



Use of Adipose-Derived Mesenchymal Stem Cells and Biomaterials in Treatment of Spinal Cord Injuries in Cats Model

JASSIM M. KHALAF ALBOZACHRI^{1*}, HAMEED A. AL-TIMMEMI²

¹Department of Veterinary Surgery and Obstetrics, College of Veterinary Medicine, University of Kerbala, Karbala, Iraq; ²Department of Veterinary Surgery and Obstetrics College of Veterinary Medicine, University of Baghdad, Iraq.

Abstract | Spinal cord injuries are a common cause of permanent neurological deficits, often resulting in severe disabilities such as complete paralysis. Current therapies for spinal cord injury frequently show limited success. This study aims to clinically evaluate the effects of human placenta (HP) and adipose-derived mesenchymal stem cells (ADMSCs) on restoring spinal cord injuries in cats. Twenty-four adult healthy cats were randomly assigned to three equal groups (n = 8 each). Under aseptic conditions, the cats were anesthetized and underwent dorsal laminectomy with left lateral hemisection at the second lumbar vertebra. The control group received no treatment, the placenta powder group was treated with 0.01 mg of HP powder, and the stem cell group received 50 µl (5 x 10⁶ cells) of ADMSCs implanted into the hemisection cavity immediately post-surgery. Motor and sensory functions, including gait, proprioceptive posture, and nociceptive responses, were assessed weekly using the open field locomotor scale from the first week until the 16th week post-operation. Throughout the study, the analysis revealed no significant differences (p < 0.05) in motor and sensory outcomes between the placenta powder and stem cell groups. However, at the 16th week post-surgery, a noteworthy distinction (p ≤ 0.05) in motor and sensory reflexes was observed between the treatment and control groups. These findings suggest that HP powder may have regenerative potential for spinal cord injuries, while AD-MSC transplantation demonstrates greater effectiveness. The results advocate for further exploration of HP powder and AD-MSCs in spinal cord regeneration following hemisection injuries, with implications for clinical application and future research.

Keywords | Spinal cord, Stem cells, Biomaterials, Adipose tissue, cats

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***Correspondence** | Jassim M. Khalaf Albozachri, Department of Veterinary Surgery and Obstetrics, College of Veterinary Medicine, University of Kerbala, Karbala, Iraq; **Email:** jasim.khalaf@uokerbala.edu.iq

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INTRODUCTION

A severe disorder, spinal cord injuries cause an abrupt loss of motor, sensory, and/or autonomic function far from the site of the lesion. (Vaquero *et al.*, 2017; AL-Ameri and AL-Timmemi, 2018; Markides *et al.*, 2018). Developing treatments for spinal cord injury is intrinsically difficult due to its complex pathobiology, which includes glial scarring,

apoptosis of neural cells continuously, demyelination, the formation of cavities or cysts, inflammatory agent invasion, and the loss of complex neural circuitry (Liu *et al.*, 2013; Helal and Hussein, 2022). The majority of spinal cord injury therapies now in use fall into one of two categories: neuro-protective or neurodegenerative. While neuroregenerative treatments rely on restoring lost or compromised capability by fixing the spinal cord's damaged neuronal circuitry, neu-

roprotective therapies aim to hinder or stop the secondary injury from getting worse (Garcia *et al.*, 2016). Tissue engineering uses biomaterials to help rebuild damaged tissues (Kabu *et al.*, 2015). Acellular placenta has the potential to be a biomaterial that is employed as a scaffold for the repair of different organs and tissues, as well as a substrate for the transfer of autologous and allogeneic cells (Roy *et al.*, 2016; Francisco *et al.*, 2013; Al-Timmemi *et al.*, 2017). Acellular amniotic membrane may be a potential biomaterial and can be used as a scaffold for various organs and tissue repair or as a substrate to facilitate autologous/allogeneic cell transfer (Roy *et al.*, 2016). Mesenchymal stem cells produced from fat have a vast range of sources, a significant capacity for multipotent differentiation, and a variety of application methods. Superior anti-inflammatory, immune-regulating, and angiogenic properties compared to other treatments and other stem cells (Sabol *et al.*, 2021; Essa *et al.*, 2020). photobiomodulation therapy after SCI can decrease the inflammation reactions in the spinal cord by regulating the migration of immune cells in the spinal cord and it can prevent the destruction of axonal myelin. Also, it can cause a decrease in the size of the central cavity and enhance motor function (Gupta *et al.*, 2015). The application of human placenta powder will result in greater functional recovery in spinal cord injury models due to its unique composition that promotes neuroprotection and regeneration. The study's objective is to clinically assess how human placenta and mesenchymal stem cells produced from adipose tissue affect the repair of spinal cord injuries in cats.

