Review Article

Ameliorative Effects of Neural Stem Cells in Spinal Cord Injury

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ABSTRACT

A deadly neurological damage known as a spinal cord injury result in weakness and loss of feeling below the site of lesion. There are two further subcategories of spinal cord damage. External trauma, such as an accident or any kind of damage to the spinal cord, causes traumatic spinal cord injury. Any acute or chronic disease activity, such as a tumour, inflammation, or ischaemia, can cause nontraumatic spinal cord injury by reducing or completely stopping the ability of neural cells to regenerate. Stem cell therapy has emerged as one of the most cutting-edge and promising methods in the study's last years. Rehabilitative care is a part of the time-dependent treatment for spinal cord injuries. The current course of treatment entails spinal cord decompression and surgical stabilisation. This research examines how neural stem cells function at various phases of spinal cord injury to explore their application in situations of severe spinal cord injury. The process by which the spinal cord damage operates is two-phase. There are two distinct phases to the acute phase. The first mechanical damage that disrupts cell membranes, axons, and blood flow causes the main phase. Following the main phase, which can induce vascular damage, ionic imbalance, necrosis and apoptosis, inflammation, and glutamate excitotoxicity in a matter of minutes to months, is the secondary phase. In this chronic phase, the second phase, cysts form, connective tissues are accumulated, and grey matter degrades. There is currently no entirely effective treatment for spinal cord lesions. Through tissue restoration, remyelination of the injured area, and stimulation of cytokine expressions, these therapies have been quite helpful in situations involving spinal cord injury.

Keywords: Spinal cord injury, Stem cells, Neural cells, Stem cell-based therapy.

1. INTRODUCTION

It's the kind of crippling illness where a person loses their motor and sensory nerves. One of the most serious neurological disorders is spinal cord injury, which can strike anyone at any time and have catastrophic consequences. Because of the consequences on patients' quality of life, the complexity of care needed, and the significant expenses connected with it, it is one of the top global health priorities. First of all, there were an estimated 0.93 million new instances of spinal cord injury in 2016, with an overall incidence of 27.04 million cases. [1] Both sexes experience similar global occurrences, albeit more males experience them in the 20–40 age range. The number of people living with spinal cord injuries is predicted to rise in the future due to the growing global population and advancements in medical care. The two main kinds of spinal cord injury are traumatic and non-traumatic. [2, 3]

Traumatic spinal cord injury results from physical impacts from the outside world. Road traffic accidents, falls, violent incidents, and sports-related mishaps are a few of the more prominent instances. With almost 50% of cases, falls are the primary cause. Diseases including tumours, infections, degenerative disc disease, etc., can result in non-traumatic spinal cord injury. We note techniques that alter neural stem cell activity after damage as a step towards the objective of improved brain healing. [4] Neural stem cell therapy has the potential to restore lost tissue and facilitate structural regeneration after spinal cord damage. Over the past 30 years, the prevalence of this disease has increased globally, rising from 236 to 1298 instances per million people. An estimated 250,000 to 500,000 spinal cord injuries occur worldwide each year. Every patient with a spinal cord injury will spend more than $3 million in their lifetime. [5, 6]

Basic Characteristic of Stem Cells: Two features of stem cells are their multipotency and ability to regenerate themselves. Because they can develop into entire bodies and continue to proliferate indefinitely, embryonic stem cells (ESCs) derived from fertilised eggs potentially meet the criteria for stem cells [7]. It has been proposed recently that induced pluripotent stem cells (iPSCs) share features with embryonic stem cells (ESCs) [8]. Pluripotent stem cells (PSCs) are these two kinds of stem cells. Adult stem cells, on the other hand, are found in organs and can repair damaged tissue [9]. As a result, the lifespan and differentiation potential of ASCs are typically restricted. MSCs and NSCs are the two types of ASCs that have been employed in clinical trials to repair the damaged central nervous system (CNS). The ability of MSCs to differentiate into mesodermal tissues, including osteoblasts, adipocytes, chondrocytes, and even other lineages, is one of their major characteristics [10]. Additionally, MSCs generate a variety of paracrine factors that support immune regulation and regeneration [11]. Nonetheless, numerous investigations have determined that their advantageous impacts stem from functional regulation rather than direct neuronal regrowth and assimilation into the damaged central nervous system. The expression of common markers like Nestin or Sox2 [12] is indicative of NSCs. They typically live in the specialised niches known as the subventricular zone and the subgranular zone [13],

where the olfactory bulb and hippocampal derived neurones are produced. NSCs have the capacity for self-renewal and contribute to adult brain neurogenesis. The brain lineages that NSCs preferentially differentiate into—neurons, astrocytes, and oligodendrocytes—are appealing for clinical application in CNS disorders [14]. Moreover, NSCs release advantageous paracrine substances that support the regeneration of the injured CNSs [15]. Because of these qualities, NSCs are a powerful and adaptable cellular medication candidate for the management of CNS injury.

