Review

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Review

Extracorporeal Shock Wave Therapy (eSWT) in Spinal Cord Injury

Józef Alphons Opara [1,*], Robert Dymarek [2], Mirosław Sopel [3] and Malgorzata Paprocka Borowicz [4]

[1] Department of Physiotherapy, The Jerzy Kukuczka Academy of Physical Education, 40-065 Katowice, Poland
[2] Department of Nervous System Diseases, Faculty of Health Sciences, Wroclaw Medical University, 50-367 Wrocław, Poland; robert.dymarek@umw.edu.pl
[3] Faculty of Medicine, Wrocław University of Science and Technology, 50-370 Wroclaw, Poland; miroslaw.sopel@pwr.edu.pl
[4] Department of Physiotherapy, Faculty of Health Sciences, Wroclaw Medical University, 50-367 Wrocław, Poland; malgorzata.paprocka-borowicz@umw.edu.pl
* Correspondence: j.opara@awf.katowice.pl

Abstract: Background: Injury of the spinal cord causes motor and sensory dysfunction, and pathological reflexes, leading to paraplegia or tetraplegia. The sequelae of traumatic spinal cord injury (SCI) is a significant burden and impact on healthcare systems. Despite constant progress in medicine, traumatic SCI still remains irreversible. Till now, no satisfying treatment that can enable neuronal regeneration and recovery of function at the damaged level has been found. Hundreds of experiments have been conducted on various possibilities of influencing spinal regeneration, some of them have yielded promising results, but unfortunately, the successes obtained in experimental animals have not translated into humans. Methods: This narrative review article presents the application of Extracorporeal Shock Wave Therapy (eSWT) in Spinal Cord Injury. The article has been divided into parts: 1. Use of extracorporeal Shock Wave Therapy for regeneration of the spinal cord after traumatic Spinal Cord Injury. 2. Application of extracorporeal Shock Wave Therapy in spasticity after Spinal Cord Injury. In both cases, the hypotheses of possible mechanisms of action will be described. Results and conclusions: A small number of clinical trials have demonstrated the potential of eSWT to influence the regeneration of the spine, as an innovative, safe, and cost-effective treatment option for patients with SCI. Some reports have shown that eSWT can improve spasticity, walking ability, urological function, quality of life, and independence in daily life.

Keywords: extracorporeal shock wave therapy; neuromodulation; neuroregeneration; recovery; spasticity; spinal cord injury

1. Introduction

Despite constant progresses in medicine, traumatic spinal cord injury (SCI) still remains irreversible. The sequelae of the spinal cord is motor and sensory dysfunction, pathological reflexes, which leads to paraplegia or tetraplegia, and a significant burden and impact on healthcare systems. For diagnostics issues commonly used is International Standards for Neurologic Classification of Spinal Cord Injury recommended by American Spinal Injury Association (ASIA) and International Spinal Cord Society (ISCoS) [1].

Till now, no satisfying treatment that can enable neuronal regeneration and recovery of function at the damaged level has been found. Main important pathophysiological mechanisms of spinal cord injury are: disruption to the microcirculation and the secondary injury due to a cascade of biochemical and pathological changes [2]. Hundreds of experiments have been conducted on various possibilities of influencing spinal regeneration, some of them have yielded promising results, but unfortunately the successes obtained in experimental animals have not translated into humans.

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The aim of drug interventions is improving of the microcirculation which can has the effect on the microenvironment and promote recovery following spinal cord injury. Recently (2024) Wang and Bai described the pharmacological interventions targeting the microcirculation following traumatic spinal cord injury. The authors listed seven categories of the drugs mentioned above: neurotrophic factor-related drugs, chemical synthetic drugs and biological agents, corticosteroids, endogenous vasoactive substance inhibitors or antagonists, matrix metallopeptidases (MMP)-related drugs, human immunoglobulin G (HIGG), and carbon monoxide (CO) donors and other drugs. Clinical testes showed that these drugs have promising effects on functional recovery after SCI, alleviating blood-spinal cord barrier (BSCB) damage, enhancing intimal protection, and inducing vascular endothelial repair and regeneration. By improving blood flow in the spinal cord, they are able to forced the injury microenvironment and support the repair of spinal cord tissue [3].

