

The effects of ultrasound and arsenic trioxide on neurogliocytoma cells and secondary activation of macrophages

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ABSTRACT

Aims and background. As a new technique for clinical therapeutics, ultrasound has synergistic effects on traditional chemotherapy. Arsenic trioxide (AS₂O₃), an apoptosis-inducing drug, has successfully been used in the treatment of some tumor types in recent years. Macrophages have both positive and negative effects on the occurrence and development of tumors. The aim of this study was to observe the effects of ultrasound and AS₂O₃ on a glioma cell line and the secondary activation of macrophages by cell death, in order to provide a theoretical basis for the clinical application of AS₂O₃ and ultrasound in glioma treatment.

Methods. Different AS₂O₃ concentrations were used solely or combined with ultrasound in rat glioma C6 cells to induce cell death. The degree of C6 cell death was determined by Annexin V-FITC and PI double staining. The intracellular arsenium concentration and the release of lactate dehydrogenase (LDH) from C6 cells were also measured. The supernatant of C6 cells was then used to stimulate macrophages. Finally, the activation of NF-κB and the secretion of TNF-α and TGF-β1 by macrophages were determined.

Results. The cell death increase in the group where ultrasound was used together with AS₂O₃ was significantly higher than that obtained by either ultrasound or AS₂O₃. The increase was also significantly higher than the sum of the increases in the ultrasound and the AS₂O₃ only groups. At the same AS₂O₃ concentration, additional treatment with ultrasound can significantly increase the intracellular arsenium concentration. The release of LDH from C6 cells showed a close, direct correlation with late apoptosis and necrosis, but did not exhibit an obvious correlation with early apoptosis. The activation of NF-κB and the secretion of TNF-α and TGF-β1 in macrophages also showed a close direct correlation with late apoptosis and necrosis.

Conclusions. This *in vitro* study demonstrates that ultrasound may synergistically enhance the cell-killing effect by promoting AS₂O₃ to enter the C6 cells. Macrophages may be activated by killed C6 cells, especially by necrotic C6 cells.

Key words: neurogliocytoma, macrophage, cell death, ultrasound.

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Acknowledgments: The project was supported by the Chinese Education Commission fund for medical instructors, grant 0220021.

Received July 25, 2008;
accepted May 11, 2009.