



Effects of Secretome Administration on Serum Interleukin-6, Neurogranin, and Neurological Outcomes in Patients with Spinal Cord Injury: A Pilot Randomized Controlled Trial

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Abstract

Spinal cord injury (SCI) can result in persistent neurological disability, while secondary inflammatory responses represent a potential therapeutic target for adjunctive interventions. This single-blind pilot randomized controlled trial investigated whether intrathecal administration of umbilical cord-derived mesenchymal stem cell (UC-MSC) secretome was associated with changes in serum interleukin-6 (IL-6), neurogranin concentrations, and early neurological outcomes following traumatic SCI. Ten patients undergoing surgery were randomly assigned to receive either standard care plus a single intraoperative intrathecal administration of UC-MSC secretome ($n = 5$) or standard care alone ($n = 5$). Serum biomarkers were measured preoperatively and at 8 hours, 2 days, and 4 days postoperatively. Neurological and functional outcomes were assessed using the American Spinal Injury Association Impairment Scale (AIS), Spinal Cord Independence Measure (SCIM), and IANR-SCIFRS before surgery and at hospital discharge. Linear mixed-effects models were used to account for repeated measurements, assessment time, age, and sex. Adjusted serum IL-6 concentrations were significantly lower in the secretome group ($\beta = -52.61$ pg/mL; 95% confidence interval [CI]: -87.19 to -18.04 ; $p = 0.043$). The association with serum neurogranin concentrations did not reach the reported threshold for statistical significance ($p = 0.057$), while improvements in neurological and functional outcomes did not differ significantly between groups. Baseline differences in biomarker concentrations, the small sample size, and the short follow-up period limited the interpretation and generalizability of these findings. Furthermore, the reported confidence interval and p -value for neurogranin required reconciliation to ensure statistical consistency. These preliminary findings suggested a potential early anti-inflammatory biomarker response following intrathecal UC-MSC secretome administration but did not establish neurological improvement or clinical efficacy in patients with traumatic SCI.

INTRODUCTION

Spinal cord injury (SCI) is a severe neurological condition characterized by impaired motor, sensory, and autonomic functions, often resulting in long-term disability and reduced quality of life (Qin et al., 2025). Although traumatic SCI initially causes direct mechanical damage to neural tissue, subsequent neurological deterioration is largely associated with secondary injury mechanisms, including inflammation, excitotoxicity, oxidative stress, vascular disruption, apoptosis, and glial scar formation (Ahuja et al., 2017; Freyermuth-Trujillo et al., 2022).

Following SCI, activated microglia, neutrophils, and infiltrating macrophages release proinflammatory mediators, including interleukin-6 (IL-6), which contribute to blood–spinal cord barrier disruption, inflammatory amplification, and secondary neuronal injury. Consequently, persistently elevated IL-6 concentrations have been proposed as potential indicators of inflammatory activity and therapeutic response following SCI (Kwon et al., 2010; Rieder et al., 2019; Wang et al., 2022).

In addition to inflammatory processes, SCI can compromise neuronal and synaptic integrity. Neurogranin is a postsynaptic calmodulin-binding protein involved in calcium–calmodulin signaling and synaptic plasticity. Although neurogranin has been investigated as a potential biomarker of synaptic injury in various central nervous system disorders, its clinical significance in SCI remains uncertain (Çevik et al., 2019; Yang et al., 2015).

Current SCI management primarily involves early surgical decompression when indicated, spinal stabilization, prevention of secondary complications, and rehabilitation. Nevertheless, neurological recovery remains limited in many patients, highlighting the need to investigate additional neuroprotective and regenerative therapeutic strategies.

Mesenchymal stem cell (MSC)-based therapies have attracted considerable interest because of their potential immunomodulatory and regenerative properties. However, their therapeutic effects are increasingly attributed to paracrine signaling rather than direct cellular replacement. MSCs release a complex secretome containing soluble proteins, growth factors, extracellular vesicles, and other signaling molecules that may contribute to tissue repair, regeneration, and intercellular communication (Dabrowska et al., 2020; Harrell et al., 2019; Teixeira & Salgado, 2020; Vizoso et al., 2017).

