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EFFECTS OF ASENAPINE ON ENDOTHELIAL FUNCTIONS AND CARDIAC CELL SURVIVE

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Purpose: Bipolar patients have an increased risk of cardiovascular diseases for lifestyle habits and the use of antipsychotics that correlates with endothelial dysfunctions, in particular the decrease of eNOS activity and plasma NO levels. We aimed to examine the effects of the new atypical antipsychotic Asenapine on NO release and oxidative stress in porcine coronary endothelial cells (CEC).

Methods: NO production was measured in CEC isolated from coronary arteries of pigs and plated in 0.1% gelatin-coated dishes with starvation medium overnight at 37 °C with 5% CO_2. Cells were treated with asenapine 10 pM-100 μM and asenapine+inhibitors. Oxidative stress was generated with 200 μM hydrogen peroxide in the presence of asenapine for 15 min. The cells undergoing apoptosis were measured and proteins extracted from cell lysates were quantified and used for electrophoresis and immunoblotting studies.

Results: Asenapine increased NO release in CEC in a time-dependent way ($p<0.05$) by the phosphorylation of eNOS and plateau was reached at 120s stimulation; no effect was observed on iNOS activation. The association of asenapine and inhibitors suggested the involvement of cAMP/PKA, PLC, p38MAPK, PI3K and ERK1/2 in the intracellular signaling and the β_2 adrenergic receptors-related pathway. Data were confirmed by Western blot analysis. Pre-treatment of CEC with asenapine prevented cell death and mitochondrial membrane potential collapse caused by hydrogen peroxide ($p<0.05$) and counteracted the activation of apoptotic markers.

Conclusions: Asenapine could play a protective role on endothelial function and cardiac cell survival, reducing the risk of cardiovascular disease in maniac patients.

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