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HARMONY IN HEALING: INTEGRATING TRADITIONAL CHINESE AND MODERN MEDICINE FOR THE FUTURE OF TSCI TREATMENT

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Abstract: Traumatic Spinal Cord Injury (TSCI) stands as a globally impactful and devastating event, often resulting in permanent disability. With an annual incidence affecting 250,000 to 500,000 individuals and an estimated 2 to 3 million people worldwide living with TSCI-related disabilities, the magnitude of its consequences is profound. Notably, the incidence of TSCI varies significantly across continents, with Asia reporting rates ranging from 12.06 to 61.6 per million, Europe from 10.4 to 29.7 per million, and North America from 27.1 to 83 per million. Motor vehicle accidents are the primary cause, although violence takes precedence in developing countries. Men, particularly young adults, bear the brunt, experiencing incidence rates 2 to 5 times higher than women.

Beyond the evident economic burden of medical costs, individuals with TSCI grapple with a spectrum of physiological, emotional, and financial challenges post-injury. Despite primarily affecting young adults, the incidence among older adults is rising, primarily due to falls. Regrettably, effective treatments to enhance functional recovery in paraplegia or quadriplegia following TSCI remain elusive. In this context, the integration of Traditional Chinese Medicine (TCM) emerges as a promising avenue, supported by both extensive experimental and clinical research.

This review explores the unique advantages of TCM in treating TSCI, presenting a new direction for scholars and clinicians alike. Modern rehabilitation measures synergistically combine with TCM approaches, including acupuncture, massage, and herbal treatments, forming a comprehensive and cost-effective TCM rehabilitation program. This holistic approach is gaining recognition for its simplicity, convenience, and efficacy in the rehabilitation process of spinal cord injuries. By examining the current landscape of TSCI, its demographic variations, and the potential of TCM interventions, this review aims to contribute to the evolving discourse on effective and inclusive approaches to TSCI management.

Keywords: Traumatic Spinal Cord Injury, Traditional Chinese Medicine, Rehabilitation, Acupuncture, Comprehensive Treatment.

1. Introduction

Traumatic spinal cord injury (tsci) is a catastrophic event that commonly leads to permanent disability worldwide [1]. It affects between 250,000 and 500,000 people each year, with an estimated 2 to 3 million people globally living with disabilities related to sci. In asia, the incidence of tsci ranges from 12.06 to 61.6 per million. In comparison, the incidence in europe is between 10.4 and 29.7 per million, and in north america, it is between 27.1 and 83 per million [2]. Motor vehicle accidents are the most common cause, whereas violence is more prevalent in developing countries. The incidence rate is 2 to 5 times higher in men than in women, with the highest rates found in young adults [3]. Besides the economic burden associated with medical costs, individuals with tsci experience physiological, emotional, and financial difficulties after the injury [4]. Although sci primarily affects young people (often due to motor vehicle collisions), an increasing number of older adults are suffering spinal injuries due to falls. Currently, there are no effective treatments to enhance functional recovery in individuals with paraplegia or quadriplegia following tsci [2]. The use and development of traditional chinese medicine (tcm), along with extensive experimental and clinical research, have shown unique advantages in treating sci, becoming a new direction for scholars. Clinically, combining modern rehabilitation measures with tcm approaches such as acupuncture, massage, and herbal treatments forms a comprehensive tcm rehabilitation program. This program is noted for its simplicity, convenience, effectiveness, and low cost, becoming an essential method in the rehabilitation process of spinal cord injuries.

2. Modern medicine in tsci research

2.1. Pathological research on tsci

Research has shown that acute tsci can be divided into primary and secondary injury mechanisms [5]. Primary mechanisms involve initial mechanical damage caused by local deformation and energy conversion, while secondary mechanisms consist of a series of physiological and biochemical processes triggered by the primary event, potentially leading to continued cell damage or even cell death.

2.1.1. Primary mechanism

The most common primary damage is a combination of initial impact followed by sustained compression. This often occurs in cases such as vertebral dislocation caused by pedicle fracture, burst fractures of vertebral bodies, firearm injuries, and acute disc herniation. In the absence of sustained compression, isolated collisions can lead to severe ligament damage due to spontaneous dislocation and realignment of the spine. Similar cases include spinal cord lacerations, contusions, compressions, or concussions mixed with the intrusion of sharp bone fragments or shrapnel into the spinal canal [6].

