GW23-e1387 **SONODYNAMIC EFFECT OF BERBERINE ON MACROPHAGES**

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Tianye Guoshuyuan. *The First Affiliated Hospital of Harbin*

Objectives Atherosclerosis (AS) is the major contributing factor that results in acute cardiovascular events, which leading to the high mortality of cardiovascular diseases, which. The pathophysiological mechanism of atherosclerosis remains unknown. Recently, many researchers implicated that infiltration of inflammatory cell involving macrophage played a critical role in vulnerable plaque. Sonodynamic therapy (SDT) that targets at the inflammatory mechanism of atherosclerosis is a new promising treatment. Berberine, extracted from traditional herbs copies, has been used as an anti-inflammatory agent in clinical practice. Whether it could be applied as a novel sonosensitizer for sonodynamic therapy (SDT) to treat atherosclerosis deserves further exploration. So, in this study, we investigated the effect of berberine-mediated sonodynamic therapy on macrophage within atherosclerotic plaque.

Methods Absorption spectrum and fluorescent emission spectrum of Berberine were measured. (2) Effect of Berberine at different concentration on the cell viability of THP-1 derived macrophages was examined. (3) The intracellular uptake of Berberine by macrophages was detected by a fluorescence microscope. (4) THP-1 derived macrophages were cultured with Berberine at a concentration of 15 g/ml for 2 h and then exposed to pulse ultrasound irradiation (2 W/cm^2 with 0.86 MHz) for 5–15 min. Six-hours later, Cell viability analysis was performed by MTT assay. (5) Six-hours after Berberine-SDT for 15 min, the nuclei were stained with Hoechst 33342 to determine apoptosis and with PI to determine necrosis. (6) Two-hours after Berberine-SDT for 15 min, morphological changes of the cytoskeleton were examined through immune fluorescence. Data were expressed as means±SD and analysis of ANOVA was performed for individual comparisons.

Results The absorption wavelength of Berberine was less than 500 nm. (2) Berberine was distributed in cytoplasm. (3) Six-hours

after treatment with Berberine-SDT for 5–15 min, unlike the cells treated with Berberine-SDT for 5 and 10 min, the viability of cells treated with Berberine-SDT for 15 min decreased significantly. And cell viability in SDT group was lower than that in ultrasound group (48.4%±5.0% vs 72.5%±6.9%, $p<0.01$).4. Six-hours after treatment with Berberine-SDT for 15 min the cells showed a typical apoptotic chromatin fragmentation. In addition, the percentage of apoptotic and necrotic cells in SDT group was higher than that in ultrasound alone group (apoptosis: 31.7%±5.7% vs 25.9%±6.2%, $p<0.05$; necrosis: 16.5%±5.3% vs 4.5%±1.8%, $p<0.01$). (6) Two-hours after treatment with Berberine-SDT for 15 min, the cytoskeleton lost its original features as the filaments dispersed and the cytoskeletal proteins aggregated. Some cells even suffered deformations as blebs. The percentage of cells with disturbed cytoskeletal filaments in SDT group was higher than that in ultrasound group (α-actin: 49.3%±4.2% vs 32.1%±4.5%, $p<0.01$; β-tubulin: 43.1%±6.8% vs 27.3±6.4%, $p<0.01$; vimentin: 40.8%±5.0% vs 29.6%±7.1%, $p<0.01$).

Conclusions The results suggested that Berberine was a novel sonosensitizer. Berberine-SDT could inhibit cell viability of macrophages, induce apoptosis and necrosis of macrophages, and lead to cleavage of cytoskeleton. Berberine-SDT could be used as a novel treatment to atherosclerosis.