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A Review on the Etiology and Management of Pediatric Traumatic Spinal Cord Injuries

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Abstract

Context: Pediatric traumatic spinal cord injury (SCI) is an uncommon presentation in the emergency department. Severe injuries are associated with devastating outcomes and complications, resulting in high costs to both the society and the economic system.

Evidence acquisition: The data on pediatric traumatic spinal cord injuries has been narratively reviewed.

Results: Pediatric SCI is a life-threatening emergency leading to serious outcomes and high mortality in children if not managed promptly. Pediatric SCI can impose many challenges to neurosurgeons and caregivers because of the lack of large studies with high evidence level and specific guidelines in terms of diagnosis, initial management and of in-hospital treatment options. Several novel potential treatment options for SCI have been developed and are currently under investigation. However, research studies into this field have been limited by the ethical and methodological challenges.

Conclusion: Future research is needed to investigate the safety and efficacy of the recent uprising neurodegenerative techniques in SCI population. Owing to the current limitations, there is a need to develop novel trial methodologies that can overcome the current methodological and ethical limitations.

Key words: Child; Neurosurgery; Pediatrics; Spinal Cord Injuries; Trauma

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Context

Pediatric traumatic spinal cord injury (SCI) is an uncommon presentation in the emergency department. The specific anatomic features of the pediatric spine and vertebral column are associated with difficulties regarding the diagnostic steps and decision-making (1). Besides that, severe injuries are associated with devastating outcomes and complications, resulting in high costs to both the society and the economic system (2-4). In general, pediatric SCI can impose many challenges to neurosurgeons and caregivers because of the lack of large studies with high evidence level and specific guidelines in terms of diagnosis, initial management and of in-hospital treatment options.

Rehabilitation from SCI is usually incomplete, especially after severe trauma, but new tools are under investigation to improve the outcomes after SCI (5). Some of these tools are being generalized into pediatric populations (6). This review aims to summarize the current practice and evidence regarding pediatric-onset spinal trauma and to give more attention to future therapies using stem cell and bioengineering.

Evidence acquisition

We searched Medline through PubMed for relevant literature about the pediatric traumatic spinal cord injuries using the following search query “spinal cord injury” AND “children [MESH]”. An expert review author from Zagazig University Hospitals, Zagazig University, Egypt, (AN) was consulted about relevant studies for inclusion. The data on traumatic spinal cord injury have been narratively reviewed.

Results

Epidemiology

Pediatric SCI is a life-threatening emergency leading to serious outcomes and high mortality in children if not managed promptly, in general, the incidence rate of SCI has increased gradually worldwide in the last years and varied from 13.0 per million to 163.0 per million people depending on the expansion of human activities among different regions in the world (7, 8). According to the WHO, there are approximately 250.000 to 500.000 people suffering from SCI annually, and about 78% of new cases are male. Age distribution of cases follows a bimodal fashion with young adults occupying the first peak and adults more than 60 years occupying the second peak (5, 9). There is a variation in the injury prevalence between developed and developing countries (10-12).

In pediatric patients, Traumatic SCI is relatively rare, representing only about 2% to 5% of all spine injuries (13-17). In young people, More than 80% of injuries occur in the cervical spine, while the percentage of cervical regions in adults is only around 30% to 40% (18).

It was also estimated that thoracic and lumbar spine injuries represent 6% to 9% of all pediatric spine trauma (19). After the age of 14, it was found that cervical injuries incidence decreased and resembled adult patient pattern (20).

These epidemiologic properties may be explained by the interference of many factors such as large head size, soft elastic tissue, and supporting structures, and horizontal facet alignment (21, 22). Moreover, mortality rate in cervical spine-injured pediatric patients was reported to range from 16% to 18 %, with higher rate in upper cervical injured patients (23, 24).