2.1.2. Secondary mechanism

The concept of tsci’s secondary mechanism started with allen's proposal in 1911, when he discovered improved neurological functions in dogs with experimental acute sci after removing hemorrhagic necrotic material from the trauma site. Three years later, allen speculated about the existence of a "biochemical factor" in hemorrhagic necrosis that initiates the current injury. This concept has developed and matured over the subsequent decades. In the 1970s, the free radical hypothesis emerged, emphasizing the critical role of free radicals in the injury process. The focus then shifted to the roles of calcium, opioid receptors, and lipid peroxidation. In the 21st century, modern research involves cell apoptosis, inhibition of intracellular protein synthesis, glutamatergic mechanisms, and countless pathophysiological pathways mediating secondary injury mechanisms, including the influence of bloodderived macrophages on spinal axonal self-repair and the impact of the gut microbiome. Evidence suggests that primary mechanical injury triggers a series of secondary injury mechanisms, including: (1) vascular changes such as ischemia, impaired autoregulation, neurogenic shock, hemorrhage, microcirculatory disturbances, vasospasm, and thrombosis [5,6]; (2) ionic disturbances, including increased intracellular calcium, increased extracellular potassium, and enhanced sodium permeability [7]; (3) accumulation of neurotransmitters like serotonin or catecholamines and extracellular glutamate [8], leading to excitotoxic cell damage [9]; (4) release of arachidonic acid and production of free radicals [10], lipid peroxidation [11]; (5) endogenous opioids [12]; (6) edema [13]; (7) inflammation; (8) loss of atpdependent cellular processes [14]; (9) programmed cell death or apoptosis [15]; (10) infiltration of bloodderived monocytes/macrophages [16]; (11) influence of gut microbiota on post-sci neural function [17]; (12) glial and astrocytic involvement [18] etc. Reduced spinal cord blood flow (scbf) and microvascular perfusion, inducing spinal cord edema, are significant factors in tsci, although the exact mechanisms behind this are unclear. Vascular spasms secondary to mechanical injury may be partly responsible [5]. Post-injury macrophage invasion and infiltration into the spinal cord, causing secondary injury, is another important factor in tsci. However, literature also shows that m2-polarized macrophages promote tissue function and reduce inducers of m1 macrophage polarization and inflammatory response, thus preventing damage to spinal axons and myelin [19]. The entry of gut microbiota into the bloodstream due to immune suppression could be a pathogenic factor for various tsci complications (lung infections, liver damage, urinary tract infections, etc.) [18]. Experiments on sci mice treated with vsl#3 showed a significant increase in cd4+, cd25+, foxp3+, t reg lymphocytes, suggesting that probiotics activate these neuroprotective mucosal immune cells, reducing injury-induced inflammation [20].

2.2. Symptoms and complications of tsci

Tsci can potentially lead to permanent paralysis or quadriplegia, causing significant functional disabilities [20]. The primary symptoms include motor, sensory disturbances, and impaired autonomic nerve function. Relatively few reports exist on the complications associated with tsci. The major secondary complications typically reported are sequelae of urinary sepsis, atelectasis, pneumonia, deep vein thrombosis, pressure ulcers, chills, and fever. Respiratory complications are among the main secondary issues following cervical spinal cord injury (csci). Damage to muscles leads to a decrease in lung capacity and coughing ability, thus resulting in secondary complications like dependent pneumonia. This also becomes one of the primary causes of early mortality post-csci. Autonomic dysreflexia (ad) is another life-threatening complication, usually caused by spinal cord segmental injury. Patients with sci at t6 or higher segments might experience autonomic reflex disorders [21]. After sci, resting blood pressure is typically lower than normal (hypotension), and a sudden rise in blood pressure to as low as 20 mm hg can lead to a life-threatening emergency. This hypertension is a symptom of ad, affecting 50%-90% of patients with paraplegia or high-level quadriplegia due to sci [21]. Compared to patients with delayed hospital admission (2-60 days post-injury), patients have a lower risk of contractures, heterotopic ossification, atelectasis, cardiac arrest, renal abnormalities, and bedsores, although the ranking of main complications remains similar. These data may have some degree of selection bias, depending on the referral patterns for more severe injuries. In comparing paraplegia and quadriplegia, the former has higher rates of urinary tract infections and pressure sores [22].