Very important role plays the comprehensive rehabilitation for SCI patients - this should be focused on participation is the optimal independence in activities of daily living (ADL) and ability of walking [4]. Recently, new innovative methods of walking recovery based on robots have appeared, one of them is robotic-assisted gait training [5,6].

For at least three decades, there has been an increasing number of experimental studies on the therapeutic effects of stem cells in SCI due to their ability to differentiate into neural cells and release neurotrophic factors. Bonosi et al. has prepared an overview consisting of an up-to-date summary of the current research status, challenges, and future directions for stem cell therapy in SCI models. The results are generally promising - stem cells-based therapy has some neuroregenerative and neuroprotective effects in SCI treatment. However, Bonosi et al. indicated some safety concerns. Following these, immunotoxicity, immunogenicity, and carcinogenicity associated with cell therapy are often discussed in preclinical studies. Limited cell survival and limited integration have been common obstacles in previous studies involving various experimental designs, including cell number, treatment time, and transplantation strategies. Genetic stability, generational consistency and storage safety of stem cells also need to be considered. To determine clinical use, the mechanism of action and biological properties must be investigated. Small sample size, limited oversight, and low quality are the most common problems in most registered clinical trials that hamper the development of stem cell therapies. Standard protocols are difficult to confirm due to heterogeneity in the type and level of injury, treatment time, and varying numbers of transplanted cells. One specific type of stem cell achieves only a limited therapeutic effect. In final conclusion the authors stated that as well use of genetic engineering technologies as cell conjugation, combination therapy with neuroprotective factors, trophic factors, biomaterials, and rehabilitation may help improve the therapeutic effectiveness of stem cells in heterogeneous patient populations [2].

In a recent review article, Rahmadian et al. described biomaterials used to treat this disease and techniques used to create nanostructured biomaterials. They said nanomedicine innovations in SCI management hold promise in bridging the gap [7]. In another recent review article, Tian et al. presented the latest advances and challenges in the treatment of SCI. They considered the future of SCI treatment and provided information on how to reduce the translation gap that currently exists between preclinical research and clinical practice. The authors concluded that clinical trials should emphasize interdisciplinary conversation and collaboration to identify optimal combinatorial approaches to maximize therapeutic benefits in humans with SCI [8]. Youseffard et al., based on a systematic review of 14 studies and 17 separate animal experiments, found that the self-assembling peptide could potentially aid in the recovery of motor function after brain injury through axonal regeneration help locomotion recovery after SCI due to axon regeneration [9].

It seems that the future belongs to the use of 3D bioprinted scaffolds for neuronal regeneration. Szymoniuk et al. performed a systematic review of preclinical in vivo studies on this topic. They found eleven animal studies describing the transection rat model of SCI; six of the included studies involved 3D bioprinted scaffolds enriched with stem cells, two studies involved 3D bioprinted scaffolds combined with growth factors, and three studies involved stand-alone 3D bioprinted scaffolds, showing varying risks of bias. All included studies observed significant improvements in functional outcomes compared to the control group. Functional recovery corresponded to changes

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that could be observed at the site of injury in histological analyses. The authors concluded that the results of this systematic review suggest that 3D bioprinted scaffolds may represent a feasible therapeutic approach for the treatment of SCI. They suggested that further evidence from other experimental SCI models is necessary before clinical translation of 3D bioprinted scaffolds [10].

This review article has been divided in to parts: 1. Use of the extracorporeal Shock Wave Therapy early after traumatic Spinal Cord Injury, and 2. Application of extracorporeal Shock Wave Therapy in spaticity post Spinal Cord Injury.

2. Use of the Extracorporeal Shock Wave Therapy after Traumatic Spinal Cord Injury

In the literature, physical methods used to regenerate a damaged spinal cord are rare. Neuromodulation in the irreversibly injured spinal cord is better known, such as: electrical spinal cord stimulation (SCS), which can be epidural or via implanted electrodes, transcutaneous spinal cord stimulation (TSCS), vagus nerve stimulation (VNS), electroacupuncture, direct transcutaneous current stimulation (tDCS), etc. Despite the literature confirming the independent benefits of such stimulation, there are reports confirming that it may be more effective in restoring motor and autonomic functions in combination with physical exercise or stem cell transplantation [11–16].

