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Focused extra-corporeal shockwave treatment during early stage of osteonecrosis of femoral head

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In recent years, increasing evidence has demonstrated that extra-corporeal shockwave therapy (ESWT) can offer an effective and non-invasive method for the treatment of musculoskeletal disorders, such as shoulder tendinopathies, lateral epicondylopathy of the elbow, greater trochanteric pain syndrome, patellar tendinopathy, Achilles tendinopathy, plantar fasciitis, and bone disorders.[1,2] As a safe, cheap, and non-invasive therapeutic method, ESWT has played a promising role in orthopedic medicine.[3-5] Inspired by this, several researchers have attempted to investigate its use for treating osteonecrosis of the femoral head. ESWT deserves being recommended as the optimal choice for osteonecrosis of the femoral head (ONFH).

ONFH was at first described as an ischemic lesion in the hip area, which may eventually progress to disability.[6] After the collapse of the femoral head, patients who desire the restoration of hip function have no choice but to resort to total hip replacement. This would cause a huge financial burden. Given this, the importance of hip-preserving procedure during the early period of ONFH should be emphasized.[7] Recent evidence has proven that ESWT has good efficacy when performed during the early stages of ONFH as a non-invasive intervention.[6,7] Within the last 5 years, several researchers have demonstrated the role of ESWT for the treatment of ONFH in published manuscripts, clinical trials, meta-analysis, and reviews.[4,8-12] However, only a few of these studies have demonstrated sufficient evidence. Randomized controlled trials are required to conclusively demonstrate the efficacy of ESWT.

Extra-corporeal shockwave (ESW) is a type of pressure wave whose energy changes rapidly within a relatively short period of time after being triggered. It has a fast rise time, high amplitude, and a short duration. In terms of technique, it could be generated using three different sources, namely electrohydraulic, electromagnetic, or piezoelectric.[2] Because of the acoustical impedance of shockwaves as it passes through the layers of different tissues, the pressure is partially absorbed which results in the decrease in pressure amplitude.[2] Because of this, ultrasonic coupling agents are required during ESWT in order to reduce the energy loss between the different media.

In term of biomechanics, ESW has been proven to be effective in inducing angiogenesis and bone remodeling, which might be the key link in the regeneration of the diseased femoral head.[13-15] From shock wave generation to the final effect phase, this procedure includes four phases, namely physical phase, physicochemical phase, chemical phase, and biological phase.[2] This procedure begins with a physical phase. A shockwave is generated using a focused shock wave device. Prior to this, the relevant parameters are set to an appropriate value in order to have an effective treatment without harming living tissue; then, in the physicochemical phase, waves transmit through the layers of media, cutaneous tissue, and subcutaneous tissue. After reaching the diseased areas, shock waves stimulate the body tissue to initiate signal pathways; next, during the chemical phase, activation of local cells induces several cytokines to be secreted around the diseased tissue. The cytokines produced by living tissue affected by the shock wave exert their effects on the surrounding tissues, such as blood vessels and extracellular environment. Lastly, but most importantly, there is an increase in local metabolism resulting in tissue repaired. The mechanism of action of ESWT is summarized in Figure 1A. Specifically, the shockwave induces

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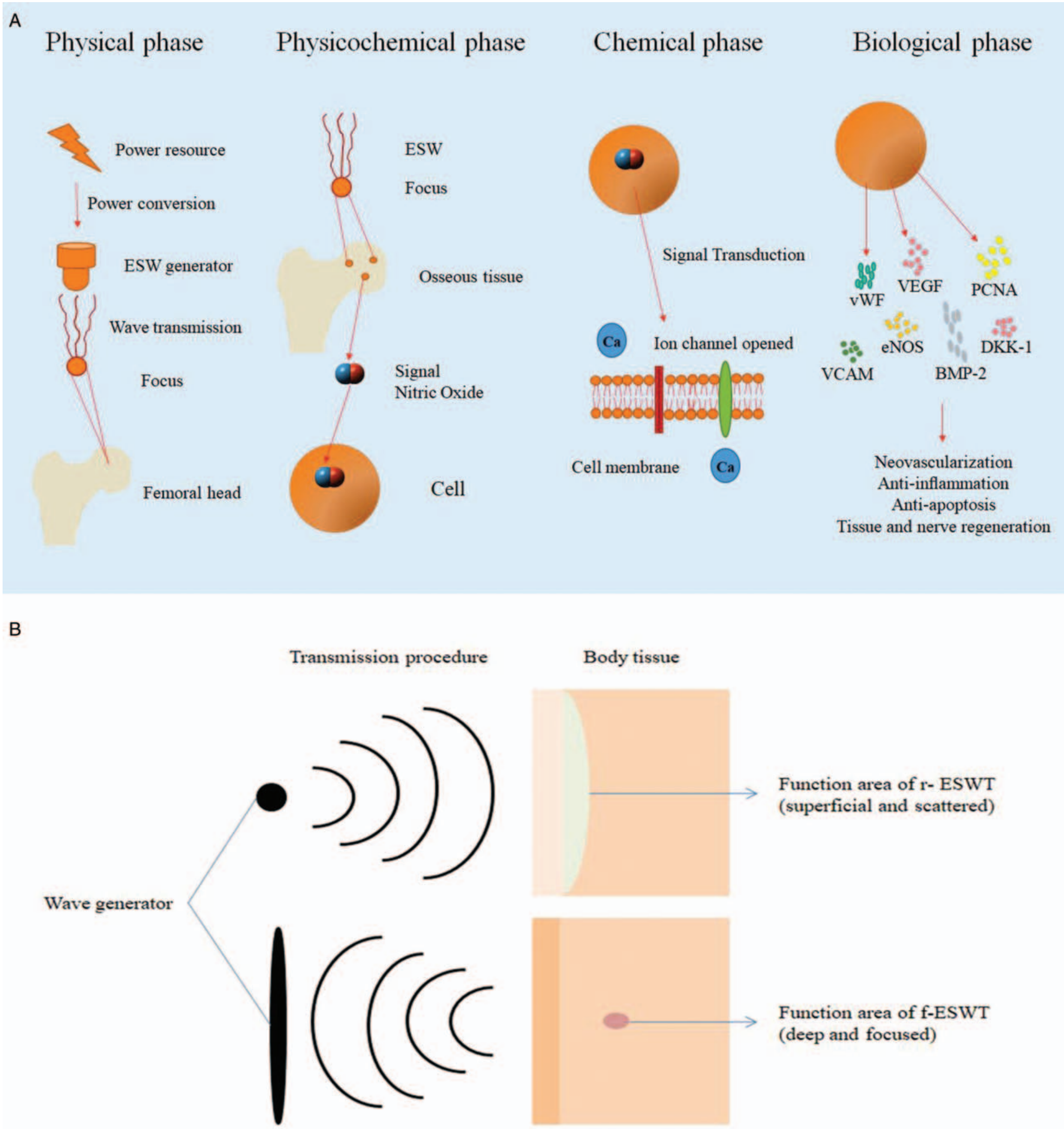