2.3. Treatment methods for tsci

2.3.1. General treatment methods for tsci

Currently, there are no standard neuromodulatory treatments for tsci. Traditional treatments mainly include bed exercises, wheelchair propulsion training, strengthening programs, joint mobility exercises, passive motion, stretching exercises, bowel/bladder function management, and higher-level functional activities aimed at reducing secondary complications and improving limb function post-injury, yet there are no universal guidelines [23]. However, in recent years, various neuromodulation methods such as epidural spinal cord stimulation (scs) [24], intraspinal microstimulation, functional electrical stimulation (fes) [25], and transcutaneous spinal cord stimulation (tscs) [26] have been extensively researched. Among these, non-invasive stimulations like fes and tscs are relatively safer and easier to implement in clinical settings compared to invasive stimulations [27]. Non-invasive tscs is a

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relatively new technology, targeting neural structures similar to its invasive counterpart scs [28]. Based on stimulation parameters, tscs can be roughly divided into two types: direct current stimulation (tsdcs) and pulsed current stimulation (tspcs). Fes is a neuromodulation technology that applies short-pulse electrical stimulation during specific simulated activities (like walking or cycling) [25], with many benefits including enhancing residual muscle strength, increasing flexibility and range of motion in joints or limbs, and reducing spasticity, thereby enhancing sensorimotor functions [29], improving cardiopulmonary health such as peak ventilation, thus enhancing airflow rate and airway pressure [30], and reducing common post-sci neuropathic or injury-related pain and spasms . It also helps in controlling bowel/bladder dysfunctions and improving erectile and ejaculatory dysfunctions, increasing blood circulation and metabolic rate, ultimately improving muscle mass and balance, and controlling posture [30], thus having a wide application in rehabilitation. Epidural scs is an effective neuromodulatory therapy that can alleviate chronic pain, reduce spasticity severity, increase specific rhythmic movement activity in lower limbs, activate respiratory muscles, improve bladder control, enhance sensory nerve activities, and affect various organs in the autonomic nervous system or viscerosomatic reflexes. However, epidural scs has its problems (with a surprisingly high incidence rate of about 28%-42% [31]), including technical defects (device malfunctions, leakage currents, and rechargeable battery failures, etc, with an incidence rate of about 5% [32]) and clinical complications (tissue damage, bleeding, hematoma, and the most common, infection, with an incidence rate of about 4%-10% [31]). To utilize the benefits of epidural scs while avoiding complications, a non-invasive spinal cord neuromodulation method called percutaneous scs has been recently developed and studied [33]. Percutaneous stimulation can induce or combine with functional therapy, leading to enhanced motor functions in patients with chronic paralysis [26]. It has the therapeutic potential to improve autonomous motor functions, enhance muscle strength in upper and lower limbs, improve standing posture and gait, reduce spasticity, improve trunk strength, and overall spinal function [34], being a relatively safe treatment method suitable for all sci patients except those with skin stimulation issues [26]. Other non-invasive spinal cord neuromodulation methods, such as tsdcs and tspcs, involving transcutaneous electrical stimulation of the spinal cord and surrounding nerves, are effective treatment options for sci and other neurological diseases, including stroke, chronic pain, spasticity, respiratory diseases, cardiovascular ischemia, neurogenic bladder, bowel dysfunctions, and upper and lower limb functions, including fine motor functions of fingers. Increasing evidence suggests that for patients with sci, tsdcs and tspcs might be potential effective treatment choices. However, the main complexity of this neuromodulatory therapy lies in the assessment and comparison of short-term and mid/long-term clinical outcomes. Although short-term effects are very promising, the mid-term or long-term impacts of this neuromodulation have not yet been evaluated and are difficult to predict [35]. Literature has summarized some possible current treatments for tsci: counteracting secondary injuries and rescuing axons throughout the injured area; using drugs, cell, or tissue grafts to repair spinal circuits; reactivating surviving but silent pathways in the injured area; using electronic multichannel bridging devices to reconstruct connections across damaged nerve bundles; using advanced devices to formulate and implement symptom-centered plans for patient recovery; using implantable electronic devices to couple peripheral nerves with the central nervous system to control muscles; using implantable electronic devices to couple peripheral nerves with the central nervous system to control mechanical prostheses; manipulating exoskeleton devices for activity, etc [36].