In a recent review article, Liu et al. presented the future of artificial hibernation medicine in protecting nerves and organs after spinal cord injury. As one of the artificial hibernation techniques, mild hypothermia has tentatively confirmed its clinical impact on SCI. Recent research shows that artificial hibernation technologies have therapeutic implications for nerve damage following spinal cord injury by inhibiting inflammation, immunosuppression, oxidative defense and possible central protection [17].

Extracorporeal shockwave therapy (eSWT) is a form of mechanotherapy with a peak pressure of about 1,000 times more than ultrasound therapy. ESWT has been firstly applied as a non-invasive, out-patient alternative to surgery for those with many joint and tendon disorders. SWT was first used in the urology clinic at the University of Munich in 1980 for lithotripsy of human kidney stones and was approved by the US Food and Drug Administration in 1984 [18]. Currently, eSWL is a treatment method that uses strong acoustic pulses , which are most often used in the treatment of kidney stones and in physiotherapy to reduce pain, increase metabolism at the cellular level, revascularize and regain normal muscle tone after various diseases (mainly in diseases of the musculoskeletal system, such as frozen shoulder, tennis elbow, degenerative knee joint, tendinopathies, low back pain, sports injuries) and orthopedics [19,20]. It has also been utilized to treat wounds, urological diseases, and male erectile rejuvenation or even in neurogenic heterotopic ossification [21].

One can divide ESWT into focused (feSWT) and radial (reSWT), based on the wave patterns used. It is first generated electrohydraulically, electromagnetically or piezoelectrically and then focused into a focal zone of tissue. As an acoustic wave, feSW is characterized by high pressure exceeding 1000 bar (100 MPa), extremely short rise time (<10 ns), short duration (<10 ms), and a wide frequency spectrum (16–20 MHz). Unlike feSW, radial extracorporeal shock wave (reSW) does not have the characteristics of a shock wave, such as short rise time, high peak pressure, and nonlinearity. ESWT is believed to cause two important physical effects on tissues: mechanotransduction and cavitation, which may play a major role in introducing shock waves into tissues and triggering physiological actions at the molecular and tissue levels, which then trigger beneficial biological events such as tissue regeneration and repair, angiogenesis, pain relief, metabolic activation and anti-inflammatory effects, leading to favorable therapeutic outcomes [22]. Considering the mechanisms of action of eSWT, Simplicio et al. indicates vascularization, protein biosynthesis, cell proliferation, neuroprotection and chondroprotection [23]. Describing eSWT as mechanotransduction d`Angelo et al. foresee new interesting and promising applications in the fields of regenerative medicine, tissue engineering and cell therapies [24]. Guo et al. published a review on the possibility of regeneration and repair of neurological disorders using the eSWT method. They said recent animal studies and clinical trials have demonstrated the potential of eSWT as an innovative, safe and cost-effective option for the treatment of neurological disorders as well as diseases of the central and peripheral nervous system. The main parameters influencing the effectiveness of eSWT treatment include air pressure (unit: bar), energy flux density (EFD)

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(unit: mJ/mm2), number of pulses (unit: pulses), and frequency (unit: Hz). EFD is a parameter indicating the energy intensity of shock waves per unit area. It was suggested that ESWT should be divided into low energy (<0.08 mJ/mm2), medium energy (<0.28 mJ/mm2) and high energy (<0.60 mJ/mm2) according to the energy (intensity) value of its EFD [25].

In a study on the treatment of chronic SCI with eSWT, Lee et al. found that behavioral tests in rats improved when stem cell therapy was combined with eSWT. In addition, feSWT at three energy levels (level 1, 0.01 mJ/mm2; level 2, 0.04 mJ/mm2; and level 3, 0.11 mJ/mm2) were applied with 1000 pulses to the spinal cords of rats. Histological examination showed that no neurological disorders occurred after the use of feSWT at these energy levels [26]. Other authors also reported that the use of eSWT in the treatment of rats with SCI reduced neural tissue damage, increased neuroprotective efficacy, promoted BDNF expression, enhanced expression of serum-derived miRNAs, and improved motor function without any harmful effects [27–30].

