membrane by interference with K+ channels and the modulation of PMCA activity and Na+/Ca2+ exchanger.

Conclusions We expect to further confirm the protective effect of Asenapine against peroxidative injuries.Implications will be discussed