MATERIALS AND METHODS

ETHICAL APPROVAL

The Research Ethics Committee at the University of Baghdad's College of Veterinary Medicine endorsed the experimental design and techniques used in this work, with ethics number 603 P.G. dated March 18, 2024, in compliance with ethical norms about animal welfare. The post-operative care uses tramadol injection to control the pain at a dose of 4 mg/kg 3 times a day (Malek *et al.*, 2012).

EXPERIMENTAL ANIMALS

Twenty-four male healthy cats aged 8-24 months and weighing 2-5.5 kg were enrolled. The cats had commercial food and water for meals and were housed in individual cages. Before the surgical procedure, the animals were allowed to acclimate for a total of fifteen days in their cages. Ceftriaxone (22 mg/kg), a broad-spectrum antibiotic, was injected intramuscularly (IM) twice daily for five days. On the first day and day 14 of acclimatization, an antihelminthic injection of 0.2 mg/kg ivermectin (Ivomec, Holland) and 0.4 ml/kg SC was administered. Three equal groups of eight cats each were randomly assigned to have a left lateral hemisection of the spinal cord at the second lum-

bar vertebra of the spinal cord and a dorsal laminectomy. The procedure of surgical dorsal laminectomy which was depended in the present study was described previously by Fossum (2013). The back of the animal extending from the last thoracic vertebra to the last lumbar vertebra of the anesthetized cat was prepared surgically with chlorhexidine gluconate, Isopropyl alcohol 70% and disinfected with 1.8 % tincture iodine. The cats were positioned in sternal recumbency. A surgical incision was made over the dorsal midline to include L1-L3 vertebrae, using a periosteal elevator to subperiosteally elevate epaxial muscles from dorsal spinous processes, laminae, articular facets, and pedicles of L2 vertebra and with aid of Gelpi retractors to facilitate gentle retraction of epaxial musculature during dissection. In the control group (group A) (n=8), the hemisection defect was left without treatment, powder group (group B) (n=8), was treated by implantation of 0.01mg human placenta powder (AL-Ameri and Al-Timmemi, 2018) impacted between proximal and the distal stumps of the hemisection site of the spinal cord and stem cells group (group C) (n=8), was treated by injection (5x10⁶) (ADMSCs) into the hemisection site of the spinal cord. Weekly assessments of motor and sensory reflexes were part of the clinical follow-up, which ran from the first week of the study to the 16th week following the procedure.

FABRICATION OF HUMAN PLACENTA POWDER

Following the signing of informed permission forms, human placentas (HP) were removed from healthy pregnant women during cesarean births. Al-Yarmouk Teaching Hospital in Baghdad, Iraq, provided the (HP) samples. Human placenta powder was prepared according to (Fan *et al.*, 2023).

ISOLATION AND CULTIVATION OF AD-MSCs

The cat was administered general anesthesia including xylazine (2%) 1 mg/kg b.w. (Aleppo-Syria) and ketamine (10%) 10 mg/kg b.w. (AlasanTM, Holland) via intramuscular injection (Allen *et al.*, 1986). The inguinal region's skin underwent aseptic surgical preparation, which was followed by a clean skin incision. Three grams of subcutaneous fat were taken out. The isolation and cultivation of stem cells according to (Dhurgham and Al-Timmemi, 2023).

CLINICAL SIGNS EVALUATION

Every week from the first week of the study to the 16th week after surgery, the injured spinal cord's clinical indications of motor reflex were evaluated. However, from the second to the 16th week following surgery, sensory reactivity was assessed once a week.

