

Guest Editorial

Spinal Cord Injury: Point-of-Care Biomarkers for Better Prognosis

Amrita Ghosh¹ Ranabir Pal²

¹Department of Biochemistry, Medical College, Kolkata, West Bengal, India

²Department of Community Medicine, Mata Gujri Memorial Medical College and Lion Seva Kendra Hospital, Kishanganj, Bihar, India

J Neurosci Rural Pract 2019;10:390–391

Spinal cord injury (SCI) is one of the most devastating injuries encountered in trauma care with the global prevalence of 750/million, and the incidence is on the rise with enormous downstream socioeconomic and psychological burden. Neurosciences experts are unanimous that, current practice of clinical and functional examination at the initial phase of evaluation, it is difficult to distinguish degree of the severity of damages for apposite definitive managements, and prognosticating neurologic recovery is not easy. In the past decades, research groups identified candidate biomarkers for the early detection of neuronal injury and attempted stepwise evaluation of SCI severity for prognostic value of managements. Precise detection and prediction of the initial damage by using these neurochemical biomarkers may help to resolve dilemma of neuroprotective interventions in the acute phase.^{1–6}

Biomarkers are expressed out in blood and cerebrospinal fluid (CSF), hours and days after mechanical damage to the tissues in and around the spinal cord disposition, as unpredictable cascade of pathophysiological changes ending in infarction with or without the paralytic sequels. The impact of trauma directly or indirectly injure the neurons, axonal fiber tracts, and glial cells to initiate the release of biochemical substances immediately denoted as lesional biomarkers; partially injured cells react to release reaction biomarkers starting sometimes later to several hours to days. Foremost lesional biomarkers are phosphorylated neurofilament subunits from fragmented cytoskeletal components of axonal neurofilament. Axonal form of the heavy neurofilament subunit NF-H (pNF-H) is a predictive lesional biomarker; for the favorable outcome, a sudden increase is observed followed by steady decline to normal values; unfavorable outcomes are predicted by gradual increase to a plateau or a progressive increase up to a peak trailed by reduction to quasinormal values. CSF concentrations of light chains of neurofilaments

(NFL, 68 kDa) and of glial fibrillary acid protein (GFAP) remain significantly higher with acute traumatic cervical spinal injuries and whiplash cases with pronounced neurological deficits. Further, literature reported other inflammatory cytokines and structural proteins, such as neuron-specific enolase (NSE), glial-specific calcium-binding β protein (S100 β), GFAP, and interleukin 8 (also known as neutrophil chemotactic factor). Their concentration in the CSF and blood samples exhibited as promising biomarkers to gauge severity in complete and incomplete SCI related with spinal cord ischemia within first few hours of injury; steadily elevated serum concentrations of S100 β indicated unfavorable functional outcomes.^{5–8}

Research groups who attempted to find reasons of heterogeneous recovery and uncertain prognosis in SCI tried with positive findings using structural protein biomarkers, namely, neurofilaments, cleaved-tau, microtubule-associated protein 2, myelin basic protein, NSE, S100 β , and GFAP in different permutation and combinations. However, positive reports were not found with ubiquitin C-terminal hydrolase-L1 and α -II spectrin breakdown products, which are widely researched in other central nervous system injuries, including traumatic brain injury. Curiously, micro-RNAs have been earmarked as candidate biomarker due to their stability in biological fluids with tissue specificity and altered expressions in SCI in animal models. There were unresolved issues relating to accuracy and their accessibility though these biomarkers showed promising results for SCI diagnosis and outcome prediction.^{5,9–12}

Many research groups are working on diagnostic biomarkers on SCI and with encouraging qualitative results. However, when there are considerations of shortcomings in the presence of confounders, for example, polytrauma, hemolysis, extracerebral sources, and poor resuscitation, quantification and validation are warranted before adding them in the clinical

Address for correspondence
Ranabir Pal, MBBS, MD, PhD, DCH,
MBA, Department of Community
Medicine, Mata Gujri Memorial Medical
College and Lion Seva Kendra Hospital,
Kishanganj 855 107, Bihar, India
(e-mail: ranabirpal1957@gmail.com).

DOI [https://doi.org/
10.1055/s-0039-1698032](https://doi.org/10.1055/s-0039-1698032)
ISSN 0976-3147.