2. PHASES OF SPINAL CORDS INJURY

A) Acute phase:

This is the initial stage. Damage to the spinal cord causes sensory and motor defects. Therefore, there is currently no effective treatment for this condition. The following scenarios can result from spinal cord injury: initial mechanical damage that damages axons; rupture of the blood-spinal cord barrier; destruction of neural parenchyma; and a series of secondary events that increase the severity of injury: vascular damage, inflammation, excitotoxicity, cell death, and activation of astrocytes. [16] This leads to the infiltration of circulatory factors and cellular contents into the spinal cord. In the initial days following injury, there is a rapid inflammatory response as a result of the local microglia's release of cytokines and chemokines in response to the blood-borne macrophages entering the spinal cord. The length of spinal cord compression and the degree of early destruction were the main factors that determined the severity of spinal cord injuries. [17]

B) Chronic phase:

The further harm following Oedema, persistent demyelination, and the development of glial scar—a mixture of cells made up of astrocytes, oligodendrocyte precursor cells, and fibroblast-like cells—are all brought on by spinal cord injuries. The glial scar's resident astrocytes multiply and move to the damage site. After the spinal cord damage, the glial scars serve both beneficial and detrimental purposes. It prevents damage from spreading, but it hinders spinal cord structural healing. An further unique gene population is expressed by an astrocyte that forms scars inside the glial scar. [18] Recent research has highlighted the dual role of glial scar and demonstrated that astrocytes can actually improve neurite outgrowth from CNS neurones following SCI. Research on myelinating cells in the peripheral nervous system has shown that NSCs play a part in the process of remyelination. Following spinal cord injury, it has been shown that NSCs and their progeny—collectively referred to as neural precursor cells—proliferate in the periventricular zone surrounding the central canal, move to the site of injury, and develop into adult neural cells. [19]

3. CLINICAL MANAGEMENT AFTER SPINAL CORD INJURY

There is currently no entirely effective treatment for spinal cord injuries, despite research efforts to find new ones. Preclinical SCI models have demonstrated some encouraging outcomes in a number of studies; however, patient administration is still debatable and unclear. Following trauma, the patient is rendered totally immobile and is under close observation to avoid a number of problems, including hypoxia, cardiovascular abnormalities, and respiratory dysfunctions. [20] SCI is surgically decompressed and gains control of the lesion site following stabilisation. For individuals with spinal cord injury (SCI), methylprednisolone sodium succinate (MPSS) was the first-line medication treatment. Fifty years later, there is still a friendly debate about this. Although preclinical studies have demonstrated a neuroprotective impact and neurological benefits following MPSS administration, patients receiving MPSS treatment are concerned about the increased risks of infection and mortality. This is especially true when it comes to safety, dosage, and timing of MPSS administration. [21] Actually, the American Association of Neurological Surgeons and Congress of Neurological Surgeons' most recent guidelines prohibited the use of MPSS in cases of acute SCI. As a result, MPSS is not a practical long-term therapeutic option, emphasising the necessity to create novel treatments that specifically target processes that take place during the acute and/or chronic phases. [22]

4. SOME TREATMENT FOR SPINAL CORD INJURY

The management of SCI gets complicated and starts with an extremely early diagnosis, transfer, and resolution of problems pertaining to the right care facilities. A quick referral to a specialised SCI centre is necessary in cases that are life-threatening. In order to evaluate TSCI injuries, radiological testing is crucial, as vertebral fractures are frequently seen. Since computed tomography has a high sensitivity and specificity for fractures, especially in difficult-to-reach regions like the cervicothoracic junction, it is recommended for use in these reconstructions, which include sagittal and coronal views. When TSCI has already occurred, magnetic resonance imaging is thought to be required to identify the specific form of TSCI, such as haemorrhage, soft tissue, ligamentous, or oedema. The pharmaceutical medicines used in modern neuroprotection techniques target inflammation and immunological responses. [23] Because of the numerous dangers involved and the scant evidence of benefit, high dose corticosteroids are no longer advised. It is critical to monitor the spinal perfusion pressure in order to avoid ischaemia. For the first seven days following an accident, guidelines advise regular haemodynamic monitoring and related measures to maintain mean arterial pressure above 85 mmHg. Normal surgical management for TSCI involves stabilisation and decompression. However, there is disagreement over the precise timing of this intervention. Early surgery aims to lessen spinal cord compression and ischaemia, albeit there is still no data to