EVALUATION OF THE MOTOR FUNCTIONS

After undergoing surgery, every animal was spared and used for analysis. The modified Tarlov Scale (Tarlov *et al.*, 1953)

and Texas Spinal Cord Injury Scale (TSCIS) (Levine *et al.*, 2009). A behavioral assessment system was used to assess locomotor recovery. Weekly assessments and records of the spinal cord injury's motor functions were made from the first week following surgery and continuing through the 16th week. Function improvement was assessed using the Knuckling scale, which ranged from normal to mild to severe (Table 1).

Table 1: Modified clinical signs grading system for motor recovery (Tarlov *et al.*, 1953; Levine *et al.*, 2009).

Clinical observation	Grad	Description
Gait	6	Complete motor activity
	5	Normal gait but inability to leap
	4	Ability to walk with minor difficulty
	3	Ability to walk with major difficulty
	2	Ability to push up on hind leg and take few steps
	1	Ability to push upon hind leg but not take steps
	0	Total paralysis of hind leg
Proprioceptive positioning "Knuckling"		Flexion of the fetlock joint and bending of digits
Normal	4	Planter surface of the foot face the ground
Mild	3	Planter surface of the foot face the ground with little flexion of digits
Moderate	2	The animal can walk with more difficulty than above grade
Severe	1	The animal dragged the limb and walked on the dorsum of foot

SENSORY FUNCTIONS EVALUATIONS

Every week from the 2nd to the 16th week following the injury, the sensory functions of spinal cord injury were evaluated. The Texas Spinal Cord Injury Scale (TSCIS), which evaluates each limb separately in cats, was created to represent the normal progression of functional loss and recovery following spinal cord injury (Levine *et al.*, 2009). The cat was put in lateral recumbency and examined to see whether deep and superficial nociception was present. A needle was used to prick the plantar surface of the foot and the lateral side of the leg to test for superficial nociception (soft tissue pain), and a forceps was used to grasp the most distal part of the digit to assess deep nociception (bone or joint pain) (Table 2).

STATISTICAL ANALYSIS

The software Statistical Analysis System (SAS, 2012) was utilized to determine how different factors affected the research parameters. In this study, the least significant differ-

ence (LSD) test (ANOVA) was utilized to compare means in a significant way, and was employed to compare percentages.

Table 2: Texas Spinal Cord Injury score (TSCIS) Modified Scoring for Evaluation the Sensory Clinical Signs by [10].

Clinical Observations	Description	Score
1. Superficial nociception	Induced by pricking the lateral aspect of leg with needle	
a. (Lateral aspect leg sensation)		
Absent deep and superficial		0
Present superficial noci.		1
Present deep nociception	Reflex induced by pricking the planter surface of foot with needle	2
Present deep and superficial		3
b. (Toe Prick)		
Absent deep and superficial	Reflex induced by pinching the most distal portion of digit with forceps	0
Present superficial noci.		1
Present deep nociception		2
Present deep and superficial		3
2. Deep nociception (Toe pinch)		
Absent deep and superficial		0
Present superficial noci.		1
Present deep nociception		2
Present deep and superficial		3

RESULTS AND DISCUSSION

NEUROLOGICAL EXAMINATION OF THE CONTROL GROUP DURING THE PERIOD OF THE STUDY

From the 1st to the 14th day after surgery, every animal had severe dysfunction (The animal dragged the limb and walked on the dorsum of foot), which included total paralysis of the pelvic limbs and dragging of the caudal portion of the body when walking (Table 3) and severe knuckling (Table 6). However, there were no documented deep or surface pain feelings in the hind leg (Table 4). According to the clinical evaluation, on day 28, all hind limb paralysis was visible, and on day 21, Because they were crawling on their rear limbs, some animals developed skin erosion on the dorsum of those limbs (Table 4). However, all animals had severe knuckling (Table 6). No sensations of the hind limb were recorded (Table 4). Three animals comprising in this group have complete paralysis of hind limbs which persisted up to the end of the study and five animals ability to push up on hind leg and take few step at end of 56th day PO (Table 3). However, knuckling became moderate on 38th day PO (Table 6). No sensations of the hind limb were recorded (Table 4). The clinical observations at the

Table 3: The Mean (score) neurologic status as evaluated by the modified Tarlov neurologic recovery in all groups (Subgroup n=4).

