

Effect of Sonodynamic Therapy With 5-aminolevulinic Acid on Malignant Gliomas

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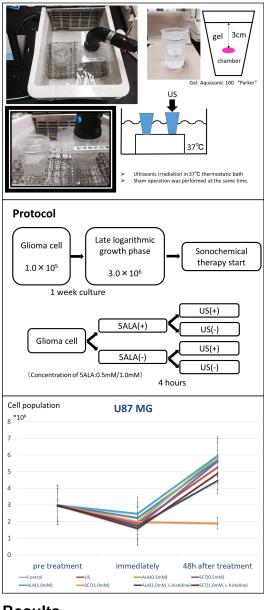


Introduction

Photodiagnosis (PD) with 5aminolevulinic acid (5-ALA) is useful to detect malignant glioma tissue during surgery. On the other hand, photodynamic therapy (PDT) with 5-ALA is not yet popular for malignant gliomas, although PDT is widely used for skin or gastrointestinal cancers. One of the problems of PDT for gliomas is the limit of penetrating distance of light. Since glioma grows invasively into deep tissue, its effect does not reach the peripheral of the tumor. Ultrasound instead can conduct its energy into the deep tissue with less attenuation and is known to activate photosensitizing drug like light. We have been investigating its application for glioma treatment and report the different effects on two glioma cell lines.

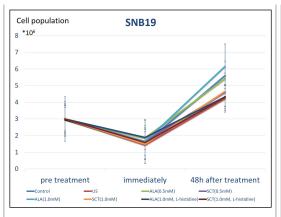
Methods

Two human malignant glioma cell lines (U-87 MG, SNB-19) were cultured in exponential growth phase. The glioma cells were treated with 5-aminolevulimic acid (5-ALA) for 4 hours and then enclosed in plastic tubes. Ultrasonic device UST-770 (ITO Co., Ltd.) was used for all experiments. Ultrasonication (US) was performed at the condition of 2.0W/cm2, 1.0MHz, 5min and the depth of 3 cm. As control, 5-ALA (-) or US(-) groups were set. The number of cells was counted immediately after SDT and after 48 hourincubation.



Results

The SDT with 5-ALA showed suppressive effect (approximately 15% by comparison with a control data) on U-87 MG. Whereas no effect was seen in other groups of U-87 MG, and all groups of SNB-19.



Discussion

-This study showed that the SDT with 5-ALA(1mM) suppressed effect on U-87 MG. On the other hand, no suppressed effect on SNB19. We have recognized the difference of treatment sensitivity in cell lines. This results were not able to indicate weather didn't show the difference of protoporphyrin ix production amount or localization in each cell lines.

- 5-ALA is metabolized finally heme in vivo. However, in tumor cells,

vivo. However, in tumor cells, protoporphyrinIX is accumulated because of decrease of converting enzyme. PpIX is considered to be able to tumor-selective treatment, and so, its effect as an ultrasonic sensitizing agent. The group of added L-histidine showed the effect on ALA-SDT was canceled out, therefore production of effect on ALA-SDT is considered involvement of active oxygen.

Conclusions

SDT with 5-ALA has the potential as an option for treatment of malignant glioma. The conditions have to be investigated for its stable effectiveness. The mechanism of action should also be elucidated to understand the differential effects on each cell lines.

Learning Objectives

By the conclusion of this session, participants should be able to: 1)
Describe the importance of sonodynamic therapy, 2) Discuss, in small groups, 5-aminolevulinic acid, 3) Identify an effective treatment of sonodynamic therapy with 5-aminolevulinic acid

References

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