

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

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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 gauze 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

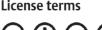
Research groups who attempted to find reasons of heterogeneous recovery and uncertain prognosis in SCI tried with positive findings using structural protein biomarkers, namely, neurofilaments, cleaved-tau, microtubule-associated protein 2, myelin basic protein, NSE, S100 β, and GFAP in different permutation 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

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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 nonexisting 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.

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