Poster

[P26-9] P26-9: Oncologic drugs (5): Pharmacokinetics, TDM practice

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[P26-9-7] Melatonin attenuates EGF-induced migration through downregulating Cathepsin S expression in human retinal pigment epithelial ARPE-19 cells

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Background

Proliferative vitreoretinopathy is a serious sight-threatening disease because of the unearthly migration in retinal pigment epithelium (RPE) cells. Melatonin, a hormone produced by the pineal gland, regulates the day-night cycles as its primary function. Previous studies indicate that melatonin can suppress migration ability of several cancer types such as lung cancer, liver cancer and renal cell carcinoma. In this paper, we explored whether melatonin attenuates EGF-induced migration in ARPE-19 cell line.

Methods

The cell viability of ARPE-19 treated with melatonin alone or combination with EGF was investigated by MTT assay in 24 and 48 hrs. The migration and invasion assay was used in Boyden chamber after treatment of melatonin and EGF in 24hrs. The protease activation was detected by protease array kit. The expression of mRNA and protein after treatment of melatonin and EGF was investigated by RT-PCR and western blot.

Results

The results showed that melatonin reduced the EGF-induced cell proliferation and did not enhance the cell toxicity in 24 and 48 hrs. Also, in Boyden chamber assay, melatonin strongly inhibit the ability of migration and invasion after EGF-induced in 24hrs. Second, the result of protease array demonstrated that the expression of cathepsin S and ADAMTS-1 was inhibited after melatonin treated the EGF-enhanced ARPE-19 cells in 24 hrs. However, PCR results showed cathepsin S, not ADAMTS-1, the expression of mRNA was reduced by treatment of melatonin after EGF-induced. Furthermore, we used Z-FL-COCHO, the cathepsin S inhibitor, in combination of melatonin to treat the EGF-enhanced ARPE-19 cells. The immunoblot results show that Z-FL-COCHO could effectively reduce cathepsin S expression. In Boyden chamber assay, the results also demonstrated that Z-FL-COCHO further enhanced the inhibitory efficacy of melatonin on migratory/ invasive abilities.

Conclusions

These results obviously demonstrate that melatonin can effectively suppress the EGF-induced migration/invasion via the inhibition of cathepsin S. In conclusion, melatonin, the hormone produced by the pineal gland, may have the potentiality for the therapy of proliferative vitreoretinopathy.