support its clinical utility. The advancements in regenerative medicine have created a whole new avenue for promising treatments for the management of traumatic brain injury (TSCI), including neuroprotection, neuro regeneration, and the use of bioactive materials and stem cells, which provide great promise for improved results. [24]

5. NEURAL STEM CELL-BASED THERAPIES

It has garnered widespread attention and optimism for regenerative medicine throughout the past two years. In essence, stem cells are a unique class of living cells found in all multicellular organisms that possess remarkable capacities for self-renewal and cell differentiation into a wide variety of specialised forms. They fall into two main categories: adult, or somatic, stem cells and embryonic stem cells, depending on where they originated. Potency, or a cell's ability to differentiate into multiple distinct cell types through the process of cellular differentiation, is another way to categorise stem cells. [25]

Based on potency, they are classified as follows:

1) Totipotent Cells: These have the highest degree of potency and are capable of forming everything—the individual down to embryonic tissues and extraembryonic tissues.

2) Pluripotent Cells: A pluripotent stem cell is able to differentiate into any cell type of the body with the exception of placental tissues.

3) Multipotent Cells (Oligopotent Cells): Those cells that have a more restricted but still very important potential of differentiation, able to give rise to a range of closely related cell types in a specific tissue or organ.

4) Unipotent Cells: Unipotent stem cells have the least differentiation capacity since they are capable of differentiating into only one particular cell type. [26]

The key difference between embryonic and somatic, or adult, stem cells have to do with their potency. Embryonic stem cells can either be Toti- or pluripotent, whereas adult or somatic stem cells can be multi-, oligo-, or unipotent. Other extra-fetal tissues from which pluripotent cells can be isolated are amniotic fluid, chorion, amnion and the umbilical cord. Development of multicellular organisms starts with one cell, a zygote. The cell undergoes regulated and rapid divisions during gestation. [27] The cells formed by the initial divisions are totipotent; they have the option of developing into embryonic tissues like embryonic disc and extra –embryonic tissues like the placenta. While cell divisions continue, they gradually lose their competence in generating extraembryonic tissues and become pluripotent stem cells, capable of giving rise to cells of the three germ layers: endoderm, ectoderm, and mesoderm. These will eventually develop into all tissues and organs of the body. However, their potency continues to drop with further development and pluripotent cells differentiating into other lineages, giving rise to multipotent, oligopotent, and finally unipotent stem cells. Unipotent stem cells, giving rise to just one cell type, still have the capacity for self-renewal. More importantly, it has been emphasized that of the many important phenomena within the purview of stem cell plasticity, an important one is that adult stem cells can give rise to cells of different lineages depending upon the microenvironment in which they are transplanted. Cells that are used in the treatment of a wide spectrum of diseases including those of the spinal cord injuries. [28]

The multicentric potential of such an induced pluripotent stem cell, identified during the last couple of years, has increased the possibilities for cellular therapy. Introducing genes that can provide pluripotency in somatic cells, iPSCs can be developed that will mimic the embryonic stem cells for their potential to grow and differentiate. It also discusses various types of stem cells, including neural progenitor cells, embryonic cells, and hematopoietic cells, and their potential applications in treating TSCI. While, for example, only neural progenitor cells—one type of adult stem cells—hold deeper differentiation potential into all three neural cell lineages and have shown promise in allowing recovery in patients with TSCI. [29] The use of mesenchymal stem cells as therapeutic intervention for Traumatic Spinal Cord Injury. Due to their characteristic multipotent nature, MSCs differentiate into several cell types of mesodermal origin, including myocytes, chondrocytes, osteoblasts, and adipocytes.