Embryology and Anatomy

In embryogenesis of the central nervous system (CNS), Ectoderm is the most important initiating player forming the neural eCTCTctoderm, which gives rise to the neural tube and neural crest, and they subsequently give rise to the brain, spinal cord, and peripheral nerves.

The spinal cord is formed from the neural plate which is constituted by three layers (25): The Ventricular layer that lines the central canal, the Mantle layer that contains neuronal bodies and forms the gray matter and the marginal layer that contains axons, giving rise to the white matter. The spinal cord is the part of the central nervous tissue from which the different spinal nerves arise. It is protected by the vertebral column which has the form of a curved rod containing 33 vertebrae and 23 intervertebral discs. It is divided into five parts: cervical, thoracic, lumbar, sacral, and coccygeal regions. Each vertebra is composed of an anterior and a posterior part. The vertebral body involves the anterior part and is the weight-bearing structure of the vertebral column, and the neural arch (pedicle and posterior elements) consists in the posterior part.

In imaging, understanding the various biomechanical properties and the developmental anatomy of the pediatric cervical spine plays an important role in interpretation. The pediatric cervical spine shows several particularities such as epiphyseal variations, unique vertebral architecture, and incomplete ossification of synchondroses and apophyses. At birth, the neural Arches of the Atlas (C1) are ossified, but the anterior arch is not (only 20%of cases). By the age of 3 to 4, the neural arches fuse posteriorly, and they fuse with the anterior arch by the age of 7 (26, 27).

In terms of the axis development (C2), the fusion of secondary ossification center (which appears at the apex of the dens by 6 to 8 years of age) with the dens fails and results in ossiculum terminal that may be accompanied with atlantoaxial instability in pediatric patients (28-31). Furthermore, the third to seventh cervical vertebrae share similar ossification features with a unique ossification center for the vertebral body and an ossification center for each neural arch, and they have five secondary ossification centers that may remain open till the adulthood (32). The ossification of partially ossified ring apophyses is completed belatedly, and they should not be confused with fractures (30, 33).

A recent review also showed the knowledge of thoracolumbar anatomy and biomechanics is essential as it plays a significant role for the prevention of damage of spine in daily activities that are correlated to low back pain and tissue degeneration (34).

Pathophysiology and Mechanisms of Injury

The pathophysiology of acute SCI occurs in two major stages: immediate mechanical injury resulting in contusions of the spinal cord by permanent or temporary compression followed by secondary phase that may result in dysfunction and neural death after hours to weeks following primary injury due to destructive and biochemical changes in the neuronal and glial cells (35-40). In general, there are three main mechanisms that can engender pediatric SCI.

- ***Acceleration / Deceleration***

Acceleration/deceleration usually result in occipito-atlantal and atlantoaxial injuries. These joints are protected against vertical distraction by the strong fibrous tectorial membrane, which is a strong fibrous ligament that fixes the axis with the

occiput, and so any rupture in this ligament requires surgical fusion (41). In young children, occipito-atlantal and atlantoaxial dislocation can occur during high-speed collisions, auto versus pedestrian and may be related to airbag injuries (42). And even if there are any partial or absent neurological deficits, the lesions are worsened by distraction through cervical collar placement and traction (43). Sagittal CT images and MRI can be helpful to detect such lesions in pediatric patients as subluxation may be radiographically occult (44).
Odontoid injuries can also occur after high-speed collisions or fall in children less than seven years and usually have a fatal outcome (45). They result from avulsion of the dens of the body of the axis, and this type of injury can be typically detected by lateral radiographs and reconstructed CT images and needs prompt immobilization with or without a halo (1).

In pediatric patients, more than eight years, injuries in the sub-axial ligaments that are usually caused motor-vehicle collisions are more common. They can be typically diagnosed with CT and MRI and usually require only conservative management with immobilization (46, 47).