Time	Control group	Placenta powder group	Stem cells group
1Wk PO	Total paralysis of hind leg	Total paralysis of hind leg	Total paralysis of hind leg
2Wk PO	Total paralysis of hind leg	Total paralysis of hind leg	Ability to push upon hind leg but not take steps
3Wk PO	Total paralysis of hind leg	Ability to push upon hind leg but not take steps	Ability to push up on hind leg and take few step
4Wk PO	Total paralysis of hind leg	Ability to push up on hind leg and take few step	Ability to push up on hind leg and take few step
5Wk PO	Ability to push upon hind leg but not take steps	Ability to push up on hind leg and take few step	Ability to walk with major difficulty
6Wk PO	Ability to push upon hind leg but not take steps	Ability to walk with major difficulty	Ability to walk with minor difficulty
7Wk PO	Ability to push upon hind leg but not take steps	Ability to walk with major difficulty	Ability to walk with minor difficulty
8Wk PO	Ability to push upon hind leg but not take steps	Ability to walk with minor difficulty	Normal gait but inability to leap
9Wk PO	Ability to push upon hind leg but not take steps	Normal gait but inability to leap	Normal gait but inability to leap
10Wk PO	Ability to push upon hind leg but not take steps	Normal gait but inability to leap	Normal gait but inability to leap
11Wk PO	Ability to push up on hind leg and take few step	Normal gait but inability to leap	Normal gait but inability to leap
12Wk PO	Ability to push up on hind leg and take few step	Normal gait but inability to leap	Normal gait to leap
13Wk PO	Ability to push up on hind leg and take few step	Normal gait to leap	Normal gait to leap
14Wk PO	Ability to push up on hind leg and take few step	Normal gait to leap	Normal gait to leap
15Wk PO	Ability to push up on hind leg and take few step	Normal gait to leap	Normal gait to leap
16Wk PO	Ability to push up on hind leg and take few step	Normal gait to leap	Normal gait to leap

end of experiment revealed no improvement up to 112th day (Table 3). Knuckling persisted until the study's conclusion at a moderate level (Table 6). Sensation remained absent (Table 4).

NEUROLOGICAL EXAMINATION OF THE PLACENTA POWDER GROUP DURING THE PERIOD OF THE STUDY

The clinical assessment for this group showed total paralysis of hind limbs from first day PO which continued to the end of 14th day PO (Table 3), and severe knuckling at the end of 14th day PO (Table 6). However, no sensations of the hind limb were recorded (Table 4). On the 21th day PO, every animal in this group demonstrated the capacity to push against their hind limb with a few steps, and they also began to be able to walk with some difficulty. (Table 3) and knuckling improved to moderate on 17th day PO (Table 6) but still, there were no sensations (Table 4). All animals could walk with minor difficulty (Table 3) and the knuckling became mild on 56th day PO (Table 6) still sensation was absent at end of 56th day PO (Table 4). One intriguing discovery was that on day 91th PO, the animals' pelvic gait motions returned to normal (Table 3) at the same time the knuckling disappeared 63th day (Table 6). However, sensation slowly progressed towards foot at the end of the study. Toe pinch reaction first showed on day 85 postoperatively, whereas lateral aspect leg and toe prick

were evident on days 99 and 105 postoperatively, respectively (Table 4).

NEUROLOGICAL EXAMINATION OF THE STEM CELLS GROUP DURING THE PERIOD OF THE STUDY

In the stem cell group, complete paralysis of hind limb movement was evident on the 6th day post-operation (PO). However, by the end of the 7th day PO, the animals began to demonstrate the ability to push with their hind legs, although they could not take any steps (see Table 3). By the 8th day PO, moderate knuckling was observed (Table 6), and no sensory response in the hind limbs was recorded (Table 4). Remarkably, by day 21, all animals in this group exhibited the capacity to push off with their rear legs and take a few steps. Progress continued, and by day 35, the animals were able to walk, albeit with some difficulty (Table 3). Knuckling improved to a moderate level by the 23rd day PO (Table 6), but sensory responses remained absent (Table 4). By day 45 PO, while all animals displayed a normal gait, they were still unable to leap (Table 3), and knuckling had reduced to a mild condition (Table 6). Sensory responses continued to be absent on the 56th day PO (Table 4). A significant finding emerged on the 84th day PO, where all animals showed normal pelvic gait movements (Table 3), and knuckling had returned to normal by day 56 (Table 6). Additionally, the toe pinch reaction was

first observed on day 78 PO, followed by responses to lateral aspect leg and toe pricks on days 93 and 95, respectively (Table 4).