They are a focus of much research in the treatment of traumatic spinal cord injury because of their regenerative and neuroprotective properties. They are derived from various tissues, which have distinct cell surface markers and therapeutic potential. A number of their advantages have been touted, which relate to their antiapoptotic, anti-inflammatory, and angiogenic properties. Mesenchymal stem cells generate factors that accomplish the functional repair of traumatic spinal cord injury by promoting cell survival, modulating the immune response, and stimulating the growth of new blood vessels. The three main sources of Mesenchymal stem cells are:

1. Bone Marrow Mesenchymal Stem Cells: These cells, considered adult progenitor cells, reside within the cavities of bones and exert important functions in bone repair, regeneration, and hematopoiesis. When transplanted into TSCI sites, a number of positivity has been noted in axonal regeneration and reduced inflammation. However, the outcome clinically has been heterogeneous, questioning dosage and safety, mechanisms of action, and interaction with a host immune system.

2. Umbilical Cord-Derived Mesenchymal Stem Cells: These are cells obtained from the umbilical cord blood, having similar effects to bone marrow cells in the reduction of apoptosis and glial scarring. It had significant functional improvement in motor and bladder function in clinical trials compared to rehabilitation alone. Grasp of transplantation timing is very important, and up until now, it has been shown that the effectiveness was influenced by

a variety of factors—like disease course, donor availability, or immunosuppressive therapy.

3. Adipose-Derived Mesenchymal Stem Cells: They are similar in morphology to umbilical cord cells but differ in proliferative capacity and availability. They direct tissue and neuronal regeneration and secrete anti-inflammatory factors. Research showed improved sensitivity in patients, although it is not always demonstrated to decrease the size of the lesion seen on MRI.

It therefore calls for more research, particularly through well-designed clinical trials to answer the various unanswered questions in Mesenchymal stem cell therapy for traumatic spinal cord injury. These pertain to dosage and safety, mechanisms of action, differentiation into neural cells, integration into the site of injury, and lastly, patient factors that may bear on response to MSC therapy. One of the major problems identified in this study is a lack of standardization of the protocols for Mesenchymal stem cell isolation and transplantation, which impinges on comparability of results from different studies. [27, 30]

In a nutshell, it illustrates the bright prospects of MSC therapy for TSCI but also brings forward the intricacies of this approach and what further research is needed.

Further, large patient number-based interventional multicenter randomized controlled trials are needed to standardize the assessment tests for a definitive conclusion.

The low incidence of the condition coupled with low patient recruitment, low rate of stem-cell production, and financial constraints pose a significant barrier to holding these essential trials.

A feature that the manuscript brought out is that though cellular transplantation may be very promising, combinatory therapies might be necessary to treat this devastating injury comprehensively. [31]

6. PRECLINICAL STUDY OF NSC FOR SCI:

It is important to plan preclinical research to examine the safety and efficacy of stem cell-based products before using them in clinical settings. Preclinical models need to be used to study the possible mechanism of action of stem cells in the disease indication, the timing of intervention in relation to the illness course, and the manner of distribution to the site of action. Numerous preclinical investigations employing NSCs in animal models of spinal cord injury have been documented in the literature [32], and under varied circumstances, the therapeutic potential, safety, and a number of technical elements of NSC transplantation have been examined.

Table 1 provides a summary of the features of NSC-based experimental research. Treatments with NSCs have been studied at acute, subacute, and chronic stages of spinal cord injury. The most commonly utilised animals are rats and mice. Non-human primates have been used as test subjects for human NSCs in a few research [33]. The most often examined area of the spine is the thoracic spinal cord, which is the site of mechanical trauma caused by falling heavy objects or compression from clips. The ideal approach for cervical SCI models is hemitransection because abrupt contusive injury to the spinal cord can be fatal. Scales for functional testing are standardised to some extent based on animal model species. The most widely used tests in mice and rats are the Basso mouse scale, also known as the Basso-Beattie-Bresnahan test, and the CatWalk gait study. Furthermore, the von Frey test has been used extensively in research to assess sensory function. Numerous investigations have also documented graft survival, differentiation, and axonal regeneration following NSC transplantation, in addition to functional recovery [34].

