Two Promising Novel Classes of Drug Treatment in Clinical Development for Acute and Chronic Spinal Cord Injury

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Editorial

Spinal Cord Injury (SCI) can occur accidentally (i.e., trauma caused by motor vehicle accident, fall, gun shot, etc.) or be caused by a disease (i.e., non-traumatic SCI associated with diseases such as multiple sclerosis, spinal tumor, vascular problems, etc.) [1].

In traumatic SCI, the initial injury results into spinal cord deformation, laceration, crush and persistent post-injury cord compression occurring within seconds to minutes post-accident. This leads to immediate cell death, axonal disruption, vascular and metabolic changes, which have subsequent effects or so-called secondary injury processes occurring within a few minutes to a few weeks of injury [2-4].

Subsequently, within a few weeks to a few months post-trauma (chronic SCI), the patient generally experiences the development of several serious medical problems. They typically develop cardiovascular problems, type II diabetes, sarcopenia, osteoporosis, immune deficiencies and other life-threatening problems [5-13]. The cellular mechanisms underlying these so-called secondary complications or comorbid problems remain unclear and no drug treatment has been developed to specifically treat these medical concerns. However, a plethora of symptomatic treatments are often prescribed to separately control some of these complications expressed in both traumatic and non-traumatic SCI patients [14].

I strongly believe that the lack of treatment in clinical development either for acute or chronic problems may be attributed to at least two factors. First, most technologies (cell-based, neurotrophic factors, etc.) identified in rodents were found, for several reasons, to lack reproducibility [15]. It is generally accepted that damage to neuronal function following SCI arises from a complex series of reactions. A key determinant of functional loss after SCI is the extent of damage to projection axons at the lesion site, and axons do not regenerate spontaneously even though their cell bodies may remain alive. Failure of self-repair is caused by growth inhibitory proteins [2-4], which are especially prevalent in regions of white matter and long axonal tracts. They act by affecting signaling pathways that regulate the growth cone cytoskeleton. As mentioned above, although a few technologies were found in animal models to reduce the inhibitory actions of growth inhibitory proteins, none has been approved. This said, a Rho inhibitor called Cethrin™ is probably the most advanced technology as of now. It is one of the rare treatment candidates that has successfully completed preclinical studies and first-in-patient safety study (Phase I/IIa) [16]. It is currently in preparation for a Phase IIb study in acute SCI patients.

Secondly, no animal model ideally suited to investigate the development of comorbid problems in chronic SCI had been developed until recently [17-21]. In fact, we have been the first group to have recently developed a model of chronic SCI in which systemic and metabolic problems were thoroughly characterized [22]. In parallel to these experiments, we also identified and developed a drug product aimed to prevent several of these chronic problems after SCI by activating pharmacologically a spinal locomotor network based in the lumbar area of the spinal cord [23-25]. This is the first and still the only drug treatment candidate in development for chronic SCI-related health problems. The technology that is called Spinalon™ has undertaken in 2012 its first clinical trials in chronic SCI patients (http://clinicaltrials.gov/ct2/show/NCT01484184?term=spinalon&rank=1).

Now, let’s only hope, after so many years of research in SCI, that these two promising technologies designed specifically for acute and chronic SCI patients respectively will succeed in moving along the difficult and risky path of clinical development. If eventually approved by regulatory authorities, they may constitute in approximately five (5) years two novel classes of safe and potent drug treatments for SCI patients.

Nearly 1.3 million people are currently living with a traumatic SCI in North America (www.Christopherreeve.org) making of SCI the first neurological problem only second to Alzheimer’s disease (4.5 million cases, www.cdc.com).

References


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