Table 4: The Mean time (Days) of sensory clinical observations during the period of the study in all groups (Subgroup n=4).

Group	(Sup. nocicep- tion) Lat. Aspect Leg Sense	(Sup. nocicep- tion) Toe prick	(Deep nocicep- tion) Toe Pinc
Control			
14 days	-	-	-
28 days	-	-	-
56 days	-	-	-
112 days	-	-	-
Placenta powder			
14 days	-	-	-
28 days	-	-	-
56 days	-	-	-
112 days	+99days	+105days	+85days
Stem cells			
14 days	-	-	-
28 days	-	-	-
56 days	-	-	-
112 days	+93days	+95days	+78days

The results are consistent with (Fukuda *et al.*, 2005), which demonstrated significant spinal cord injury and the development of cavities encircled by high-collagen scar tissue, resulting in permanent paraplegia in cats for 12th weeks following SCI. However, among the treatment groups the placenta powder group (91 days) and the stem cells group (84 days) the gait returned to normal. Clinical motor symptoms, such as the capacity to walk by the pain's intensity (which was divided into inflammatory and neuropathic pain). According to the current study, the gait of the stem cell group returned to normal more quickly than that of the placenta powder group. This finding indicated that the use of stem cells may have therapeutic benefits for improving the functional recovery of injured spinal cords by releasing a variety of neurotrophic factors that support the formation of myelin sheaths, neovascularization, decreased inflammatory response, and decreased edema, all of which help to relieve pain associated with spinal cord injuries. The knuckling vanished in each of the treatment group's animals. But vanished after 63 days in the placenta powder group and 56 days in the stem cell group. Conversely, until the conclusion of the trial, knuckling continued in the control group. This might be due to the placenta powder and stem cells are beneficial for functional recovery at the location of hemisection defects in SCI patients. It has been demonstrated that they enhance the early innervation of

the flexor and extensor muscles, which control proper limb movement and promote the growth of neovascularization and myelin sheaths. This improvement may be attributable to stem cells' capacity to hasten axon regeneration and re-building, as well as to reduce the production of neuropathic pain through the release of neurotrophic, angiogenic, and anti-apoptotic substances (Yousefifard *et al.*, 2016; Hussein and AL-Bayati, 2022). According to Mannoji *et al.* (2014), the infusion of mesenchymal stem cells in spinal cord injuries will stop the development of heat and mechanical allodynia. All of the main immune cell populations' functions can be modulated by the immunosuppressive qualities of stem cells. Stem cells may have an impact on inflammatory pain, which interacts with all immune system cell types. This interaction may occur directly or through soluble substances that impede all immune response mechanisms and shorten the duration of inflammatory pain. (Sotiropoulou and Papamichail, 2007; Al-Timmemi *et al.*, 2011). Additionally, stem cells fight several detrimental processes including inflammation and apoptosis to produce a milieu that is favorable for neural regeneration (Parr *et al.*, 2007; AL-Qaisy *et al.*, 2014). According to Zhou *et al.* (2016); Dhurgham and Al-Timmemi (2023), stem cells can promote axonal regeneration in two main and distinct ways: either by differentiating or by encouraging transdifferentiation into neurons or glial cells, or by releasing a variety of trophic factors, such as factor (BDNF), NGF, VEGF, FGF-2, TGF- β , and IGF-1, through a paracrine effect.