Leister et al. initiated a two-arm, three-stage, adaptive, prospective, multicenter, randomized, blinded, placebo-controlled clinical trial in 2020 to evaluate the effects of eSWT therapy in acute SCI on motor and sensory functions within 6 months after injury. A total of 82 acute SCI patients were to be recruited for the first phase at 15 participating hospitals in a two-arm, three-stage adaptive trial design. Concentrated eSWT (energy flux density: 0.1-0.19 mJ/mm2, frequency: 2-5 Hz) is applied once at the level of the lesion, five segments above/below and on the plantar surface of both feet during the first 48 h after resentment. The primary endpoint of the study is the degree of improvement in motor and sensory functions 6 months after the injury. Secondary endpoints include routine blood chemistry parameters, spasticity score, walking ability, urological function, quality of life, and independence in daily living. Scientists believe that the use of eSWT activates neural tissue regeneration involving a wide variety of biochemical and cellular events and leads to a reduction in neuronal loss. They hypothesized that eSWT could help improve the treatment of acute SCI in future clinical application [31].

3. The Application of Extracorporeal Shock Wave Therapy in Spasticity after Spinal Cord Injury

Spasticity is a common disabling sequela of upper motor neuron injury, this is why as well as diagnosis and treatment are essential to prevent contractures, minimize pain and maximize functional recovery. The incidence of spasticity after spinal cord injury has not been precisely estimated. Dragojlovic et al. conducted a retrospective study on the incidence of spasticity during the first admission to inpatient rehabilitation in 285 patients with acute stroke, traumatic brain injury, and traumatic brain injury. In SCI, the incidence of spasticity was 48% on admission and 46% on discharge [32].

Based on a 5-year follow-up of 350 patients with an average age of 46 ± 19 years and an average time from spinal cord injury to hospital discharge of 108 ± 95 days (range 1–728 days), Mills et al. created the first predictive model for the development of problem spasticity. These are: age and first documented Glasgow Coma Scale at the time of injury; whether admitted to a rehabilitation facility prior to hospital discharge or discharged directly from an acute hospital to the community; whether the person was taking anti-spasticity medications at the time of discharge; at hospital discharge, neurological status (i.e., neurologic level, motor level, AIS grade, and change in AIS motor score), spasm frequency, and patient-reported impact of pain on activity, sleep, and quality of life [33].

It turned out that no recommendations regarding electrical stimulation parameters in SCI spasticity could be made precisely due to the wide variability of the methodology. Future studies that are better designed and at the highest methodological level are needed. There are several reports on the use of repetitive transcranial magnetic stimulation (rTMS) and transcranial direct current stimulation (tDCS) in SCI. Chen et al. published the results of a systematic review and meta-analysis assessing the effects of non-invasive brain stimulation (NIBS) on motor function after brain injury. A total of 14 randomized controlled trials with 225 participants were included in the study. Nine studies used rTMS and five studies used tDCS. A meta-analysis showed that NIBS can improve lower extremity strength and balance and reduce spasticity. However, upper limb motor ability in the NIBS groups was not statistically significant compared to the control group. Functional mobility in the

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NIBS groups did not reach statistical significance compared to the sham NIBS groups. The authors concluded that NIBS appears to positively affect lower limb motor function in patients with spinal cord injury, despite a marginal P value and high heterogeneity. They recommend further high-quality clinical trials to support or refute the use and optimize NIBS stimulation parameters in clinical practice [34].

Adeel et al. described the effects of paired stimulation with specific waveforms on cortical and spinal plasticity in individuals with chronic spinal cord injury (at least 1 year after injury). Recruited SCI patients underwent three therapeutic interventions in a random order for 4–20 min, followed by 30 min of cycling (control, rTMS) at 20 Hz with transspinal direct current stimulation (tsDCS) and intermittent theta burst stimulation (iTBS) with tsDCS with a 1-week break. The TMS method was used to record the resting motor threshold (RMT), with 90% of its value taken as the stimulation intensity, and the Hoffman (H) reflex was measured by stimulating the tibial nerve in the popliteal fossa. RMT, motor evoked potential (MEP) latency, MEP peak-to-peak amplitude, and H-reflex latency as primary variables, and the Lower Extremity Motor Scale (LEMS) and Modified Ashworth Spasticity Scale (MAS) as secondary variables were analyzed before and after the interventions. Results: MEP latency, MEP amplitude, and LEMS were significantly improved with rTMS-iTBS/tsDCS or rTMS-20 Hz/tsDCS protocols ($p < 0.050$) compared to the control intervention. All other outcome measures, including RMT, H-reflex latency, and MAS score, showed some change but did not fully reach significance. Authors' conclusion: combined rTMS-iTBS/tsDCS stimulation was equally effective in inducing a neuroplastic effect in people with chronic SCI compared to the conventional TMS-20 Hz/tsDCS intervention [35].