- ***Rotational Injury***

Falls or collisions can give rise to Atlantoaxial rotatory fixation (AARF) leading to occipito-atlanto dislocation regarding the axis and also functional fixation (44).
There are four types of fixations. In Type I, the atlas is rotated on the odontoid with no anterior displacement. Type II, the atlas is rotated on one lateral articular process resulting in minimal anterior displacement. Type II occurs by rotation of the atlas on both lateral articular processes with an anterior displacement more than 5 mm. Finally, type IV is characterized by rotation and posterior displacement of the atlas (48). CT and MRI are used for diagnosis of these for types of injury and type I improves with a soft collar with or without traction, whereas the other three types require surgical stabilization (49).

- ***Flexion/Extension***

Lateral flexion can result in cervical cord neurapraxia, which is a common type of injury is in contact sports. It is also considered as a mild form of SCI without radiographic abnormality (SCIWORA) and may be accompanied by transitory sensory and motor symptoms in one or all extremities, so it usually requires immobilization for two weeks as a sufficient treatment (50, 51).

Imaging

Plain radiographs are considered the tool of choice in screening for pediatric patients with normal neurological examination while decreasing the dose of radiation and subsequently, the risk of malignancy decrease.
The sensitivity of the lateral film is 73% in young children and increases to reach 93% in children more than eight years old (52). Therefore, the lateral view has the capacity of detecting around 80% of injuries (53). The anteroposterior (AP) view can also be used but has a little role as well as the flexion/extension films.
In children younger than nine years, the odontoid view also has a little role as in this age dens fractures can be detected by the lateral film (54). A retrospective study published in 2017 has reported that CT is superior to X-rays in detecting cervical spine injuries (CSI) in both clinically significant and insignificant injuries independent of the age of patient and injury location (55). However, the use of CT is associated with increasing doses of ionizing radiation and the subsequent risk of malignancy.
MRI of cervical spine continues to be the best imaging modality for the diagnosis of soft tissue injuries as ligamentous and cord injuries when compared with CT (56-58).
Applications of the Canadian C-Spine rule and nexus low criteria in emergency condition have widely spread, and this may be due to inadequate cervical spine radiography which reinforces the debate about its utility (59). The last meta-analysis done to evaluate the accuracy of Triage tools for detecting CSI in pediatric patients concluded the lack of enough evidence to determine the accuracy of Canadian C-Spine rule or nexus criteria. Only three cohort studies were eligible for analysis, and so additional studies with large sample size are required to determine their accuracy (60).

SCI without radiographic abnormality (SCIWORA)

SCIWORA in children was defined as the presence of objective signs of acute traumatic myopathy in the absence of spinal column injury on plain radiographs and CT scan (61, 62). Children usually develop SCIWORA from falls and pedestrian versus motor vehicle accidents. It is also important to note that most of the patients may have a significant injury in the spinal cord in spite of normal neuroimaging and normal physical examination, and they present with blunt trauma to the spinal cord with the previous history of transient neurologic deficits or presented by transient numbness, paresthesias, and paralysis that has resolved at the time of initial evaluation, Therefore, clinicians must retain a high suspicion for that and

a radiographic follow up is recommended for all patients with SCIWORA . In this regard, a case report presented six years old child with delayed clinical presentation, unusual neuroimaging, and a moderately uneventful clinical course that was diagnosed as SCIWORA (63).
However, with the advance of MRI, the diagnosis of SCIWORA becomes less common. It was found that in cases of clinical-radiologic mismatch or SCIWORA, it is highly recommended to do an MRI of the spine (64). MRI also allows subdivision of SCIWORA cases into detectable intramedullary or extramedullary pathology and those without neuroimaging abnormalities (SCIWONA), but yet there is no implicit prognostic value of MRI findings to guide treatment (65, 66).
A meta-analysis in 2015 showed that the extent of initial neurologic status has a significant association with specific MRI patterns and subsequent outcome. It also recommended an MRI for all pediatric patients experiencing SCI without radiographic abnormality (67).

Management

Steps in the management of patients with acute traumatic SCI are divided into pre-hospital and in-hospital measurements (68).