Even though several studies have shown encouraging outcomes when using NSCs to treat SCI, there is still a long way to go before NSCs are used in actual clinical settings. Finding the discrepancies between the animal model and human SCI and bridging the gap created by the model's intrinsic limitations should be the first step towards moving from bench to bedside. Generally speaking, human disease cannot be accurately predicted by animal models. The best option in such cases is to use a model that most nearly reflects the important aspects of the targeted indication. The majority of SCI instances in humans result from mechanical trauma. [35] As a result, we have created a number of animal models of spinal cord injury utilising mechanical trauma. However, each species has a different spinal cord's physical dimensions and capacity for regeneration. With the poor understanding of the pathophysiological mechanism of SCI, several animal models are required to adequately address the toxicity, delivery, effectiveness, and tumorigenicity of NSCs in SCI treatments. [36]

7. CLINICAL TRIALS USING NSCS:

There have been few clinical trials of NSC treatment in SCI patients that have been published in the literature, in contrast to the relative quantity of preclinical studies on NSC transplantation in animal models of SCI (Table 2). The fact that multiple studies have documented both the procedural safety and a partial success rate in terms of functional recovery following NSC transplantation in SCI patients is encouraging [52]. However, it is challenging to determine the therapeutic efficacy of NSCs, particularly in acute phase SCI, due to the small number of patients enrolled in the trials and the inclusion of only patients in the subacute (within 1 week to 6 months from the injury) and chronic (over 6 months from the injury) phases of SCI.

Table 1: Summary of preclinical studies using neural stem cells/neural progenitor cells in animal spinal cord injury models in literature

Species	SCI model	Injury location	Transplantation time after SCI	Types of Cells	Source of cells	Route and dose	Combination	Functional evaluation	Observation
Rat	Transection	Cervical	8 Weeks	Auto/ allogenic NPCs	Rat brain	Intralesional injection, 2.4× 10^5 cells	Fibroblasts	N/A	Showed substantial axonal regeneration[37]
Rat	Transection	Thoracic	0 Day	NSCs	Rat brain, spinal cord	Intralesional grafts, N/A for cell dose	Chitosan channel	BBB test	Astrocytic, oligodendrocytic differentiation observed in the channels. No functional improvements [38]
Rat	Transection	Thoracic	0 Day	NSCs	Rat brain	Intralesional grafts, 4.76 × 10^5 cells	PLGA polymer scaffold	BBB test	Facilitated axonal regeneration No functional recovery [39]
Rat	Clip compression injury	Thoracic	3 Weeks	NSCs	SC of transgenic rats	Intralesional, 1 × 10^6 cells	Chitosan channel	BBB test	No functional improvements[40]
Rat	Transection	Thoracic	0 Day	NSCs	Hippocampus of rat pups	Cord lesion site, cell dose not specified	PLGA scaffold LacZ, NT-3, TrkC gene modification	BBB test Inclined-grid climbing test.	Transfected NSCs, co-cultured with scaffold showed the smallest tissue defects at the injury site. Functional improvements observed. Limited ability of corticospinal tract axonal regeneration [41]
Rat	Drop weight contusion injury	Thoracic	0 Day	Human NSCs	Human fetal NSCs	Either intrathecal or perilesional SC lesion, 5 × 10^5 cells	None	BBB test	Functional improvements in both intrathecal and perilesional injections. [42]
Rat	Balloon-induced compression injury	Thoracic	1 Week	Human NSCs	Human fetal spinal cord	Intralesional, 5 × 10^5 cells	ISD	BBB, Plantar, walking-beam test	Significant motor, sensory function recovery. Showed robust cell survival and partial lesion filling. [43]
Monkey	Drop weight contusion injury	Thoracic	10 Days	NSCs	Monkey brain	Intralesional injection, 1 × 10^6 cells/kg	None	Tarlov scale and tail movements. Limb and tail pinch test	In all scales, transplanted group was faster in recovery. [44]
Mouse	Clip compression injury	Thoracic	1 Week	NSCs	Murine embryonal stem cell	Perilesional injections, 5 × 10^4 cells	ISD	BMS score, Cat-Walk test, von Frey test	Differentiation to oligodendrocytes Promote remyelination and axonal function. Motor function improvements[45]
Rat	Drop weight contusion injury	Thoracic	4 Weeks	Human NSCs	Human fetal NSCs	Either intrathecal or perilesional SC lesion, 5 × 10^5 cells	None	BBB test	Functional improvement in intrathecal group. No functional improvements in perilesional injection group. [46]
Rat	Hemi-section	Cervical	2 Weeks	Human NSCs	Human ESCs	Perilesional injections (6 points around lesion cavity), 2.5 × 105 cells, each	Growth factor cocktail	Forepaw placements on gridwalk task	More than a year later, forelimb motor function improved and astrocytes migrated to host tissue. [47]

