Comparison of Anti-cancer Effects of Atorvastatin on Hormone Receptor-Positive and Triple Negative Breast Cancers: An in-vitro Study

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Elevated serum cholesterol levels have been identified to implicate oncogenesis in breast tissues. Studying the impact of altering the cholesterol synthesis in breast tissue microenvironment *in vitro* as a potential anticancer treatment option holds significance. Research problem: Can widely prescribed statins exert anticancer effects and if so, differently on different breast cancer (BC) cells *in vitro*? A concentration series of active ingredient atorvastatin calcium (10-160 $\mu moldm^{-3}$) was prepared in complete cell culture media. Prepared concentrations were treated on seeded triple-negative MDA-MB-231 and hormone-receptors positive MCF7 BC cells, and nontumorigenic mammary epithelial cell line MCF10A (n=6) in 96 well plates separately. The treated cells were incubated at 37° for 24, 48 and 72 hours. The cell viability was assessed with 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) assay. Dose effect curves were derived and half maximal inhibitory concentrations (IC_{50}) of atorvastatin were calculated at 24, 48 and 72 hours, compared to negative controls. Induced apoptosis was assessed with acridine orange ethidium bromide (AO/EB) staining. The IC_{50} derived from the dose effective curves at 24, 48, and 72 hours were as follows; for MDA-MB-231; 125.8, 33.9 and 9.5 $\mu moldm^{-3}$, for MCF7; 117.0, 98.5, and 78.3 $\mu moldm^{-3}$ and for MCF10A; 177.9, 90.6 and 13.9 $\mu moldm^{-3}$, respectively. At 24 hours atorvastatin exerts more cytotoxicity on MCF7 cells than on MDA-MB-231 cells. The IC_{50} decreased with prolonged incubation in all the cell lines. However, the decrease in IC_{50} was more prominent in MDA-MB-231 cells than in MCF7 indicating more cytotoxicity to triple-negative BC cells in a time-dependent manner. In the AO/EB staining cytoplasmic blebbing, nuclear fragmentation, and loss of membrane integrity were noted at the IC_{50} concentrations at 24-hour incubation confirming that the loss of cell viability is due to induced apoptosis. The anticancer effect exerted by atorvastatin on hormone receptor-positive BC cells is higher than the hormone receptor-negative BC cells, at 24 hours.

Keywords: Breast Cancer, *In Vitro*, Atorvastatin, Anti-Cancer

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