The Potential Role of Erythropoietin versus Human Umbilical Cord Blood Stem Cell Therapy Following Sciatic Nerve Injury In Rats

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Summary

Erythropoietin (EPO) and its receptor have been shown to be expressed in the nervous system. Many in vitro and in vivo studies suggest that EPO has a neuroprotective impacts against various neural insults including peripheral nerve injuries. Mesenchymal stem cells (MSCs) are emerging as a new effective therapeutic approach to a wide range of neural insults since they act as a source of stem-like and progenitor cells. The aim of the present study was to demonstrate the neuroprotective effect of EPO administration, human umblical cord blood (HUCB) Mesenchymal Stem cells transplantation and their Co-treatment in injured sciatic nerve in albino rats. Sixty adult male albino rats, weighing ٢٠٠ (±٥٠) grams each, were studied in this work. The rats were classified into **five groups**; **the first group** was the normal control group and **the second group** was sciatic nerve injured non-treated group in which rats had Standardized crush injury of the left sciatic nerve by a standard surgical hemostat for one minute, **the third group** was sciatic nerve injured EPO- treated group in which sciatic nerve injury rats were treated with ٥٠٠٠٠ units per kg of body weight of recombinant human erythropoitien intra lesional once at the time of the surgery, **the fourth group** was sciatic nerve injured mesenchymal stem cells - treated group in which sciatic nerve injury rats were treated with intralesional injection of mesenchymal stem cells in a dose of ٣×١٠^{٥} cells/µl grafted into each injured sciatic nerve and finally, **the Fifth group** was sciatic nerve injured rats co-treated with both EPO and MSCs with the previous doses.

In each of the previously mentioned groups: functional evaluation, electrophysiological recording, expression of BDNF mRNA in the injured nerve by RT-PCR technique, and expression of synapsin I mRNA in the injured nerve by semiquantitative PCR technique. At the end of the experiment (after ٨ weeks), the rats were sacrificed and sciatic nerves were excised for histopathological studies.

The results showed that significant improvement in functional evaluation, electrophysiological evaluation, expression of brain derived neurotrophi factor (BDNF) mRNA by RT-PCR, expression of synapsin I mRNA by semiquantitative PCR by intralesional injection of EPO and umblical cord blood mesenchymal stem cells transplantation and their Co-treatment when compared with sciatic nerve injured non treated group. No significant difference noticed when EPO treated group and MSCs treated group were compared to each other in the functional evaluation, while the co-treated group showed a significant functional improvement when compared to either EPO treated or MSCs treated groups. Concerning the electrophysiological evaluation; the nerve conduction velocity results showed no significant difference between the three treatment groups, also the electromyography results showed no significant improvement in the amplitude between the three treatment groups while the latency decreased significantly in both MSCs treated and co- treated groups in comparison to EPO treated group.

Concerning the PCR results; BDNF mRNA showed significant elevation among the treatment groups, MSCs group showed superiority over the EPO group and the co-treated group showed superiority over both the EPO and MSCs treated groups separately. Synapsin I mRNA results showed no significant elevation when EPO and MSCs groups

were compared to each other while significant elevation observed when the co- treated group was compared to either EPO or MSCs treated groups.

Histopathological examination with H&E stained sections and toludine blue sections from the sciatic nerve of EPO treated group showed "Onion bulb" formations that are concentric layers of Schwann cell processes and collagen around the axon due to repetitive segmental demyelination and regeneration of myelin with moderate degree of *Wallerian degeneration***.** MSCs treated group showed lesser degree of *Wallerian degeneration*; Fragmentation and loss of myelin and axons with evidence of axonal regeneration, surrounded by thin layer of perineurium, and normal Schwan cells umber. The Co- treated groups showed more axon regeneration, minimal *Wallerian degeneration* and no macrophages.