Review Article

Effects of Extracorporeal Shockwave Therapy on Systemic Sclerosis: A Review Study

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Abstract

Background: Systemic sclerosis (SSC) is an uncommon chronic autoimmune disorder that can involve several organs. The manifestations of SSC occur due to fibrosis in the tissue. Patients with SCC experience stiffness in skin, muscles, and calciumic mass that are known as calcinosis cutis. Extracorporeal shock wave therapy (ESWT) is a safe rehabilitation method that is used in different disorders. The use of ESWT in SSC has not been well-assessed. In this study, we aimed to review the effects of ESWT on systemic sclerosis.

Materials and Methods: We reviewed studies that were published from 2010 to 2023. Five studies were found that evaluated the effects of ESWT on SSC. Fifty-nine patients were assessed in these studies.

Results: The results of studies demonstrated that ESWT reduced pain and skin stiffness. It has remarkable effects on endothelial progenitor cells, endothelial cells, endothelial growth factor, and von Willebrand factor. No side effects were reported in the studies.

Conclusion: ESWT is a suitable method for SSC management. This method can be used safely in patients with SSC to improve their quality of life.

Keywords: Extracorporeal shockwave therapy, Systemic scleroderma, Systemic sclerosis

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Introduction

Systemic sclerosis (SSC) or scleroderma, which is characterized by a complex and poorly understood pathogenesis, is an uncommon connective tissue disease[1]. SSC is a multifaceted condition that impacts various systems, exhibiting a broad spectrum of clinical manifestations. Diffuse cutaneous SSC is generally associated with more pronounced symptoms and elevated mortality rates in comparison to limited cutaneous SSC. Furthermore, the severity of SSC is often greater in males, African Americans, and those who experience a later onset of the disease. Limited SSC or CREST syndrome is characterized by the presence of calcinosis, esophageal dysmotility, Raynaud's phenomenon, telangiectasia, and sclerodactyly. Diffuse SSC is characterized by cutaneous thickening that can impact regions proximal to the face, elbows, knees, and trunk. Both limited and diffuse forms of cutaneous SSC are related to various systemic manifestations[2-4].

There is currently no exact treatment or disease-modifying agent capable of altering the natural progression of the disease. Timely diagnosis is essential

for enhancing patient outcomes. A thorough clinical assessment, along with the identification of impacted organs and the progression of the disease, is vital for ensuring the effectiveness of treatment. Additionally, treatment objectives should adopt a holistic approach, customized to enhance the quality of life for patients, as the manifestations of the disease significantly reduce their quality of life[1].

Extracorporeal shockwave therapy represents a minimally invasive intervention that has demonstrated efficacy in alleviating pain due to persistent lesions of calcinosis that are not candidates for surgical treatment, primarily through the mechanism of nerve decompression[5]. In this study, we aimed to review the effect of extracorporeal shock wave therapy on the rehabilitation of patients with SSC.

Methods

This study aimed to assess the effect of shock waves for the rehabilitation of patients with systemic sclerosis. We searched PubMed/MEDLINE, Web of Science, EMBASE/Elsevier, Scopus, and CENTRAL from the start of 2010 to the end of 2023. The search keywords were as follows: “shockwave”, AND/OR “extracorporeal shockwave”, AND/OR “systemic sclerosis”, AND/OR “systemic scleroderma”.

The full text of the articles was reviewed, and data about the effect of extracorporeal shockwave on the patient’s life were assessed. If there was no access to the full text of an article, the article was excluded from the current review.

Results

We found five articles on the issue of assessment of extracorporeal shockwave effects on systemic sclerosis. Fifty-nine patients were evaluated. Four studies were conducted only on patients with SSC[6-9], and one study was done on patients with calcinosis cutis that may be present due to SSC[10]. The methods were different, and in this section, we review the studies one by one.

Blumhardt et al.[9] performed extra-corporeal shock wave therapy (ESWT) for four patients with SSC for 12 weeks without pre-ESWT or during ESWT analgesic use. The ESWT was administered in three sessions on the calcinosis cutis of fingers. A significant decrease in pain was observed in the treated fingers of two patients. Additionally, there was a significant reduction in the size of the calcinosis. No adverse events were found[9].