MSC-derived secretome has emerged as a potential cell-free therapeutic approach that may offer advantages over direct cell transplantation, including fewer concerns regarding transplanted cell survival, differentiation, and unintended cellular effects. The umbilical cord-derived mesenchymal stem cell (UC-MSC) secretome used in this study was described as containing bioactive components, including stromal cell-derived factor 1 (SDF-1), keratinocyte growth factor (KGF), fibroblast growth factors (FGFs), vascular endothelial growth factor (VEGF), and procollagen, which are associated with tissue repair and regenerative signaling.

Although preclinical studies have demonstrated promising immunomodulatory and neuroprotective effects of MSC-derived secretome (Zhai et al., 2021), clinical evidence supporting its application in patients with SCI remains limited. In particular, the effects of intrathecal UC-MSC secretome administration on circulating inflammatory biomarkers, markers of neuronal and synaptic injury, and early neurological outcomes have not been adequately established (Akhlaghpasand et al., 2024; Semita et al., 2023).

The research gap extends beyond the limited number of clinical studies investigating MSC-derived secretome. Specifically, insufficient evidence is available to determine whether changes in early circulating inflammatory biomarkers are accompanied by corresponding changes in synaptic injury markers and neurological function following traumatic SCI. Although experimental findings provide biological support for the potential therapeutic effects of MSC-

derived secretome, they do not establish clinical efficacy. Furthermore, neurogranin has not been validated as a surrogate marker of neurological recovery in patients with SCI. Simultaneously examining inflammatory, synaptic, and functional outcomes is therefore particularly important when evaluating an invasive intervention for which human clinical evidence remains preliminary.

Accordingly, this pilot randomized controlled trial aimed to investigate the effects of adjunctive intrathecal UC-MSC secretome administration on serum IL-6 concentrations, neurogranin levels, and early neurological outcomes in patients with traumatic SCI. The study specifically sought to characterize serial changes in inflammatory and synaptic biomarkers alongside short-term neurological and functional assessments within a small randomized clinical sample. Given its exploratory design and limited sample size, the investigation was intended to generate preliminary evidence rather than provide confirmatory conclusions regarding therapeutic efficacy.

The novelty of this pilot investigation lies in its combined assessment of serial serum IL-6 and neurogranin concentrations alongside standardized neurological and functional outcome measures within a randomized clinical comparison. Its primary objective was to explore short-term biomarker responses and neurological outcomes following adjunctive intrathecal UC-MSC secretome administration rather than establish definitive therapeutic efficacy. The clinical relevance of this investigation arises from the need to identify potential biological responses to emerging treatments for traumatic SCI while distinguishing biomarker changes from clinically meaningful neurological improvement. Nevertheless, the preliminary nature of the evidence, limited sample size, and short observation period underscore the importance of further investigations incorporating comprehensive safety assessments, larger patient populations, and longer follow-up periods before conclusions regarding clinical benefit can be established.

METHOD

This study was designed as a single-blind, parallel-group pilot randomized controlled trial conducted at Prof. Dr. R. D. Kandou General Hospital, Manado, Indonesia. The study was conducted in accordance with the Declaration of Helsinki and was approved by the institutional ethics committee.

Adult patients with traumatic spinal cord injury (SCI) requiring surgical decompression and stabilization were recruited from the emergency department, inpatient wards, and surgical units. Patients with active systemic infections, malignancies, conditions that could interfere with neurological assessment, or other contraindications to the intervention were excluded.

After written informed consent was obtained, participants were randomly assigned to two parallel groups using computer-generated block randomization.

The intervention group received standard SCI management combined with a single intraoperative intrathecal administration of umbilical cord-derived mesenchymal stem cell (UC- MSC) secretome, whereas the control group received standard SCI management alone.

Participants were blinded to treatment allocation, whereas surgeons and personnel administering the intervention were not blinded because of the nature of the procedure.

The intervention consisted of a cell-free secretome preparation derived from human UC-MSCs. The product was obtained from qualified UC-MSC sources and supplied as a sterile solution in a 1.5-mL cryovial.

