# Early therapies for acute traumatic spinal cord injury

# St.M. Iencean<sup>1</sup>, Al. Tascu<sup>2</sup>, A.St. Iencean<sup>3</sup>, I. Poeata<sup>1</sup>

<sup>1</sup>"Grigore T. Popa" University of Medicine and Pharmacy Iasi, Romania

#### **Abstract**

Early therapies for acute traumatic spinal cord injury has some key points:

- 1. Immediately or soon after the injury is recommended a hemodynamic support to maintain mean arterial pressure at 85 90 mmHg and monitoring in an intensive care unit for the first week after spinal cord injury.
- 2. Immediate surgery for spinal cord decompression is of high importance for the prognosis and evolution of spinal cord injury.
- 3. The recommendation is to treat all patients with spinal cord injury according to the local protocol, methylprednisolone is not standard of care anymore, it is a treatment option that should only be undertaken with knowledge of the potential complications.

**Key words**: methylprednisolone, spinal cord injury.

In April in Canadian Medical Association Journal was published an excellent review of the acute traumatic spinal cord injury problem: "Emerging therapies for acute traumatic spinal cord injury" written by Jefferson R. Wilson, Nicole Forgione and Michael G. Fehlings (CMAJ, vol. 185 no. 6, pp.485 - 492, 2013).

In the beginning the article show the incidence and prevalence of traumatic

spinal cord injury in Canada; for us this is a serious problem! We have not a situation of these cases in Romania, therefore we have not a national perspective on the incidence and prevalence of spinal cord injury in our country. Neurosurgical and neurorehabilitation departments must keep track of cases of spinal trauma and each statistic should be centralized.

Following the protocols developed for the spinal cord injury patients the care on the first 72 hours of injury are the most important and all must prevent secondary complications.

After a good triage protocols and trauma systems of care, including prehospital triage, spinal stabilization during emergency transport and early immobilization of all patients with a potential spinal injury, patient arrives at the spinal cord injury center. Initial prehospital management of traumatic acute spinal cord injury is crucial for the morbidity and mortality following acute spinal cord injury.

The radiographic evaluation of patients following spinal cord injury consists of the images of the entire spine and to perform MRI of the known or suspected ares of spinal cord injury.

In the spinal cord injury center the patient receives "aggressive medical and surgical methods to maintain cord perfusion, avoiding complications, decompressing the spinal cord and restoring stability." (citare Emerging). The

<sup>&</sup>lt;sup>2</sup>"Carol Davila" University of Medicine and Pharmacy Bucharest, Romania

<sup>&</sup>lt;sup>3</sup>"N. Oblu" Emergency Hospital Iasi, Romania

authors recommend to maintain mean arterial pressure at 85 - 90 mmHg and monitoring in an intensive care unit for the first week after spinal cord injury. These recommendations are consistent with recommendations of the American Association of Neurological Surgeons: that patients' mean arterial pressure must be maintained at 85-90 mmHg for the first 7 days after injury, published since 2002, in article: "Blood pressure management after acute spinal cord injury" Neurosurgery. "when volume replacement is inadequate to achieve this goal, intravenous vasopressor medications introduced. Patients, particularly those with severe cervical injuries, should receive treatment in an intensive care unit (ICU) with continuous cardiac, hemodynamic and respiratory monitoring for the first 7–14 days after injury. In observational studies, the standardized admission of patients with spinal injuries to an ICU has been associated with reduced mortality and morbidity, in addition to improved neurologic recovery." (citare Emerging).

The surgical treatment (ideally - within eight hours of the injury occuring) must remove the tissues causing spinal cord compression, must correct the misalignment and must stabilize the spine.

Immediate surgery for spinal cord decompression is of high importance for the prognosis and evolution of spinal cord injury. STASCIS, the Surgical Timing in Acute Spinal Cord Injury Study, was a prospective study that compares patients who underwent either early (< 24 h after injury) or late ( $\ge$  24 h after injury) surgical decompression and the results were early surgery were associated with better neurologic recovery at 6 months.



Figure 1
C5 cervical spinal fracture with traumatic acute spinal cord hemorrhage, tetraplegia

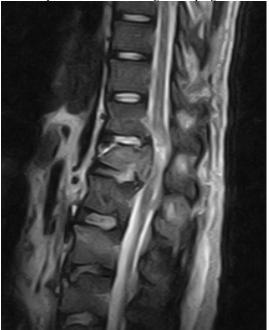


Figure 2
T 10 fracture with traumatic acute spinal cord injury, paraplegia

Thefore the conclusion is that: "decompressive surgery within 24 hours after injury has been shown to be safe and feasible; in prospective nonrandomized trials, it has been associated with improved rates of neurologic recovery."

There are still other drugs which can be used and the recommendation is to treat all patients with spinal cord injury according to the local protocol.

If steroids are recommended, they should be initiated within 8 hours of injury with the following steroid protocol: methylprednisolone 30 mg/kg bolus over 15 minutes and an infusion of methylprednisolone at 5.4 mg/kg/h for 23 hours beginning 45 minutes after the bolus. Methylprednisolone is not standard of care anymore, "optional at best, although could still be considered in view of the lack of other treatment options".