Tinazzi et al.[8] evaluated the effects of ESWT on progressive systemic sclerosis in 30 patients. Modified Rodnan score was used for the evaluation of skin involvement in this study. Twenty-eight patients completed three sessions, and two patients completed two sessions. They found that the Rodnan score significantly reduced after the first session. Pain was significantly reduced during the treatment. Based on the visual analogue scale (VAS 0-100), the mean pain was 47.2±14.9 at the baseline, and it had a decreasing trend after the 30th day (31.4±17.3). Vascularity and skin thickness didn’t change during and after the study period. Tinazzi et al. also evaluated the effects of ESWT on the laboratory data of the patients, and they found that levels of circulating endothelial cells and endothelial progenitor cells were significantly increased at 30th and 90th days[8].

Belloli et al.[7] evaluated the effect of 4 sessions of ESWT on 6 SSC females. They reported that von Willebrand factor and vascular endothelial growth factor in serum significantly decreased after the first session, but it was stable in other sessions. Total Rodnan score did not change at the end of the study, but fingers' Rodnan score significantly reduced. Cutaneous wellness was assessed based on VAS, and it was found that it improved significantly by ESWT[7].

Saito et al.[6] performed ESWT for nine patients with SSC for nine sessions, weekly. They assessed the effect of ESWT on skin ulcers, and no patient had calcification. At the baseline, there were 5.4 ulcers per patient. The average number of ulcers/patients was 2.3±0.5 at the 4th week, and at the 9th week, it was 1.1±0.4 ulcers/patient, which demonstrated that the number of ulcers significantly reduced. At the 20th week, the ulcer reappeared, and the average value of ulcer/patient reached 2.2±1.1. It should be highlighted that there was a significant difference in terms of the number of ulcers between baseline and the 20th week. Large ulcers were found in 18 patients, and at the 9th week, only eight patients had large ulcers, and ten of them didn’t have large ulcers. The baseline VAS score was 43.3±9.3 at the baseline, and it significantly

decreased to 18.1±6.4 in the last session, but it gradually increased and reached 30.2±11.3 at the 20th week. Assessment of Rodnan skin score at 9th and 20th weeks demonstrated that it significantly improved. Disability of patients was assessed by the EuroQol 5 dimensions (EQ-5D) and Health Assessment Questionnaire (HAQ). Although HAQ didn't change significantly after the treatment, EQ-5D significantly improved at the 9th session and at the end of the study. The mean finger-tip temperature didn't change during and after the sessions. ESWT had no side effects[6].

Sultan-Bichat et al.[10] evaluated three sessions of ESWT on calcinosis cutis due to different diseases. They assessed eight patients, including one patient with amyopathic dermatomyositis, four patients with chronic venous insufficiency, and 3 SSC. They found that there was no significant decrease after 6 months of the last session in terms of the calcinosis cutis area. There was no remarkable side effect. Sultan-Bichat et al. mentioned that although no significant radiologic or biologic changes occurred in the patients following ESWT, the VAS score for pain reduction was observed in the patients[10].

Discussion

Systemic sclerosis (SSc) is marked by the progressive development of fibrosis affecting both the skin and internal organs, which can result in organ failure and alterations in the morphology and function of blood vessels. It is important to note that SSc is not a homogeneous condition; it encompasses various clinical forms, primarily limited systemic sclerosis (lSSc) and diffuse systemic sclerosis (dSSc). The prevalence of SSc is relatively low, with global incidence rates estimated to range from 3 to 24 cases per 100,000 individuals. The disease exhibits a significant gender disparity, as women are 3 to 5 times more likely to be diagnosed with SSc compared to men, with the highest incidence occurring between the ages of 35 and 55 years[11-13].

At present, there is an absence of curative therapies or medications that can effectively halt or substantially slow the progression of the disease. Nevertheless, over the past few decades, there has been a modest improvement in the survival rates of patients diagnosed with SSc. This enhancement can be attributed to the implementation of organ-targeted therapies, which are grounded in the understanding of the intricate nature of treatment and the necessity for personalized approaches that consider both the duration of the disease and the extent of organ involvement[14].

