

Proliferative Effect of Some Calcium Channel Blockers on the Human Embryonic Kidney Cell Line

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Abstract : Introduction: Numerous epidemiological studies have shown a positive as well as negative association and no association in some cases between chronic use of calcium channel blockers and the increased risk of developing cancer. However, these associations were enmeshed with controversies in the absence of laboratory based studies to back up those claims. Aim: The aim of this study was to determine in mechanistic terms the association between the long-term administration of nifedipine and diltiazem and increased risk of developing cancer using the human embryonic kidney (HEK293) cell line. Methods: Cell counting using the Trypan blue dye exclusion and 3-(4, 5-Dimethylthiazol-2-yl)-2, 5-diphenyl-tetrazolium bromide (MTT) assays were used to investigate the effect of nifedipine and diltiazem on the growth pattern of HEK293 cells. Protein assay using modified Lowry method and analysis of intracellular polyamines concentration using Liquid Chromatography - Tandem Mass Spectrometry (LC-MS) were performed to ascertain the mechanism through which chronic use of nifedipine increases the risk of developing cancer. Results: Both nifedipine and diltiazem significantly increased the proliferation of HEK293 cells dose and time dependently. This proliferative effect after 24, 48 and 72-hour incubation period was observed at 0.78, 1.56 and 25 μM for nifedipine and 0.39, 1.56 and 25 μM for diltiazem, respectively. The increased proliferation of the cells was found to be statistically significantly ($p < 0.05$). Furthermore, the increased proliferation of the cells induced by nifedipine was associated with the increase in the protein content and elevated intracellular polyamines concentration level. Conclusion: The chronic use of nifedipine is associated with increased proliferation of cells with concomitant elevation of polyamines concentration and elevated polyamine levels have been implicated in many malignant transformations and hence, these provide a possible explanation on the link between long term use of nifedipine and development of some human cancers. Further studies are needed to evaluate the cause of this association.

Keywords : cancer, nifedipine, polyamine, proliferation

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