STATISTICAL ANALYSIS OF MOTOR CLINICAL SIGNS OBSERVATIONS

Proprioceptive positioning-related hind leg posture responses and a change in gait score were not seen in the control group during neurologic testing. After transplanting of human placenta powder or stem cells the total Modified Tarlov scores and Texas Spinal Cord Injury Scale score were improved. However, the cats on the 14th day PO, in the stem cells group reached an average Tarlov score (1.00 ± 0.00) that was significant ($p < 0.05$) than placenta powder (0.25 ± 0.12) and control (0.00 ± 0.00) groups.

On the 28th day PO stem cells (2.00 ± 0.00) were more significant ($p < 0.05$) than the placenta powder (1.25 ± 0.25) and control (0.00 ± 0.00) group (Table 5). In addition, on 56th day 56 PO, in placenta powder (4.25 ± 0.25) and stem cells (4.50 ± 0.28) groups was higher significant ($p < 0.05$) than control group (0.50 ± 0.28). On the 112th day PO, the placenta powder (6.00 ± 0.00) and stem cells group (6.00 ± 0.00) was significantly higher ($p < 0.05$) than the control group (1.25 ± 0.25). There were no significant differences between the placenta powder and stem cell groups at the 8th and 16th weeks. However, the cats regained normal pelvic gait movement with no recurrence of neurological disorders in the placenta powder group on the 91th day and the stem cells group on the 84th day (Table 5).

Table 5: Statistical analysis of motor clinical observations on days the study period in all groups (Subgroup n=4).

Groups Days	Mean ± SE			LSD value
	Control	Placenta powder	Stem cells	
14	C 0.00±0.00b	D 0.25±0.12b	D 1.00±0.00a	0.461*
28	C 0.00±0.00c	C 1.25±0.25b	C 2.00±0.00a	0.461*
56	B 0.50±0.28b	B 4.25±0.25a	B 4.50±0.28a	0.884*
112	A 1.25±0.25b	A 6.00±0.00a	A 6.00±0.00a	0.533*
LSD value	0.50*	1.284 *	1.105 *	-----
* (P= 0.023)				

^{a,b,c}Values (Mean ± SE) having with the different small letters in same row and big letters in same column differed significantly at $p \leq 0.05$.

Table 6: Statistical analysis of knuckling function tests on days the study period in all groups (Subgroup n=4).

Groups Days	Mean ± SE			LSD value
	Control	Placenta powder	Stem cells	
14	C 1.00±0.00b	B 1.63±0.05a	C 1.75±0.03a	0.455 *
28	C 1.00±0.00c	B 1.75±0.04a	C 1.88±0.03a	0.431 *
56	B 1.75±0.04c	A 2.38±0.05b	B 3.14±0.06a	0.502 *
112	A 2.38±0.08b	A 3.75±0.11a	A 3.88±0.08a	0.833 *
LSD value	0.489*	0.507 *	0.574 *	-----
* (P=0.013)				

^{a,b,c}Values (Mean ± SE) having with the different small letters in same row and big letters in same column differed significantly at $p \leq 0.05$.

Table 7: Statistical analysis of sensory clinical observations at the end of experimental study in all groups (Subgroup n=4).

Sensory Signs	Control	Placenta powder	Stem cells
Lat. Aspect	0±0 ^a	1±0 ^b	1±0 ^b
Leg Sense			
Toe pinch	0±0 ^a	1±0 ^b	1±0 ^b
Toe prick	0±0 ^a	1±0 ^b	1±0 ^b

^{a, b} Values (Mean ± SE) with different superscript within same row are significantly different at $p \leq 0.05$.

While proprioceptive positioning was observed, on the 14th day PO severe knuckling in the placenta powder (1.63 ± 0.05) and stem cells group (1.75 ± 0.03) which was significant ($p < 0.05$) compared to control (1.00 ± 0.00) groups. In addition, on the 28th day PO moderate knuckling was shown in the placenta powder (1.75 ± 0.04) and stem cells (1.88 ± 0.03) groups which were significant ($p < 0.05$) than the control group (1.00 ± 0.00) (Table 4). However, knuckling disappeared in the stem cells (3.14 ± 0.06) group which was significant ($p < 0.05$) compared to placenta powder (2.38 ± 0.05) and control (1.75 ± 0.04)

groups on 56th day PO (Table 6). On 112th day PO normal response (Planter surface of the foot face the ground) the placenta powder (3.75 ± 0.11) and stem cells (3.88 ± 0.08) groups, which was highly significance ($p < 0.05$) than control group (2.38 ± 0.08) (Table 6). Moreover, knuckling disappeared after 63th day PO in Placenta powder group and 56th day PO in stem cells group.