According to the manufacturer's product information, the secretome contained bioactive components, including stromal cell-derived factor 1 (SDF-1), keratinocyte growth factor (KGF), fibroblast growth factors (FGFs), vascular endothelial growth factor (VEGF), and procollagen.

The secretome was administered through a single intrathecal injection following spinal decompression and stabilization and before surgical wound closure.

Neurological impairment was assessed using the American Spinal Injury Association Impairment Scale (AIS), in accordance with the International Standards for Neurological Classification of Spinal Cord Injury (Rupp et al., 2021). Functional independence was evaluated using the Spinal Cord Independence Measure (SCIM) (Catz et al., 1997), while neurological and functional recovery was further assessed using the International Association of Neurorestoratology Spinal Cord Injury Functional Rating Scale (IANR-SCIFRS) (Huang et al., 2020).

Neurological and functional assessments were performed preoperatively and repeated at hospital discharge to evaluate short-term changes following treatment.

Blood samples were collected to assess inflammatory and neuronal injury biomarkers. Serum interleukin-6 (IL-6) and neurogranin concentrations were measured using enzyme-linked immunosorbent assays (ELISAs) according to the manufacturer's instructions.

Blood samples were collected preoperatively and at 8 hours, 2 days, and 4 days postoperatively.

The primary outcome was the between-group difference in serial serum IL-6 concentrations during the early postoperative period. Secondary outcomes included between-group differences in serial serum neurogranin concentrations, neurological impairment assessed using the AIS, and functional outcomes evaluated using the SCIM and IANR-SCIFRS.

Continuous variables were summarized as means $\pm$ standard deviations or medians with interquartile ranges, depending on their distributions.

Baseline characteristics were summarized descriptively without formal statistical significance testing.

Serial serum IL-6 and neurogranin concentrations were analyzed using linear mixed-effects models to account for repeated measurements within participants. The models included treatment group, measurement time, age, and sex as explanatory variables.

Given the exploratory nature of this pilot randomized controlled trial and its limited sample size, additional regression analyses with bootstrap resampling were performed to assess uncertainty in the estimated treatment effects. A two-sided p-value of less than 0.05 was considered statistically significant.

The observation period was limited to biomarker measurements obtained through postoperative day 4 and neurological and functional assessments conducted at hospital discharge. Consequently, the study was designed to explore early between-group differences rather than establish sustained neurological recovery or long-term therapeutic efficacy. Although linear

mixed-effects models accounted for repeated measurements and the specified covariates, the small sample size of five participants per group increased the sensitivity of the estimates to baseline imbalances and modeling assumptions. Furthermore, the available study documentation did not provide comprehensive information on investigational product potency characterization, systematic adverse-event reporting, or long-term follow-up. These limitations were therefore considered when interpreting the preliminary findings and assessing their clinical implications.

RESULTS AND DISCUSSION

Ten patients with traumatic spinal cord injury were included in the final analysis between March and August 2025. Five patients were allocated to the UC-MSC secretome group and five patients to the control group.

The mean age of participants was 52.4 ± 19.8 years, with three males (30%) and seven females (70%). Injury levels ranged from cervical to lumbosacral, with thoracic injury being the most frequent level (40%). According to the American Spinal Injury Association Impairment Scale (AIS), four patients (40%) had complete injury (AIS grade A), while six patients (60%) had incomplete injury (AIS grade C–D).

Baseline neurological and functional scores showed moderate-to-severe impairment, with mean IANR-SCIFRS and SCIM scores of 22.3 ± 12.8 and 51.8 ± 23.3 , respectively.

Baseline serum IL-6 and neurogranin concentrations were 403.2 ± 42.6 pg/mL and 406.7 ± 48.2 pg/mL, respectively.

Baseline characteristics are summarized in Table 1. Baseline neurogranin concentrations were higher in the control group than in the UC-MSC secretome group (438.4 ± 43.0 vs 375.0 ± 29.5 pg/mL), while baseline IL-6 concentrations were also numerically higher in the control group (418.5 ± 55.5 vs 387.9 ± 20.6 pg/mL). Given the small sample size, potential baseline imbalances should be considered when interpreting the biomarker findings. The group differences already present before dosing make comparisons of absolute postoperative biomarker concentrations vulnerable to baseline imbalance, despite randomized allocation.