There are few reports on the use of eSWT in the treatment of spasticity after spinal cord injury. Comino-Suárez et al. published a case report and literature review on the use of sSWT in the treatment of plantar flexor spasticity in spinal cord injury. The authors claimed that approximately 65–78% of patients with spinal cord injury develop any symptoms of spasticity. Their aim was to investigate the tolerability and short-term effects of rESWT on plantar flexor spasticity in an 18-year-old male with incomplete SCI after five sessions of rESWT. Passive range of motion (A-PROM) increased by 15 degrees at T1 and 25 degrees at T2 compared to T0. The passive drag force on ankle dorsiflexion at low speed decreased in the gastrocnemius and soleus muscles. It also decreased in the gastrocnemius muscle at high speed. However, there was little change in the soleus muscle. Authors' conclusions: the results showed that rESWT combined with conventional therapy is well tolerated and can effectively improve A-PROM and passive resistance force in ankle dorsiflexion in the short term. Further randomized, controlled trials with longer follow-up are needed to confirm the results obtained in patients with SCI [36].

4. Discussion

As can be seen from the above review, there are many methods of spinal cord regeneration, but unfortunately the promising results do not translate to humans. There are many hypotheses trying to explain the mechanisms of possible spine regeneration. Drug interventions targeting microcirculation may improve the microenvironment and facilitate recovery from spinal cord injury. These include: drugs derived from neurotrophic factors, synthetic chemical drugs and biological agents, corticosteroids, endogenous inhibitors or antagonists of vasoactive substances, drugs derived from matrix metallopeptidases (MMP), human immunoglobulin G (HIGG), carbon monoxide (CO) donors and other drugs.

It is believed that the therapeutic effect of stem cells in SCI is due to their ability to differentiate into neural cells and release neurotrophic factors. Many authors express the opinion that the use of genetic engineering technologies, cell conjugation, combination therapy with neuroprotective factors, trophic factors, biomaterials, and rehabilitation may help improve the therapeutic effectiveness of stem cells in heterogeneous populations of SCI patients.

It seems that the future belongs to the use of nanotechnology, artificial hibernation techniques, self-assembling peptide, 3D bioprinted scaffolds and extracorporeal shock wave therapy (eSWT). The newest one – eSWT – is a previously known form of mechanotherapy

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mainly from use in urology and musculoskeletal diseases. It works through mechanotransduction and cavitation, which can cause beneficial biological events such as tissue regeneration and repair, angiogenesis, pain relief, metabolic activation and anti-inflammatory effects, leading to favorable therapeutic outcomes. Due to the lack of clinical reports, future research is needed to precisely determine the optimal parameters of eSWT: air pressure, energy flux density, number of pulses and frequency.

Gollmann-Tepeköylü et al. presented the results of an experimental study on mice. Shock wave therapy (SWT) has demonstrated potent regenerative properties for bone fractures, wounds, myocardial ischemia, and spinal cord injury through activation of innate immune receptor 3 (TLR3). SWT improved motor function and reduced lesion size in wild-type (WT) mice, but not in TLR3 −/− mice, by inhibiting neuronal degeneration and interleukin 6 (IL6)-dependent recruitment and differentiation of neural progenitor cells. Stimulation of both SWT and TLR3 increased neuronal sprouting and improved neuronal survival, even in human spinal cord cultures. Scientists have identified TLR3 as a key factor in enhancing spinal cord regeneration in zebrafish. These findings indicate that TLR3 signaling is involved in spinal cord neuroprotection and repair and suggest that TLR3 stimulation via SWT may become a potent regenerative treatment option [37].

The pioneer of electrical stimulation in spasticity was Hufschmidt who in 1966 described the reduction of spasticity by rhythmic electric shock rectangular electric current of spastic muscles, and then their weakened antagonists during relaxation of spastic muscles. Hufschmidt looked for a mechanism reduction of spasticity of the central component (in addition to the peripheral effect) [38]. In Faculty of Electrical Engineering, University of Ljubljana, Slovenia, various methods of spinal cords electrical stimulation was originated especially electrical functional stimulation (FES) enabling walking in paraplegic persons.