- ***Pre-hospital Management of Pediatric spinal cord injuries***

For pediatric patients, the evidence needed to make recommendations is insufficient. Management of the injured pediatrics needs certain skills and may differ from adults' treatment (69).

- ***<u>Proper immobilization</u>***

Immobilization is one of the most important pre-hospital procedures. It helps prevent more spinal cord injuries and neurological deficit. Traditionally, cervical injuries immobilization is done as in adults by placing the patient over a spinal board and applying cervical collar with bags on both sides of the head (70). However, children may be in severe pain, so, application of collar will be dangerous and difficult. The suitable approach for such cases is pragmatic, allowing the child to find his position then providing manual stabilization.

- ***<u>Pediatric respiration and airway</u>***

Airway control is more important in pediatrics than adults as the major cause of cardiac arrest in them is due to hypoxia secondary to respiratory failure compared to cardiac troubles in adults (71). For this reason, early management of respiration is recommended, but unfortunately, pre-hospital providers usually have limited experience in managing the airway in pediatrics.

- ***<u>Pediatric metabolism</u>***

The pediatric metabolism differs from that of the adults, and O_2 consumption is higher due to the increased surface area to size ratio in children. After SCI, hypothermia is frequently seen. It may lead to higher O_2 consumption resulting in lactic acidosis and affecting the coagulation system. Avoiding such complications and maintaining euthermia are essential for life-support (69).

- ***<u>Pediatric cardiovascular system</u>***

Controlling blood pressure and maintenance of blood volume by the administration of IV fluid are lifesaving steps. The first fluid bolus, as reported in Pediatric Advanced Life Support guidelines, recommended being up to 60 mL/kg of isotonic crystalloid for initial resuscitation (72). The fluid should be warmed to prevent hypothermia. Crystalloids should be administered carefully; excessive fluids may enhance bleeding and coagulopathy.

- ***Hospital Resuscitation***
  - ***<u>Initial hospital evaluation</u>***

After arrival and while maintaining Advanced Trauma Life Support guidelines and spinal precautions, the patient state should be evaluated by emergency, surgery, and neurointensive departments. After ABC stability, the team proceeds with a rapid neurologic evaluation. Then attention is given to the spinal cord. The patient entire spinal cord is assessed. At this time, the backboard is removed because of problems associated with prolonged use. There are several tools have been developed to provide a rapid and accurate assessment of the severity of SCI (73). The American Spinal Injury Association (ASIA) scoring system and the ASIA Impairment Scale (AIS) are the most valid and the most widely used (74). The ASIA score form aims at assessing the level of injury and its severity. Certain confounding factors may influence the accuracy of the ASIA scale, such as age, level of consciousness, and other injuries (75).

- ***<u>Initial radiographic analysis</u>***

After resuscitation of acute SCI patients, further diagnosis and radiographic evaluation of the spine is needed. Patients should be placed on the spinal board and immobilized until the establishment of the radiographic evaluation; then the patient must be taken off the board to prevent ulcers. This evaluation provides essential information and is needed for decision-making regarding the treatment options.

- ***<u>Respiratory management</u>***

Respiratory problems are one of the most frequent causes of morbidity and mortality in children with SCI trauma (76). Pediatrics have smaller lungs and higher metabolism than the adults so pediatrics can tolerate apnea for 2-3 minutes then hypoxia occurs, but the adults can tolerate apnea for a longer duration up to 5 minutes before developing of hypoxia (77). Rapid airway management is a key element in managing patients, and it follows the next steps

- ***Positioning***

The injured child is positioned at the sniffing position that can be established by a simple extension of the neck, rolling the shoulder, adding headrest, glabella and chin are horizontally aligned. Also, the mouth and oropharynx should be cleared from any debris or secretions.