Table 1. Baseline Characteristics of Patients with Spinal Cord Injury by Treatment Group (N = 10)

Characteristic	Control (n = 5)	Secretome (n = 5)
Sex		
Male, n (%)	1 (20)	2 (40)
Female, n (%)	4 (80)	3 (60)
Age, years, mean (SD)	53.0 (19.5)	51.8 (22.4)
Injury level		
Cervical injury, n (%)	0 (0)	2 (40)
Thoracic injury, n (%)	3 (60)	1 (20)

Characteristic	Control (n = 5)	Secretome (n = 5)
Sex		
Male, n (%)	1 (20)	2 (40)
Thoracolumbar injury, n (%)	1 (20)	0 (0)
Lumbar injury, n (%)	1 (20)	1 (20)
Lumbosacral injury, n (%)	0 (0)	1 (20)
AIS grade A, n (%)	2 (40)	2 (40)
AIS grade C, n (%)	1 (20)	0 (0)
AIS grade D, n (%)	2 (40)	3 (60)
IANR-SCIFRS, mean (SD)	24.4 (10.4)	20.2 (15.8)
SCIM, mean (SD)	56.0 (12.6)	47.6 (31.9)
Interleukin-6, pg/mL, mean (SD)	418.5 (55.5)	387.9 (20.6)
Neurogranin, pg/mL, mean (SD)	438.4 (43.0)	375.0 (29.5)

Note. Data are presented as mean (SD) or n (%). Baseline characteristics are presented descriptively; formal significance testing was not performed because treatment allocation was randomized. AIS = American Spinal Injury Association Impairment Scale; IANR-SCIFRS = International Association of Neurorestoratology Spinal Cord Injury Functional Rating Scale; SCIM = Spinal Cord Independence Measure.

Both groups showed numerical clinical improvement from the preoperative assessment to hospital discharge, without a statistically detectable between-group difference. IANR-SCIFRS rose by 10-11 points overall (secretome +8.3 vs. control +12.9; $p = 0.564$), and SCIM rose by approximately 17 points overall (secretome +15.2 vs. control +18.8; $p = 0.511$). No significant between-group difference in AIS improvement was detected.

Serial measurements showed declining mean IL-6 and neurogranin concentrations over time in both groups. The UC-MSC secretome group had lower absolute mean concentrations than the control group from baseline through postoperative day 4 (Figure 1).

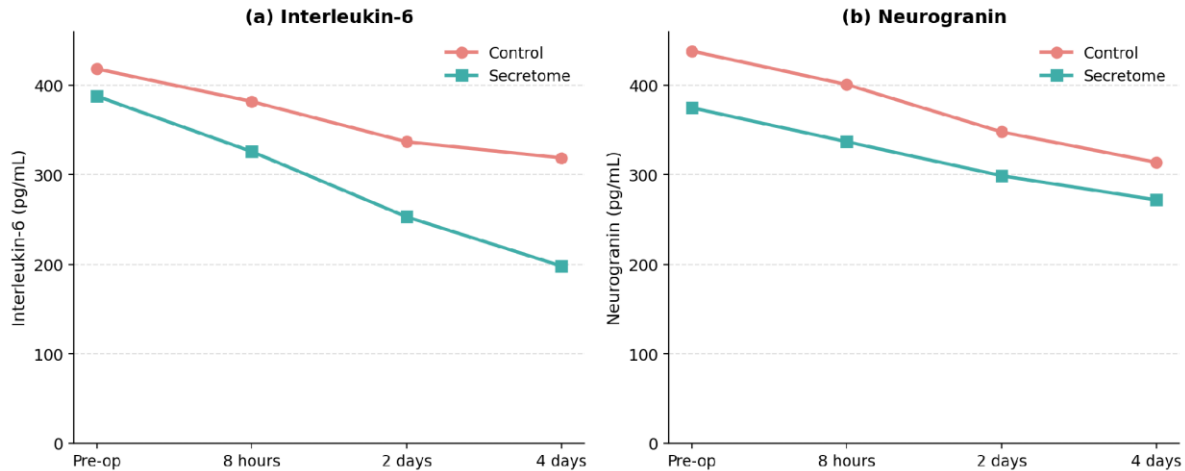


Figure 1. Mean serum interleukin-6 and neurogranin concentrations during the early postoperative period. (A) Serum IL-6 and (B) serum neurogranin concentrations were measured preoperatively and at 8 hours, postoperative day 2, and postoperative day 4. Lines represent mean concentrations for the control and UC-MSC secretome groups.