Rat	Clip compression injury	Thoracic	7 Weeks	Human NPCs	Human bone marrow somatic cells	Intralesional injection, 4 × 10^5 cells	Chondrotinase ABC	BBB test, Cat-Walk behavioral test, von Frey test	Enhanced NPC survival, migration and oligodendrogenic differentiation. Promoted synapse preservation, and enhanced myelination of axons. Showed functional improvements. [48]
Rat	Balloooninduced compression injury	Thoracic	1 Week	NPCs	Human fetal spinal cord	Intralesional, 5 × 10^5 cells	ISD	None	TNF-α downregulation, p65 NF-κB inhibition. Reduction of glial scar and cavity size [49]
Rat	Transection	Thoracic	0 Days	NSCs	Rat fetal brain	Perilesional injections (2 points rostral, caudal to lesion), 5 × 10^5 cells	Wnt5a transfection	BBB test	Wnt5a-induced NSC differentiate into neurons and promote motor functional and histological recovery [50]
Rat	Drop weight contusion injury	Thoracic	3 Days	NSCs	Rat enteric nervous system	Perilesional injection, 1 × 10^6 cells	Chondrotinase ABC	Horizontal ladder test	Gastrointestinal tract could be a viable option for cell source. Cotreated with Chondrotinase ABC showed highest regenerative effect with modest functional improvement. [51]
Rat	Transection	Thoracic	0 Day	NSCs	Rat fetal brain	Cord lesion site	3D bioprinting sodium innateate/ gelatin scaffold OLGs	BBB test	Improved hindlimb motor function. Promoted neural regeneration.[52]

SCI, spinal cord injury; NPC, neural progenitor cell; N/A, not available; BBB test, Basso-Beattie-Bresnahan test; NSCs, neural stem cells; PLGA, poly-lactico-glycolic acid; SC, spinal cord; BMS, Basso mouse scale; ISD, immunosuppressant drugs; EGF, epidermal growth factor; bFGF, basic fibroblast growth factor; ESC, embryonal stem cell; PDGF-AA, platelet-derived growth factor; MSC, mesenchymal stem cell; NT-3, neurotrophin-3; 3D, 3-dimensional; OLG, oligodentrocyte; iPC-NP, induced pleuripotent stem cell derived neural precursor cell.

Table 2: Summary of published clinical trials using neural stem cells in spinal cord injury patients in literature

Clinical phase	Treatment timing	Injury location	Types of Cell	Source of Cell	Administration route	Results
Phase I	Chronic*	Cerivcal/thoracic	Autologous NSCs	-	Feeding artery infusion	Functional recovery was shown in 5/8 patients. [53]
Phase I/II	22–213 days after SCI	Cervical	hNSPCs	Human fetal brain	Intralesional injection	Partial improvements in sensorimotor function. [54]
Phase II	At least 4 months after SCI	Cervical/thoracic	NSCs (HuCNS-SC)	Human fetal brain	Intralesional injection	Improvements in overall mean functional outcomes measures [55]
Phase I	4–24 months after SCI	Cervical/thoracic	NSCs (HuCNS-SC)	Human fetal brain	Intralesional injection	A manual injection technique are safe and feasible [56]
Phase I	1–2 years after SCI	Thoracic	NSCs (NSI-566)	Human fetal spinal cord	Intralesional injection	Can be transplanted safely [57]
Phase II	4–24 months after SCI	Cervical	NSCs (HuCNS-SC)	Human fetal brain	Intralesional injection	Motor functional gains in the treated participants [58]

HuCNS-SC, human fetal-derived central nervous system neural stem cell; NSCs, neural stem cells; NSI-566, NSI-566 cell line human spinalcord-derived neural stem cell; hNSPCs, human neural stem/progenitor cells; SCI, spinal cord injury; USA, United States of America.

8. CONCLUSION

Mesenchymal stem cell therapy should be recommended for patients with traumatic spinal cord injury, especially when leading to neurological improvement at short and medium follow-up. But whether it is long-term safe and clinically significant for these patients remains largely in question. To draw definitive conclusions regarding the treatment recommendations, more multicenter trials are undoubtedly needed, including larger patient populations and standardized test batteries of assessments; however, temporary issues such as low patient recruitment and financial limitations exist. NSCs replace damaged neural tissue and provide neurotrophic factors to ensure repair of the spinal cord injury, which needs a lot more study in order to conform to any neurological benefit, safety assurance through an optimal dose setting, and choice of the best cellular sources. Combination therapies may be an essential comprehensive treatment, wherein clinical trials can bridge the gap between preclinical models and human spinal cord injury.

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