SSc, like other chronic disorders, significantly impacts the quality of life of affected individuals in various dimensions. Among the challenges faced are persistent fatigue, restrictions in the capacity to engage in daily activities, particularly those requiring manual dexterity, and the erratic progression of the disease, notably in its diffuse form. Patients often experience psychological distress associated with skin and internal organ complications, as well as sleep disturbances. Additionally, there is a struggle with accepting alterations in facial and overall physical appearance, which can contribute to diminished self-esteem. A lack of understanding regarding the disease further exacerbates difficulties in effective self-management[15,16].

Shock wave therapy represents a non-invasive treatment modality that employs a brief, single-impulse acoustic wave lasting approximately 1 microsecond. This technique targets various areas of the body to induce analgesia and promote healing through a process known as mechanotransduction. The application of shock waves is recognized as a practical, non-invasive approach that is both economically and temporally efficient in its therapeutic outcomes[17,18].

The precise physiological mechanisms underlying the therapeutic effects of shock wave therapy remain incompletely elucidated. However, this modality induces a biological response, known as mechanotransduction, as it traverses various tissues. This process results in several beneficial outcomes, including analgesia, osteogenesis, neovascularization, and tissue repair. Notably, the therapy is associated with pain relief, enhanced protein synthesis, increased vascularization, improved cellular proliferation, the breakdown of calcium deposits in tissues, and a protective influence on both cartilage and bone[19,20]. Although the effect of ESWT was assessed on different disorders, few studies were conducted on SSC.

Mentioned effects of ESWT, like analgesia and neovascularization[19,20], were assessed in the studies reviewed in the current report. All reviewed studies

reported that ESWT significantly decreased pain in patients with SSC[6-10]. Vascularity and skin thickness were assessed by Tizzani et al., and they did not change significantly. However, the levels of circulating endothelial cells and endothelial progenitor cells were significantly increased on the 30th and 90th days (8), which differed from the effects mentioned for ESWT[19,20]. Circulating endothelial cells and endothelial progenitor cells are important factors for vasculogenesis. Although not fully understood, some studies demonstrated that impairment in these factors is associated with SSC[21,22]. Since all studies about the effects of ESWT on SSC had low sample sizes, the results of these studies should be re-evaluated in further studies with a larger population.

In terms of blood serum parameters, Belloli et al.[7] reported that von Willebrand factor and vascular endothelial growth factor in serum significantly decreased. Up-regulation of factors like endothelial growth factor (VEGF) was found in SSC[23]. Also, the disease is associated with increased von Willebrand factor[24]. The study by Belloli et al. demonstrated that ESWT can decrease the factors affecting SSC.

Blumhardt et al. found a significant decrease in the size of the calcinosis[9]. Saito et al. evaluated the effects of ESWT on SSC ulcers. They found that ESWT significantly reduced the number of ulcers. Assessment of Rodnan skin score at 9th and 20th weeks demonstrated that it significantly improved. HAQ didn't change significantly after the treatment, EQ-5D significantly improved at the 9th sessions and at the end of the study[6]. Belloli et al. showed that the total Rodnan score didn't change by ESWT, but the fingers' Rodnan score significantly reduced[7]. The modified Rodnan skin score serves as an assessment of skin thickness and is utilized as either a primary or secondary outcome measure in clinical trials focused on systemic sclerosis[25]. EQ-5D is a method for health-related quality of life assessment[26]. Therefore, based on these studies, ESWT can increase the quality of life of patients with SSC by reducing ulcer size, pain, and/or increasing skin elasticity.

Sultan-Bichat et al.[10] evaluated the effects of ESWT on calcinosis cutis of amyopathic dermatomyositis, chronic venous insufficiency, and SSC. They reported that the calcinosis cutis area didn't change by ESWT, and ESWT only had sound effects on pain relief[10]. The results of this study (except for pain) were in contrast with those of other studies. The cause of this difference may be related to the samples that were evaluated in this study, because not all patients were involved with SSC. All studies reported that the ESWT has no adverse effect, and all confirmed that it is a safe method[6-10].

Conclusion

Although there are few studies with short sample sizes regarding the effects of ESWT on SSC, these studies have demonstrated that ESWT is an effective method for managing SSC, which can improve patients' quality of life by reducing pain, increasing cutaneous elasticity, and decreasing calcinosis size. The ESWT also regulates serum factors that are associated with disease activity, like endothelial progenitor cells, endothelial cells, VEGF, and von Willebrand factor.

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Conflict of interest

The authors further declare that they have no conflict of interest.

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