Source: Not specified in the original manuscript

Regarding neurogranin, UC-MSC secretome administration was associated with a decrease of 54.49 pg/mL in the univariate analysis (95% CI 9.14–99.84; $p = 0.048$); however, this effect shifted to 55.06 pg/mL ($p = 0.057$) after adjustment for other variables.

Table 2. Linear Mixed-Model Estimates for the Effect of UC-MSC secretome and Time on Serum Interleukin-6 and Neurogranin

Outcome	Predictor	Adjusted β (95% CI)	p
Interleukin-6	Secretome vs. control	-52.61 (-87.19, -18.04)	0.043
Interleukin-6	8 hours vs. pre-op	-49.14 (-88.25, -10.04)	0.023
Interleukin-6	2 days vs. pre-op	-108.21 (-147.32, -69.11)	<0.001
Interleukin-6	4 days vs. pre-op	-144.50 (-183.61, -105.39)	<0.001
Neurogranin	Secretome vs. control	-55.06 (-98.77, -11.34)	0.057
Neurogranin	8 hours vs. pre-op	-37.71 (-58.78, -16.65)	0.002
Neurogranin	2 days vs. pre-op	-83.19 (-104.25, -62.13)	<0.001
Neurogranin	4 days vs. pre-op	-114.02 (-135.09, -92.96)	<0.001

Note. CI = confidence interval. Estimates are from linear mixed models adjusted for age, sex, and measurement time (reference category: pre-operative).

Exploratory regression analyses with bootstrap resampling did not demonstrate a statistically detectable effect of UC-MSC secretome administration on changes in AIS, SCIM, or IANR-SCIFRS. Treatment-effect estimates were imprecise, with wide confidence intervals

reflecting the small sample size.

The principal finding of this pilot randomized controlled trial was that adjunctive intrathecal UC-MSC secretome administration was associated with lower serum IL-6 concentrations during the early postoperative period compared with standard treatment alone. In contrast, the association with neurogranin was not statistically robust after adjustment for covariates, and no significant between-group differences were detected in short-term neurological or functional outcomes assessed using AIS, SCIM, and IANR-SCIFRS. Taken together, these findings suggest an early biological signal involving inflammatory activity, whereas a corresponding short-term neurological or functional benefit could not be demonstrated within the limited observation period.

The association between UC-MSC secretome administration and lower serum IL-6 concentrations can be biologically explained, given the central role of inflammation in secondary spinal cord injury. Following the primary mechanical trauma, disruption of the blood-spinal cord barrier, activation of resident microglia, recruitment of circulating immune cells, and the release of pro-inflammatory cytokines contribute to progressive neural tissue damage (Ahuja et al., 2017; Freyermuth-Trujillo et al., 2022). MSC-derived secretomes contain soluble mediators, growth factors, extracellular vesicles, and regulatory molecules capable of modulating inflammatory signaling and creating a post-injury microenvironment that is more conducive to repair processes (Dabrowska et al., 2020; Harrell et al., 2019; Teixeira & Salgado, 2020; Vizoso et al., 2017).

Previous research on patients with traumatic spinal cord injury (SCI) supports the role of IL-6 as a marker of the early inflammatory response. Rieder et al. (2019) evaluated serum biomarkers in 52 patients with traumatic SCI and found that serum IL-6 levels were significantly elevated within 48 hours post-injury but were no longer significantly elevated by day 7. Notably, biomarker concentrations during the early phase did not correlate with subsequent neurological or functional outcomes; this indicates that IL-6 may reflect acute inflammatory activity without necessarily serving as a reliable long-term prognostic marker.