2.3.2. Limb movement therapy in tsci treatment

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Research by shimura, through two trials, found that the manipulation positions in proprioceptive neuromuscular facilitation (pnf) stimulate cortical and spinal activation prior to voluntary movement, leading to a reduction in electromyographic reaction time (emg-rt) and changes in excitability reflected in motor evoked potentials (mep), thereby having therapeutic effects on tsci [5]. Beekhuizen's clinical trial research showed that extensive upper limb functional exercises with incoming neural signals, in the form of sensory inputs related to movement or peripheral nerve stimulation, can induce beneficial neural plasticity. This plasticity may promote the optimal use of residual pathways conducting neural impulses through the injured spinal cord region in patients with incomplete sci [6].

3. Status of traditional chinese medicine (tcm) research in tsci

3.1. Tcm understanding of tsci

In traditional chinese medicine, there is no specific term equivalent to "traumatic spinal cord injury." based on "traditional chinese internal medicine", the "tcm diagnosis and treatment plan for incomplete spinal cord injury (trial)" formulated by the national tcm key specialty collaboration group in 2016, and the "tcm disease and syndrome diagnosis and treatment effectiveness standards" issued by the national administration of traditional chinese medicine in 1994, the condition is diagnosed as "wei zheng (impotence syndrome)" [37]. Tcm conceptualizes tsci as damage to the governor vessel leading to local meridian blockage, blood stasis obstruction, meridian malnutrition, and, in later stages, insufficient blood and qi to nourish muscles, resulting in limb paralysis or weakness, categorized as "wei zheng (impotence syndrome)". Texts like "huangdi neijing" mention: "when a person falls, bad blood stays inside" and "yilue cunzhen" states: "modern cases of wei... Numbness below the waist, swelling in the lower abdomen, difficulty in urination" etc. The guiding principle of "zhi wei du qu yangming (treating impotence by focusing solely on yangming)" is proposed in these texts. Academician shi xuemin views traumatic spinal injuries as resulting from external force causing spinal fractures and dislocations, leading to spinal cord injury, primarily characterized by limb paralysis and urinary and bowel dysfunction, traditionally called "ti duo". The condition is often categorized among stasis syndrome, bi syndrome, and governor vessel disorders. The pathogenesis relates to qi and blood stasis, meridian obstruction, governor vessel malfunction, and malnourishment of tendons and bones. The tcm pathogenesis of tsci as yu xue zu zhi (blood stasis) and the treatment principle of "zhi wei du qu yangming (treating impotence by focusing solely on yangming)" align with the modern medical understanding of central nervous system damage under early-stage local ischemia and hypoxia, where the maximal activation of camkii aggravates nerve damage, and inhibiting the expression of camkii is considered a potential treatment for sci [38].