Jusic and Fronjek published in 1970 about their own succesive modification of Hufschidt`s tonolysis in 32 spastic patients [39]. Franek et al. also described their own metods of electrostimulation in spastic paraplegic patients [40]. However, a recommendation of the stimulation parameters cannot be accurately assumed because of high variability in the methodology, design, and heterogeneity of the included studies – stated Bekhet et al. Twenty-three clinical and nonclinical trials were included with 389 subjects. Neuromuscular electrical stimulation/ functional electrical stimulation provided reductions in spasticity by 45%-60% with decrease in electromyography activity and increase in range of motion after spinal cord injury. The identified stimulation parameters were frequency of 20-30 Hz, pulse duration of 300-350 μs, and amplitude of the current greater than 100 mA. Neuromuscular electrical stimulation/ functional electrical stimulation provides an effective rehabilitation strategy in managing spasticity. They included in a systematic review twenty-three clinical and nonclinical trials with 389 subjects appearing spasticity after SCI. Neuromuscular electrical stimulation or functional electrical stimulation provided reductions in spasticity by 45%-60% with decrease in electromyography activity and increase in range of motion. The identified stimulation parameters were frequency of 20-30 Hz, pulse duration of 300-350 μs, and amplitude of the current greater than 100 mA. The authors concluded that neuromuscular electrical stimulation and or functional electrical stimulation provides an effective rehabilitation strategy in managing spasticity [41]. But future, better designed and presenting top methodological level studies are needed.

Massey et al. made a systematic review and meta-analysis for comparing neurophysiological with clinical outcome measures of the impact of electrical stimulation on spasticity in SCI: transcutaneous electrical nerve stimulation (TENS), transcutaneous spinal cord stimulation (TSCS), functional electrical stimulation (FES) cycling and FES gait. Primary outcome measures were the Ashworth scale (AS), Modified Ashworth scale (MAS), Pendulum test and the Penn spasm frequency scale (PSFS), while secondary outcomes were the Hoffman (H)- reflex, motor-evoked potentials (MEPs) and posterior-root reflexes (PRRs).

It occured that activation of the muscle was not necessary to reduce spasticity; there was no correlation between clinical and neurophysiological outcomes [42].

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These are few reports on using repetitive transcranial magnetic stimulation (rTMS) and transcranial direct current stimulation (tDCS) in SCI, further high-quality clinical trials to support or refute the use and optimize the stimulation parameters of NIBS in clinical practice are recommended.

There is a little amount of reports on application of eSWT in spasticity after SCI.

Further randomized controlled clinical trials with long period of follow-up are necessary to confirm the results obtained. These are much more reports on application of eSWT in poststroke spasticity, Multiple Sclerosis, and cerebral palsy.

In 2021, Polish researchers, based on their own 20 years of experience, described the current state of knowledge on the clinical and methodological aspects of eSWT in the treatment of post-stroke spasticity. A total of 21 reports were found, including 432 patients after stroke - 10 reports regarding the treatment of upper limb spasticity (249 patients) and 11 reports regarding the treatment of lower limb spasticity (183 patients). Reviewers focused their attention on the clinical and methodological aspects of this issue. Many types of devices are produced: electromagnetic, electrohydraulic, piezoelectric or pneumatic, using concentrated SWT or radial SWT. Different SWT parameters are used regarding the number of impulses, pressure, frequency and energy, a different number of sessions, different places of application - the spastic abdominal muscle, the distal or proximal muscle attachment. Various timing of this intervention was observed: in some reports, eSWT was initiated one month after the onset of stroke, and on the other hand, 198 months after the onset of stroke. Various inclusion criteria were used. Dozens of primary and secondary outcome measures were used. Some studies did not use a control group. It was found that eSWT effectively reduces muscle tension in people with spastic limb after stroke, and is safe and free from unwanted side effects. The mechanism of action of eSWT on muscles affected by spasticity is still unknown. To date, no standard parameters for eSWT in post-stroke spasticity regarding intensity, frequency, location and number of sessions have been established. It was concluded that further research to the highest standards is needed to establish the recommended parameters for muscle stimulation using eSWT [43].