- ***Ventilation and Breathing***

If the spontaneous ventilation by the positioning is not adequate, hence the child needs assistance. Bag valve mask (BVM) can be a successful procedure. It's a hand device used for manual resuscitation by providing positive pressure, which helps in the breathing. If there is airway obstruction, BMV will be un-useful till re-opening of the airway either by jaw thrust or chin lift.

- ***Laryngoscope Blades***

There are two types of blades, straight and curved. Straight blades insertion into the child's mouth is easier, but the thinness of this blade makes the manipulation of a large tongue difficult. The curved blade is large and bulky so, it retracts the tongue easily and may be useful in certain pediatric populations when the tongue is larger or bulkier than usual.

- ***Endotracheal Intubation***

In endotracheal intubation, a flexible plastic tube is placed in the superior airways through the mouth or nose and usually used in respiratory failure. Rapid sequence intubation (RSI) is the use of some steps including sedatives and neuromuscular blocking agents to facilitate successful intubation and decrease risks of aspiration; Some studies concluded that intubation without some steps of RSI has a lower success rate and higher complication in children and adults (78, 79).

- ***Cardiovascular system management***

SCI patients can suffer from different degrees of shock. Differentiating between neurogenic shock (NS) from hemorrhagic shock is a crucial step for adapted management. The incidence of NS depends on the severity of the injury (80). It results in hypotension without tachycardia, and patients respond to intravenous fluid and vasoactive support. Pharmacological support, in this case, is based on α agonists to treat hypotension and β agonists for managing bradycardia. Some patients may have persistent bradycardia due to the loss of sympathetic. Impairment of supra-spinal sympathetic reflex may also occur (81, 82). Postural hypotension may persist after hemodynamic instability resolves. These patients are characterized by reduced catecholamine level (83). Spinal cord recovery can improve postural hypotension, and the adaptation of the renin-aldosterone system can solve the problem (84). On the other hand, hemorrhagic shock requires primary control of the source of hemorrhage and aggressive fluid administration, including colloid and crystalloid.

SCI and immobilization may increase the risk of venous thromboembolism (VTE) with a higher incidence in adults than in young people. There is no evidence about VTE prophylaxis and the use of mechanical or pharmacological prophylaxis depending on the clinical presentation of each patient (85).

- ***Autonomic nervous system management***

SCI patients suffer from autonomic dysfunction due to unopposed afferent nerve stimulation distal to the injury level leading to hypertension and headache (84). Autonomic dysfunction can occur repetitively and may be asymptomatic. Some SCI patients may experience adrenal insufficiency and must be supplied with hydrocortisone.

- ***Current pharmacological treatments for SCI***

Some medications are used in SCI in adult patients, but there is no clear evidence on the use of these drugs in pediatrics so, further trials targeting this population are necessary. A list of the commonly used drugs in the management of SCI is shown in table 1 (86-102).

- ***Rehabilitation***

Rehabilitation after pediatric SCI is becoming a major step in patients' care. It requires the collaboration of professionals from many disciplines. Its main goal is to decrease the dependency and to improve the quality of life of the patient. Rehabilitation usually includes inpatient measurements such as wheelchair skills and bed motility and outpatient measurements, which are also called post-discharge measurements (103, 104).

The concept of neuroplasticity has improved SCI management in both adult and pediatric populations by encouraging more scientists and clinicians to investigate the different tools of rehabilitation (105). Excessive research generated one of the most important rehabilitation processes, which are Activity-Based Therapy (ABT). Thanks to the NeuroRecovery Network, 7 ABT centers were implemented in the United States (106). The primary rehabilitation tools for pediatric

Table 1: The list of the commonly used drugs in the management of spinal cord injuries