Similarly, Kwon et al. (2010) evaluated cerebrospinal fluid biomarkers during the first 72 hours following acute spinal cord injury (SCI) in humans and demonstrated that IL-6 levels along with several other markers of inflammation and neuronal injury increased in correlation with injury severity. Therefore, the temporal pattern of IL-6 during the initial days post-injury appears to reflect the intensity of the acute inflammatory response and may provide biological information regarding the severity of the injury.

Preclinical evidence also supports the potential anti-inflammatory effects of products derived from UC-MSCs. In experimental models of spinal cord injury (SCI), extracellular vesicles derived from human umbilical cord MSCs have been shown to reduce levels of pro-inflammatory cytokines including IL-6, TNF- α , and IL-1 β and promote macrophage/microglia polarization toward the M2 phenotype, a process associated with improved functional recovery (Zhai et al., 2021). Although extracellular vesicles represent only one component of the total MSC secretome and cannot be considered equivalent to the intact secretome used in this study, these findings provide a mechanistic basis for the low IL-6 concentrations observed in the

secretome group.

Neurogranin concentrations also declined progressively during postoperative follow-up; however, the association with UC-MSC secretome administration did not remain statistically robust after adjustment. Interpretation is further complicated by the baseline imbalance between groups, with higher neurogranin concentrations in the control group before treatment. Therefore, persistent differences between groups during follow-up cannot be attributed confidently to secretome administration alone.

Clinical evidence regarding circulating neurogranin in human SCI remains extremely limited. Most available human data have been derived from traumatic brain injury rather than spinal cord injury. Yang et al. (2015) evaluated serum neurogranin in 76 patients with acute traumatic brain injury and 150 non-TBI controls and found significantly higher serum neurogranin concentrations in patients with TBI, supporting its potential role as a circulating marker of acute neuronal or synaptic injury.

Similarly, Çevik et al. (2019) reported significantly higher serum neurogranin concentrations in patients with mild traumatic brain injury who had structural intracranial lesions on computed tomography compared with patients without CT-detectable lesions. These findings suggest that circulating neurogranin may reflect acute neural or synaptic disruption; however, its kinetics and clinical significance following SCI have not been adequately characterized.

Accordingly, the progressive decline in neurogranin observed in both groups in the present study may reflect temporal changes in neural injury rather than a specific therapeutic effect of UC-MSC secretome. The baseline imbalance, short observation period, and absence of established reference kinetics for serum neurogranin after human SCI further limit interpretation. Neurogranin should therefore be regarded as an exploratory biomarker in the present study rather than an established marker of treatment response in SCI.

Human clinical evidence involving cell-free MSC-derived therapies in SCI remains very limited. The study most closely related to the present intervention was the first-in-human phase I trial reported by Akhlaghpasand et al. (2024). Nine patients with complete subacute SCI received intrathecal allogeneic human umbilical cord MSC-derived exosomes and were followed for 12 months. Significant improvements from baseline were observed in ASIA pinprick and light-touch sensory scores, SCIM-III total score, and neurogenic bowel dysfunction score, with no early or late adverse events attributed to the intervention. However, the study was single-arm and open-label without a control group, limiting causal attribution of the observed neurological and functional improvements to exosome administration. Importantly, exosomes constitute only one extracellular-vesicle component of the broader MSC secretome and should not be considered equivalent to the whole UC-MSC secretome evaluated in the present trial.

Clinical studies using direct MSC transplantation have also demonstrated heterogeneous neurological and functional responses. Albu et al. (2021) conducted a randomized, double-blind, crossover, placebo-controlled phase I/IIa trial involving 10 patients with chronic complete thoracic SCI. Following intrathecal administration of Wharton's jelly-derived MSCs, significant improvement was observed predominantly in pinprick sensation below the neurological level of

injury, whereas no meaningful changes were detected in motor function, quality of life, or measures of functional independence, including SCIM.