Of the articles published in 2023, three seem interesting. Afzal et al. presentedsystematic review and meta-analysis of the effects of eSWT on spasticity, gait, and quality of life in post-stroke lower limb spasticity. A total of five studies with 389 participants were considered for inclusion. In the experimental group, compared to the control group, a beneficial effect of eSWT on spasticity, mobility (assessed with the TUG test) and motor function of the lower limbs was observed. However, there is uncertainty about its effectiveness on walking performance [44].

Lee and Kim systematically reviewed a total of 33 articles from 2003 to 2023 on balance, pain, and spasticity after stroke. Positive therapeutic effects of several shock wave generation methods and their application have been demonstrated on various aspects of rehabilitation of stroke patients, such as improving balance, reducing pain, reducing spasticity and increasing muscle control, as well as strengthening the functional activities of the upper and lower limbs. The effectiveness of eSWT may vary depending on the patient's condition, application method, and treatment area [45].

Based on a systematic review and meta-analysis of thirteen studies involving 677 participants, Ou Yang et al. found that spasticity significantly improved after eSWT throughout the follow-up period, and the effect could persist for up to 3 months. Limb functionality improved significantly in the short follow-up period and could persist for at least 2 weeks. Patients with a stroke duration of less than 45 months may benefit from eSWT in terms of improved limb function at all follow-up periods [46].

Khan et al. through a review of 18 systematic reviews, assessed the evidence for a range of non-pharmacological interventions used to treat spasticity in a variety of neurological conditions. They found "moderate" evidence for the effectiveness of neuromuscular stimulation and acupuncture as an adjunct therapy to conventional routine care (pharmacological and rehabilitation) in people after stroke. 'Low' quality evidence for spasticity-targeted rehabilitation programs (such as induced movement therapy, stretching, dynamic elbow splinting, occupational therapy) for stroke and other neurological conditions; eSWT in brain damage; tDCS in the jump; TMS and transcutaneous electrical nerve stimulation (TENS) for other neurological conditions; physical activity programs and rTMS for people with multiple sclerosis, vibration therapy for SCI and stretching for other neurological

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conditions. For other interventions, the evidence was inconclusive. However, they concluded that further research is needed to evaluate the effect using appropriate study designs, time and intensity of methods, and associated costs of these interventions [47].

There are several articles in the literature attempting to explain the potential theoretical mechanism of eSWT's analgesic effects. Based on their review of the literature, Chamberlain and Colborne highlighted the complexity of trying to explain the effects of eSWT at the cellular and molecular levels. They focused on what appear to be key players in the promotion

repair, namely runt-related transcription factor 2 (RUNX2), bone morphogenetic proteins (BMPs), vascular endothelial growth factor (VEGF) and the mitogen-activated protein kinase (MAPK) cascade. The MAPK pathway involves protein kinase cascades that are activated by genotoxic stress and growth factors, including chemotherapeutic compounds [48].

The electrophysiological mechanisms of the antispastic action of eSWT still remain unclear. It should be emphasized that, to the best of recent knowledge, there are currently no observations of the resting bioelectrical activity of treated spastic muscles using surface ElectroMyography (sEMG) and the distribution of surface temperature in the area of the examined muscles using infrared thermometry (IRT) imaging. In accordance with these findings, it is justified to continue research on specialized and non-invasive tools (e.g. sEMG and IRT imaging) that allow for precise registration of some important phenomena and factors regarding the potential antispastic mechanisms of eSWT [49].

5. Conclusions

Hundreds of experiments have been carried out on various possibilities of influencing the regeneration of the spine, some of them gave promising results, but unfortunately the successes obtained on experimental animals did not translate into humans. This narrative review article explores the use of extracorporeal shock wave therapy (eSWT) for spinal cord injuries. The article is divided into parts: 1. The use of extracorporeal shock wave therapy in the regeneration of the spinal cord after traumatic spinal cord injury. 2. Use of extracorporeal shock wave therapy in spasticity after spinal cord injury. A small number of clinical trials have demonstrated the potential of eSWT as an innovative, safe and cost-effective treatment option for patients with SCI. Some reports have shown that eSWT can improve spasticity, walking ability, urological function, quality of life and independence in daily life. In both cases, one can only hypothesize possible mechanisms of action.

To date, no standard parameters for eSWT of spastic muscles after spinal cord injury have been established regarding intensity, frequency, location and number of sessions. Further research is needed to evaluate the impact of eSWT on SCI using appropriate study designs, method time and intensity, and associated costs.

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