STATISTICAL ANALYSIS OF SENSORY CLINICAL OBSERVATIONS

On days 14, 28, and 56 PO, sensory reflexes, including superficial and deep nociception, did not manifest. On the 112th day PO, animals in the placenta powder and stem cell groups displayed significantly stronger sensory responses ($p < 0.05$) than the control group (Table 7). On the other hand, the placenta powder group's return of deep and superficial sensations of pain in the left hind limb revealed that toe pinch response first came on day 85 PO, while lateral aspect leg and toe prick were evident on days 99 and 105 PO, respectively. Toe pinch response came on day 78 PO, but the lateral aspect limb in the stem cells group displayed toe pricks on days 93 and 95, respectively (Table 4).

Placenta powder or stem cells may have contributed to the better recovery of locomotor and sensory function by increasing the production of neurotrophic factors like NGF and BDNF at the site of injury. It is well known that these compounds support spinal cord regeneration and cell survival. The same results were achieved by Zaminy *et al.* (2013), who verified that Schwann cells were engrafted via collagen scaffold in the hemisected rat spinal cord after allogenic stem cells were differentiated. Surprisingly, sensory perception showed signs of recovery, and hind limb motor skills showed modest improvement. These improvements have been attributed to the induced Schwann cells and the scaffold's capacity to produce neurotrophic substances, which support spinal cord regeneration. The scaffold plays a role in cell behavior modulation when in contact with the scaffold and the control of its diffusing ability into the scaffold (Loh and Choong, 2013). In addition, it may play a role in increasing angiogenesis and rates of axonal regeneration. However, prior research has demonstrated that VEGF plays a significant role in angiogenesis, which might lessen spinal cord damage by reducing inflammation and enhancing healing following spinal cord injury (Park *et al.*, 2016). The ability of stem cells to create a variety of growth factors, neuroprotective cytokines, and chemokines, such as VEGF, NGF, FGF, BDNF, and HGF, may be responsible for the functional advantages of stem cell transplantation (Awad *et al.*, 2015). Zhou *et al.* (2018), showed that stem cells are a productive source of HGF and hypothesized that the hormone these cells release may have a role in the therapeutic benefits of stem cell transplantation. Jeong *et al.* (2012); Al-Mutheffer *et al.* (2023) demonstrated that the hepatocyte growth factor inhibited the production of

certain chondroitin sulfate proteoglycan (CSPG) species and reduced the release of transforming growth factor- β (TGF- β) from activated astrocytes. Kitamura *et al.* (2018), reported that the spinal cord's hemisection lesions' surrounding glycosaminoglycan chain deposition and neuron expression were significantly reduced when transplanting HGF-overexpressing stem cells. HGF-MSc-treated animals had improved functional recovery and enhanced axonal development.

CONCLUSIONS AND RECOMMENDATIONS

The biological implant of HP (Human Placenta) powder has shown promise in promoting the regeneration of spinal cord injuries. Additionally, Adipose-Derived Mesenchymal Stem Cells (AD-MSCs) transplantation appears to be more effective than HP powder alone.

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NOVELTY STATEMENTS

Researchers have isolated stem cells from the adipose tissue of cats and used in treatment of spinal cord.

AUTHOR'S CONTRIBUTIONS

Jassim M. Khalaf Albozachri conceived and planned the experiments. Hameed A. AL-Timmemi, contributed to sample preparation. In addition to leading the paper writing effort and offering insightful criticism, Jassim M. Khalaf Albozachri and Hameed A. AL-Timmemi, helped analyze the data and shaped the study, analysis, and manuscript.

ABBREVIATIONS

AD-MSCs: Adipose-derived mesenchymal stem cells.
Hp: Human placenta
TSCIS: Texas Spinal Cord Injury Scale
PO: Post operation
SCI: spinal cord injury

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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