ABSTRACT

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The anti-angiogenic effect of atorvastatin loaded exosomes on glioblastoma tumor cells: An in vitro 3D culture model.

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Exosomes are endogenous nanoparticles with a lipid bilayer membrane whose natural function as carriers of biological materials has attracted much attention. The ability of exosomes to cross biological barriers, especially the blood-brain barrier, has highlighted them as tools of drug delivery to brain tumors. In a previous study, we isolated and characterized exosomes derived from human endometrial mesenchymal stem cells (hEnMSCs exosomes). In the present study, we used hEnMSCs exosomes as carriers for atorvastatin and investigated its pro-apoptotic and anti-angiogenic effects on U87 glioblastoma spheroids 3D co-cultured with Human Umbilical Vein Endothelial cells (HUVECs). In the study of HUVEC proliferation by using MTT assay, cell treatments with concentrations of 5 and 10 μM of free atorvastatin and atorvastatin-loaded hEnMSCs exosomes (AtoEXOs) showed significant differences in inhibition of proliferation compared to other concentrations. Also, 5 and 10 μM of AtoEXOs inhibited HUVEC migration in both scratch closure and transwell migration assays significantly more than that of free atorvastatin. In addition, in vitro HUVEC capillary tube network formation was inhibited by 5 and 10 μM treatment of AtoEXOs significantly more that of free atorvastatin. Moreover, a significant decrease in VEGF secretion and a significant increase in Bax/Bcl2 expression ratio were observed in U87 spheroids 3D co-cultured with HUVECs, especially for 10 μM AtoEXOs compared to other treated cell groups. Our results showed that hEnMSCs exosomes loaded with atorvastatin not only mimicked the anti-tumor effects of free atorvastatin but also potentiated its anti-tumor effects on glioblastoma cells. The enhanced pro-apoptotic and anti-angiogenic capabilities of atorvastatin loaded in hEnMSCs exosomes offer promising new perspectives for the treatment of glioblastoma.

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