Riluzole	It is a glutamate receptor agonist that acts by blocking sodium channels. FDA did not approve its use in SCI, but ongoing trials (NCT01597518, NCT00876889, and NCT02859792) are testing its usage in humans. In a pre-clinical trial, Riluzole had promising results in terms of damaged neurons repair (86).
Ketorolac	It is a non-steroidal anti-inflammatory drug (NSAID) that inhibits the cyclooxygenases (COX1 and COX2). Ketorolac can exert a neuroprotective function as it reduces neuronal death at the site of ischemia (87).
Minocycline	This antibiotic can have a neuroprotective effect by providing some anti-inflammatory properties and by regulating cytokines metabolism in the central nervous system tissue. Three ongoing trials (NCT00559494, NCT01828203, and NCT01813240) test its usage in SCI, and one published trial (NCT00559494) proved its feasibility in SCI.
Fingolimod (FTY720)	This drug is a sphingosine receptor agonist. A study illustrated its efficacy in SCI model and showed that its use was associated with motor function improvement (88).
Magnesium	Magnesium is a neuroprotective agent that acts as an antagonist for N-methyl D-aspartate (NMDA) receptor and as a calcium channel blocker (89). A study has reported that Mg improves motor function on spinal cord rodent models (90).
Methylprednisolone	This corticosteroid has anti-inflammatory and antioxidant properties. Methylprednisolone can increase the blood flow to the spinal cord but has no role in reversing the problem of neuronal death (91).
Gacyclidine (GK-11)	This molecule has the role of an N-methyl-d-aspartate receptor antagonist. It had a neuroprotective function in rodent models and improved motor and sensory performance in some model studies (92, 93). Further clinical trials are needed to determine its efficacy.
GM-1	It is a ganglioside found in the neuronal cell membrane. Some trials showed up an improvement in ASIA motor score after its usage (94, 95).
Baclofen	It is γ-aminobutyric acid agonist that inhibits both monosynaptic and polysynaptic reflexes at the spinal level. It can decrease excitatory neurotransmitter release from afferent terminal nerves. Intrathecal baclofen can be used for treating SCI associated spasticity (96, 97).
Dantrolene	It is a peripheral skeletal muscle relaxant used in muscle spasticity that may have neuroprotective effects after SCI (98, 99).
Botox	It is made from a neurotoxin secreted by Clostridium botulinum bacteria. Botox is safe and effective in reducing neuropathic pain associated with SCI (100).
Tizanidine	It is an alpha 2-adrenergic agonist usually used for the treatment of muscle spasticity associated with SCI (101). A study found that Tizanidine is effective in improving walking in higher functioning patients (102).

populations are not thought to provide “natural recovery” because stabilizing the patients in the same position and restricting their movements makes them dependent to the different devices and adds to their paralysis (103, 107). The application of ABT resulted had a positive impact on the improvement of adults’ mobility functions after spinal cord injuries. It is based on the activation of the nervous system with many tools such as intense task-specific practice (108). Collaboration between caregivers and scientists in this field contributed to the extension of activity-based therapy into the pediatric population. They showed up that motor training leads to a significant change in the motility abilities and participation in home and community activities — function outcomes. Function outcomes after rehabilitation can be influenced by many factors such as age, sex, the severity of the injury, and socioeconomic factors.

As a consequence, many scaling systems have been developed to predict functional outcomes (ICF and FIM) (6, 104, 109, 110). These scores and scales aim to measure the assistance needed for each patient to improve his performance. NRS is an outcome measure designed for ABT. It has a high psychometric level in adults, and its pediatric version is under development (111).

- ***Surgical treatment***

The surgical interventions in adult traumatic spinal injuries in adults are well detailed and standardized by surgical societies. The spine injuries in young patients must be distinguished from those in adults because of anatomical considerations. However, in a cohort of 75 pediatric patients, the surgical methods and modalities did not differ (112). Pediatric spinal injuries are managed conservatively in most cases. They are useful in stable fractures without neurological lesion and even isolated ligamentous injuries (113, 114). Conservative treatment of the cervical spine may include external stabilization with a soft cervical, a semi-rigid collar, or a halo fixation device (44).