Figure 1: The four-stage process of shock waves acting on human tissues (A), and different working mode of extra-corporeal shock wave and radial pressure wave (B). BMP-2: Bone morphogenetic protein-2; DKK-1: Orthogenesis factor Dickkopf-1; eNOS: Endothelial nitric oxide synthase; ESW: Extra-corporeal shock wave; f-ESWT: Focused extra-corporeal shock wave; PCNA: Proliferation cell nuclear antigen; r-ESWT: Radial extra-corporeal shock wave; VCAM: Vascular cell adhesion molecules; VEGF: Vascular endothelial growth factor; vWF: Von Willebrand factor.

regeneration of local vessels and bone tissue by up-regulating angiogenic and orthogenetic factors, such as von Willebrand factor, vascular endothelial growth factor, cluster of differentiation 31, Winless 3a, bone morphogenetic protein-2, osteocalcin, alkaline phosphates, insulin-like growth factor, and proliferation cell nuclear antigen, while down-regulating anti-inflammation markers such as inter-cellular cell adhesion molecules, vascular cell adhesion molecules, and orthogenesis factor Dickkopf-1.[13,14,16]

Wang *et al*[17] stated that ESWT could be the most effective intervention for non-traumatic ONFH based on their meta-analysis where ESWT was compared to core decompression, multiple drilling decompression, vascularized fibular grafting, free-vascularized fibular grafting, inverted femoral head grafting, vascular iliac pedicle bone grafting, osteotomy, and tantalum implantation. This suggests that ESWT alone was the better choice for early-stage ONFH.

Based on the mechanism, there are two types of shockwave therapy that is used currently. In addition to focused shockwave, there is the radial pressure shockwave (RPW) which is termed radial ESWT (r-ESWT).[3] (The difference between the two waves is shown in Figure 1B.) The biological effects of RPW on living tissue are different from ESWT and are related to the pressure waveform. While focused ESWT targets at a specific point deep in the body, RPW has effects on a large but superficial area by generating cavitations where simple vibrations are unable to.[18,19] Hence, focused ESWT is recommended for ONFH, while r-ESWT is unable to have its therapeutic effects in the deep layer where the femoral head is located.

As a non-invasive treatment, according to systematic review which analyzed plenty of studies on shockwave therapy, no severe adverse events happened.[18] From previous research, neither local nerve and muscle damage nor ESWT-related systemic problems occur in patients undergoing ESWT.[5,7] Some of these patients experience temporary ecchymosis and local mild swelling after treatment.[11] As for patients who undergo high-energy ESWT, 32.4% of them had the problem of mild local swelling and erythema. However, all these events resolved within a few days.[11] Damage to the femoral artery, vein, and nerve was observed in dogs' hips if the energy flux density of the shock wave was beyond 0.47 mJ/mm^2. The most significant effect is the damage to the muscular medium layer.[20] Hence, physicians are likely to select the back approach to perform ESWT so as to reduce the damage to important major vessels and nerves right before the femoral head in the inguinal region. Prior to ESWT, ultrasonography was used to locate vessels and nerves.[11] No apparent vessel or nerve injuries have been observed in recent clinical studies.[1,7-9,11] Physicians should be aware of acute pain or discomfort apart from the presence of lesions in order to cease operation on time.

In conclusion, the current literature indicates that ESWT is indeed an effective method for the treatment of early stage of ONFH and is superior to other methods of preserving the hip because it is inexpensive, non-invasive and easy to operate. Looking to the future, as the relevant trials have partly explained the principles of the ESWT but not thoroughly, we need further researches to figure it out. In terms of clinical use, it requires multi-center clinical trials with large samples to develop guidelines for its usage in the treatment of ONFH.

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Conflicts of interest

None.

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