Efficient promotion of autophagy and angiogenesis by combination therapy with low-energy shockwaves and mesenchymal stem cells in the treatment of erectile dysfunction

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Objective(s): Mesenchymal stem cells therapy (MSCT) and low-energy shock wave therapy (ESWT) has been shown to ameliorate erectile dysfunction (ED). However, the research of combination between MSCT and ESWT is relatively less, and the mechanisms of action remain unclear. To investigate the mechanism of action of MSCT and ESWT in a diabetic ED rat model induced by streptozotocin (STZ).

Material and Method(s): Sprague-Dawley rats were randomly divided into 4 groups. (n=10 per group): 1) DM group, 2) DM+ESWT group, 3) DM+MSCT group, 4) DM+ESWT+MSCT group. And the normal group is the control group. Erectile function and other expression experiments were carried out after STZ injection of 8 weeks. Immediately after recording of intracavernous pressure (ICP), the penis was then harvested for histologic analysis, ELISA and western blotting.

Result(s): The ratio of ICP/MAP was significantly higher in the ESWT+MSCT group than in the ESWT and MSCT only treated groups (P<0.05). The quantitative result of the ESWT+MSCT group is very close to the result of the control group. The treatment stimulated angiogenesis and vasodilatation in corpus cavernosum. The result was significantly higher in the ESWT+MSCT group than in the ESWT and MSCT only treated groups, which proved that it could stimulate the angiogenesis and vasodilatation. ESWT increased the quantity of MSCs in the corpus cavernosum and also induced MSCs to express more VEGF in vitro and vivo. VEGF activated the PI3K/AKT/mTOR and NO/cGMP signaling pathway in the corpus cavernosum. The treatment stimulated autophagy and decreased apoptosis in the corpus cavernosum. Furthermore, it can promote the MSCs recruitment by inducing penile tissues to express more SDF-1 and PECAM.

Conclusion(s): Combination of ESWT and MSCT can get a better result than a single way by expressing more VEGF which can take part in autophagy by triggering the PI3K/AKT/mTOR signaling pathway. This cooperative therapy can provide a new research direction in ED treatment for the future.

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