©2019 Association for Helping
Neurosurgical Sick People

License terms



practice guidelines as a sensitive prognostic tool through further clinical trials.⁴ Further, across SCI injury severity, the variability in spontaneous neurologic recovery is quite high, though conventionally, it is accepted that outcomes depend on the severity of primary injury; yet, secondary injuries are reported up to one-fourth of SCI consequent after the initial injury during transit to dedicate facilities or during initial management.¹³

The addition of diagnostic and prognostic biomarkers of SCI in the clinical practice guidelines from the primary care level would help us about label severity of SCI. Furthermore, it will corroborate and correlate with empirical decisions based on the clinical observations, followed by precise treatment from the prehospital care, and transport to higher centers. Some proteins and related components of anatomical structures of the nervous system are recognized as prospective biomarkers of the central nervous system injury, both in CSF and serum. The central problem lies in acquiring CSF through a lumbar puncture that is significantly invasive in suspected spinal cord damage and may aggravate the clinical picture. In the above scenario, ongoing researches in SCI have focused mainly on lesional biomarkers than reaction biomarkers, as lesional biomarkers can identify SCI immediately after impact, and reaction biomarkers are released after a brief period of injury; several hours postinjury period, both coexist and become problematic to distinguish them.^{5,8}

To sum up, injury to the spinal cord is considered as a public health problem that generates high cost of life to the person, family, and community in the context of almost nonexistent prehospital care in the developing countries, in particular. Further, with the current medical practice, clinical acumen remains key activity for initial assessments of the severity of lesions in the victims. Hence, identification of point-of-care biomarkers is extremely important to demarcate the severity of injury for better prediction of neurological outcome from site of injury to definitive neurocare centers.

Funding

None.

Conflict of Interest

None declared.

References

- 1 Fehlings MG, Vaccaro A, Wilson JR, et al. Early versus delayed decompression for traumatic cervical spinal cord injury: results of the Surgical Timing in Acute Spinal Cord Injury Study (STASCIS). *PLoS One* 2012;7(2):e32037
- 2 Nanclares BVC, Padilla-Zambrano HS, El-Menyar A, et al. WACEM consensus paper on. Deep venous thrombosis after traumatic spinal cord injury. *J Emerg Trauma Shock* 2019;12(2):150–154
- 3 Ihegihu C, Ugezu A, Ndukwu C, Chukwuka N, Ofiaeli R, Ihegihu EY. A review of traumatic spinal cord injuries at the Nnamdi Azikiwe University Teaching Hospital, Nnewi, Nigeria. *Trop J Med Res* 2014;17(1):31–36
- 4 Pouw MH, Hosman AJ, van Middendorp JJ, Verbeek MM, Vos PE, van de Meent H. Biomarkers in spinal cord injury. *Spinal Cord* 2009;47(7):519–525
- 5 Rodrigues LF, Moura-Neto V, E Spohr TCLS. Biomarkers in spinal cord injury: From prognosis to treatment. *Mol Neurobiol* 2018;55(8):6436–6448
- 6 Alizadeh A, Dyck SM, Karimi-Abdolrezaee S. Traumatic spinal cord injury: an overview of pathophysiology, models and acute injury mechanisms. *Front Neurol*. 2019; 10: 282.
- 7 Yılmaz T, Turan Y, Keleş A. Pathophysiology of the spinal cord injury. *J Clin Exp Inv* 2014;5(1):131–136
- 8 Iencean SM, Iencean AS. Biomarkers in traumatic spinal cord injury. In: Wang M, Witzmann F, eds. *Role of Biomarkers in Medicine*. London, United Kingdom: IntechOpen; 2016
- 9 Yokobori S, Zhang Z, Moghieb A, et al. Acute diagnostic biomarkers for spinal cord injury: review of the literature and preliminary research report. *World Neurosurg* 2015;83(5):867–878
- 10 The Miami project to Cure Paralysis. Biomarkers for acute spinal cord injury. Available at: <https://www.themiamiproject.org/research/what-are-clinical-trials/clinical-trials/biomarkers-for-acute-spinal-cord-injury/>. Accessed on December 20, 2018
- 11 Kwon BK, Casha S, Hurlbert RJ, Yong VW. Inflammatory and structural biomarkers in acute traumatic spinal cord injury. *Clin Chem Lab Med* 2011;49(3):425–433
- 12 Quiñones-Ossa GA, Padilla-Zambrano H, Pal R, et al. Biomarkers in acute brain trauma: a narrative review. *J Acute Dis* 2019;8(1):1–6
- 13 Theodore N, Hadley MN, Aarabi B, et al. Prehospital cervical spinal immobilization after trauma. *Neurosurgery* 2013;72(Suppl 2):22–34