Surgical treatment is mainly indicated in unstable injuries, irreducible fractures or dislocations, progressive neurological deficits resulting from compression, progressive deformity, and in patients aged more than eight years (115, 116). Early surgery may be mandatory in unstable lesions (15). But as a general rule, the indication of surgical therapy for pediatric spinal trauma, particularly in small children with injuries of the cervical spine, remains strictly individual (117).

- ***Stem Cell Therapy***

Mesenchymal stem cells are characterized by their rapid division and high differentiation potency. They exceptionally engender immunoreactive responses after their transplantation. However, the mechanism in which stem cell therapy enhances synapse formation has not been determined yet (118). Researchers think that they provide neurotrophic support and some autocrine and paracrine effects by their secretome. For example, these cells can give an anti-inflammatory power by secreting multiple anti-inflammatory cytokines, including neurotrophin 3 factor (NT-3), IL-10, IL-13, and IL-17E. They can also inhibit the release of pro-inflammatory cytokines by the host or increase the level of IL-10 and promote the polarization of macrophages to an anti-inflammatory phenotype. The anti-inflammatory potential of MSCs, added to their neuroprotection effect, help prevent neural degeneration, and promote neurogenesis and remyelination (119-121).

Since the first attempts of stem cell transplantation SCI, scientists and lab investigators multiplied their efforts in this field (118). A variety of cells were used, such as bone marrow and umbilical cord mesenchymal cells (122, 123). Cellular populations obtained from the cord blood or the umbilical cord resulted in neurotrophic properties in SCI animals (124, 125). The intrathecal transplantation is being tested in a multicenter randomized trial (NCT03521336). Furthermore, Amniotic Fetal mesenchymal stem cells and Adipose-derived mesenchymal stem cells showed limited effects in animal models (126-129). To sum up, Stem cell technologies promote neuronal repair processes with minimal side effects. However, financial and ethical issues can form a real burden against their general application (118).

DISCUSSION

- ***Future directions for treating SCI***

Many promising neuroregeneration interventions have been designed to restore the normal functions after brain and spinal injuries (130). The administration of chondroitinase, which is a bacterial enzyme metabolizing CSPGs, with neural precursor cells, can enhance the axonal remyelination process (131, 132). This remyelination potential has been shown to improve sensorimotor functions in rats (133). Furthermore, the use of NOGO receptor antagonists to block the action of myelin protein NOGOA improved axonal regeneration in animals with spine injury (134, 135). Scientists examined its safety and efficacy in SLA patients (136, 137). Transplant hydrogel polymers constitute a modern method of neurodegeneration. Many molecules have been tested in SCI such as collagen, agarose, fibrin, and hyaluronan (138-142). The use of hydrogel polymers showed a promising result, especially when it was combined with the administration of biological molecules such as growth factors and immunomodulatory factors (143, 144). The results can be explained by the fact that the biomechanical properties of hydrogels delivery systems can promote cellular migration in the spinal cord tissue (145). They can also enhance cell differentiation and stop the immune response after SCI (130).

- ***Limitations of recent research into SCI treatment***

Recent research into SCI is a bit limited by several ethical and methodological challenges. The small sample size of the published studies as well as the lack of comparison against a control group, make it difficult to draw informative conclusions to guide the clinical practice. Withholding a beneficial intervention in SCI patients to test a novel regenerative treatment might be challenging from ethical and methodological points of view. Future researchers should solve this problem by suggesting novel trial methodologies that can overcome the current methodological and ethical limitations. Future research is needed to investigate the safety and efficacy of the recent uprising neuroregenerative techniques in SCI population.

Conclusions

The management of pediatric traumatic spinal cord injuries have been challenged by the lack of class-one evidence about the safety and efficacy of the present treatment options. In addition, the uprising neurodegenerative techniques might hold a promise for treating traumatic SCI in children. Owing to the current limitations, there is a need to develop novel trial methodologies that can overcome the current methodological and ethical limitations.

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Authors' contribution

All authors participated in drafting and revising the article.

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