Similarly, Saini et al. (2022) evaluated intraoperative intramedullary transplantation of bone marrow-derived MSCs in acute complete SCI using a randomized placebo-controlled design. Although 27 patients were initially randomized, only 13 were available for final analysis. Six patients in the MSC group improved by at least one ASIA grade compared with one patient in the placebo group, and sensory ASIA scores also improved substantially in the MSC group. However, there was no significant between-group difference in SCIM scores at six months.

Taken together, the findings of Akhlaghpasand, Albu, and Saini illustrate that regenerative interventions may produce measurable sensory or neurological changes without necessarily resulting in parallel improvement in functional independence. They also demonstrate that clinical changes, when observed, are generally evaluated over several months rather than only until hospital discharge (Akhlaghpasand et al., 2024; Albu et al., 2021; Saini et al., 2022). Direct comparison with the present study should nevertheless be made cautiously because the therapeutic products, routes of administration, injury severity, injury chronicity, and study designs differ considerably across trials. The study does not establish clinical effectiveness or procedural safety, because the sample is small, discharge outcomes are short term, and adverse-event results are not reported. Subsequent trials should standardize secretome potency and dose, assess safety systematically and extend neurological follow-up.

No statistically detectable between-group differences in AIS, SCIM, or IANR-SCIFRS were demonstrated in the present study. This finding should not be interpreted as proof of treatment ineffectiveness. The sample consisted of only five patients per treatment group, resulting in limited statistical power and wide uncertainty around treatment-effect estimates. In addition, neurological and functional outcomes were assessed only until hospital discharge, providing a relatively short in-hospital follow-up period.

Neurological recovery after SCI depends on processes such as axonal remodeling, remyelination, synaptic reorganization, neuroplasticity, and rehabilitation-dependent adaptation, which evolve over weeks to months rather than days (Silva et al., 2014). In contrast to the 6- to 12-month follow-up periods used in previous human studies (Akhlaghpasand et al., 2024; Albu et al., 2021; Saini et al., 2022), the present clinical assessment extended only to hospital discharge. Consequently, the current study cannot determine whether UC-MSC secretome has longer-term neurological or functional effects.

The three clinical instruments used in this study provide complementary information. AIS primarily reflects neurological impairment and completeness of SCI, whereas SCIM assesses SCI-specific functional independence in domains such as self-care, respiration, sphincter management, and mobility. IANR-SCIFRS provides a broader evaluation of neurological and functional recovery (Catz et al., 1997; Huang et al., 2020; Rupp et al., 2021). The lack of a treatment-specific difference across these measures therefore indicates that no clear short-term clinical signal was demonstrated despite the observed difference in IL-6.

The present findings should therefore be considered preliminary and hypothesis-generating.

Larger multicenter randomized controlled trials are required to determine whether the early inflammatory biomarker signal observed after UC-MSC secretome administration translates into clinically meaningful neurological or functional benefit. Future studies should incorporate stratified randomization according to injury level and AIS severity, standardized rehabilitation protocols, blinded clinical outcome assessment, comprehensive characterization of the secretome product, and longer follow-up periods of at least 6–12 months. Evaluation of optimal dose, timing, and delivery route will also be important to define the potential role of UC-MSC secretome as a cell-free regenerative therapy for SCI.

CONCLUSION

In this pilot randomized controlled trial, adjunctive intrathecal administration of umbilical cord-derived mesenchymal stem cell (UC-MSC) secretome was associated with lower serum interleukin-6 (IL-6) concentrations during the early postoperative period compared with standard treatment alone, suggesting a potential early anti-inflammatory response. However, the association with serum neurogranin concentrations was not statistically significant after adjustment, and no statistically significant between-group differences in American Spinal Injury Association Impairment Scale (AIS), Spinal Cord Independence Measure (SCIM), or International Association of Neurorestoratology Spinal Cord Injury Functional Rating Scale (IANR-SCIFRS) outcomes were observed at hospital discharge. These preliminary findings suggested a potential biological response to UC-MSC secretome administration in patients with traumatic spinal cord injury but did not establish clinical efficacy or neurological benefit. Larger randomized controlled trials with extended follow-up periods and comprehensive safety assessments are warranted to determine whether the observed inflammatory biomarker changes are associated with improvements in synaptic integrity, neurological recovery, and functional outcomes.

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