3.2. Application and efficacy of tcm in tsci

3.2.1. Application of chinese herbal medicine in tsci

Chinese herbal medicine in sci involves inhibiting inflammatory responses, improving microcirculation, inhibiting lipid peroxidation, reducing neuronal apoptosis, promoting neuronal repair and regeneration, and inhibiting the formation of glial scars [38]. Research indicates that extracts like rhubarb and angelica sinensis, and alkaloids such as ligustrazine from chuanxiong, can reduce inflammation by inhibiting inflammatory factors, thereby alleviating local tissue damage and promoting the recovery of injured spinal cord function. Studies suggest that hif-1 α and vegf play crucial roles in neurological recovery post-sci. Ligustrazine, ferulic acid, and bu yang huan wu tang can influence the gene expression of hif-1α and vegf, promoting neovascularization, improving spinal cord microcirculation, and reducing ischemic and hypoxic damage to the spinal cord. Extracts of saffron, ginsenoside rg1, and icariin can enhance sod activity in spinal cord tissue, inhibit the production of mda, and exhibit significant anti-free radical damage capabilities. They can reduce oxidative damage caused by free radicals post-spinal cord injury, decrease cavity area, and reduce the activation and infiltration of inflammatory cells, thereby promoting post-injury repair. Astragalus, icariin, and paeoniflorin can inhibit the expression of pro-apoptotic proteins bax and caspase-3, reducing the number of apoptotic cells in spinal cord tissue, thereby protecting nerve functions and promoting the recovery of hindlimb function, sensation, and reflexes in rats [39].

3.2.2. Application of acupuncture in tsci

Beijing hospital of traditional chinese medicine treated over 500 patients with traumatic paraplegia from 1969 to 1980, using a formula mainly consisting of the du mai shi san zhen (governor vessel thirteen needles), hua tuo jia ji xue(hua tuo's paravertebral points), wu zang shu (five viscera backshu acupoint), ge shu (bl17), and baliao xue (ba liao points), achieving an overall efficacy rate of 84.3% [40]. Li and others [37] combined acupuncture with medical sports therapy to treat 124 patients with traumatic paraplegia, showing recovery in patients' limb motor functions and bladder/bowel functions. Han and others treated 374 spinal cord injury patients primarily with acupuncture, combined with acupoint injection, electroacupuncture, infrared radiation, and low-frequency magnetic therapy, significantly improving patients' limb motor functions and bladder/bowel functions post-treatment [41]. Wang used acupuncture combined with pulsed electrical stimulation to treat 149 patients with traumatic paraplegia, with twice-daily acupuncture treatments for 30-45 days per course, showing improvement in most patients after 3-6 courses [42]. Additionally, wang ling conducted a comparative study on the efficacy of acupuncture and rehabilitation exercises in 176 patients with high cervical spinal cord injury, showing significant improvements in nerve function compared to those only undergoing rehabilitation exercises [42]. Min youjiang and others adopted the "three-tong acupuncture method" (tong du, tong (intestinal) fu, tong tiao bladder) for treating patients with paraplegia in the recovery phase of spinal cord injury, showing a significantly higher effective rate compared to ordinary acupuncture therapy [43].

4. Conclusion and prospects

The complexity and severity of traumatic spinal cord injury (tsci) make it a significant medical challenge worldwide. Modern medicine has made remarkable progress in understanding the mechanisms and treatment methods of tsci, particularly in the field of neuromodulation technology and non-invasive spinal cord neuromodulation methods. Although these technologies are still in the early stages, they have shown potential in improving functional recovery in patients. Traditional chinese medicine (tcm) offers a different perspective on the treatment of tsci. Utilizing acupuncture, chinese herbal medicine, and other traditional methods, tcm focuses on holistic recovery and bodily balance. While the efficacy and mechanisms of these methods in western medicine still require further validation, preliminary research suggests they may have potential value in improving the quality of life for some tsci patients. Integrating tcm and modern medical approaches could provide a more comprehensive solution for tsci treatment. Bridging the gap between these two methodologies requires a collaborative approach, where practitioners from both traditions share knowledge and research methodologies. This integration faces challenges, including the need for more rigorous scientific research to validate the efficacy and safety of tcm methods, standardization and quality control of tcm treatments, and ensuring consistent and safe practices. The future of tsci treatment lies in a more integrated approach, where modern medicine and tcm converge to offer a comprehensive treatment model. This model would not only address the physical aspects of the injury but also cater to the emotional and psychological well-being of patients. With continued research and collaboration, there is hope for more effective treatments, better recovery outcomes, and improved quality of life for those living with tsci. The goal is to move beyond merely managing symptoms to truly enhancing the lives of individuals affected by this challenging condition. More scientific research and clinical trials are needed to verify the efficacy and safety of this integrated approach. Future research should focus more on the synergistic effects of these two methods and how to most effectively use these medical approaches to address the challenges posed by tsci.

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