Other drugs with therapeutic potential in acute spinal cord injury are:

- Naloxone, an opioid antagonist that blocks the neurotoxic effects of the endogenous opioid.
- Nimodipine, as a L-type calciumchannel blocker and it prevents activation of calciumdependent

apoptotic enzymes and blocks presynaptic release of glutamate

- Minocycline promotes functional recovery, enhances axonal survival, and reduces injury-site lesion size.
- GM-1 ganglioside (Sygen) decreases injury-induced, over-release of damage-perpetuating excitatory substances.
- Riluzole, a sodium-channel blocker used for the treatment of amyotrophic lateral sclerosis (ALS), in which it reduces motor neuron degeneration and in preclinical models of spinal cord injury it decreases secondary injury by blocking

pathological activation of sodium channels and reducing the release of neuronal glutamate.

- Erytropoietin has neuroprotective effects and contributes to neurons regeneration
- Neotrofin stimulat es growth-factor production, enhances proliferation of CNS stem cells, and protects neurons from the release of excitatory substances.

The implant in the site of spinal cord injury or the transplantation of stem cells and autologous non–stem cells has been studied in preclinical injury models.

The cellular subtypes used for this purpose include:

- Bone marrow-derived stem cells,
- Olfactory ensheathing cells,
- Schwann cells,
- Activated autologous macrophages,
- Tissue-derived adult neural stem cells.

The results are promising, but further studies are needed on larger groups of patients with spinal cord injury.

### Conclusions

The patient with spinal cord injury must reach in the spine surgery service as early as possible to evaluate the need for immediate decompression and stabilization surgery. Methylprednisolone is not standard of care anymore, optional at best, although could still be considered in view of the lack of other treatment options. The patient with spinal cord injury must admitt to an intensive care unit with continuous cardiac, hemodynamic and respiratory monitoring for the first 1–2 weeks.

This article about early treatments in acute traumatic spinal cord injury is part of the grant: "Immediate neuroprotective therapy in acute traumatic spinal cord

injury", that won the 2011 national competition of National Research Council (CNCS), Ideas, grant number: PN-II-ID-PCE-2011-3-0569, funded by CNCS – UEFISCDI Romania

Corresponding author: A.St. Iencean Neurosurgery, "Prof. Dr. Nicolae Oblu" Hospital Iasi, andrei\_steffan@yahoo.com

## References

- 1. Wilson JR, Forgione N, Fehlings MG Emerging therapies for acute traumatic spinal cord injury Can MAJ, vol. 185 no. 6, pp.485 492, 2013
- 2. St.M. Iencean, I. Poeata, Didona Ungureanu, D. Cuciureanu,B. Costachescu, Al. Chiriac, Traumatic spinal cord injuries: neuroprotection and recent outcomes Romanian Neurosurgery (2012) XIX 3: 210 216
- 3. Marklund Niklas: Spinal cord regeneration current and future treatment options for traumatic spinal cord injury, EANS Training Course- Leeds, 26 30 August 2012
- 4. Bunge MB. Novel combination strategies to repair the injured mammalian spinal cord. J Spinal Cord Med. 2008;31(3):262-9;
- 5. Noonan VK, Fingas M, Farry A, et al. The incidence and prevalence of spinal cord injury in Canada: a national perspective. Neuroepidemiology 2012;38:219-26
- 6. Furlan JC, Noonan V, Cadotte DW, et al. Timing of decompressive surgery of spinal cord after traumatic spinal cord injury: an evidence-based examination of pre-clinical and clinical studies. J Neurotrauma 2011;28:1371-99.

- 7. Fehlings MG, Vaccaro A, Wilson J, 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:e32037.
- 8. Bracken MB, Shepard M, Holford T, et al. Administration of methylprednisolone for 24 or 48 hours or tirilazad mesylate for 48 hours in the treatment of acute spinal cord injury. Results of the Third National Acute Spinal Cord Injury Randomized Controlled Trial. National Acute Spinal Cord Injury Study. JAMA 1997;277:1597-604.
- 9. Yoon SH, Shim YS, Park YH, et al. Complete spinal cord injury treatment using autologous bone marrow cell transplantation and bone marrow stimulation with granulocyte macrophage-colony stimulating factor: phase I/II clinical trial. Stem Cells 2007; 25: 2066-73.
- 10. Syková E, Homola A, Mazanec R, et al. Autologous bone marrow transplantation in patients with subacute and chronic spinal cord injury. Cell Transplant 2006;15:675-87.
- 11. Hugenholtz H, Cass D, Dvorak M. High-dose methylprednisilone for acute closed spinal cord injury only a treatment option. Can J Neurol Sci 2002; 3:227-35.
- 12. Fehlings MG, Wilson JR, Frankowski RF, et al. Riluzole for the treatment of acute traumatic spinal cord injury: rationale for and design of the NACTN Phase I Clinical Trial. J Neurosurg Spine 2012;17:151-6.
- 13. Lammertse DP, Jones LA, Charlifue SB, et al. Autologous incubated macrophage therapy in acute, complete spinal cord injury: results of the phase 2 randomized controlled multicenter trial. Spinal Cord 2012;50:661-71.
- 14. Iencean St M, Ciurea AV. Autologous Bone Marrow Implant into Traumatic Chronic Spinal Cord Injury. Am J of Neuroprotection and Neuroregeneration, Vol 1, No 1, pp. 73-77, 2009.