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Combination therapy with astaxanthin and epidermal neural crest stem cells improves motor impairments and myelin levels - Leila Mohaghegh Shalmani - Shahid Beheshti University of Medical Sciences - Iran

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Spinal cord injury (SCI) can lead to temporary or permanent loss of neurologic function. Nevertheless, the ideal treatment has not found for SCI. Since the SCI is a complex, multifaceted disease process so, combinatorial treatments can be a promising approach. Epidermal neural crest stem cells (EPI-NCSCs) are unique candidates which isolated from bulge hair follicles in adults due to the possibility of autologous transplantation. We evaluated whether combination of a potent antioxidant such as Astaxanthin (AST) and (EPI-NCSCs) transplantation could affect (SCI). The sever SCI induced by dropping a metal rod onto the exposed dorsal surface of the spinal cord on male rats witch treated by Ast (0.2mM) and EPI-NCSCs (106/10µl PBS) alone and combined. The Basso, Beattie and Bresnahan (BBB) test on days 1, 3, 7, 14, 21, 28, 35 and 42 post-injury was used for assessing of Motor function. The Motor neurons number and the myelin level were investigated on days 14 and 42 using Nissl and Luxol Fast Blue staining. All treatments improved motor function on days 7, 14, 21, 28, 35 and 42 compared to SCI. However combination therapy was more effective than Ast or EPI-NCSCs individually in behavioral improvement. Decreased the motor neurons number following SCI, increased by Ast, Cell and Ast+Cell, but combination therapy significantly had better effects. Although all treatment increased white matter compared to SCI, treatment with Ast+Cell had increased myelin levels.

Introduction:

Spinal cord injury (SCI) a multifactorial disease and it is also a debilitating condition in which it can leads to temporary or permanent loss of neurologic function and it also causes continuous neurological deficits and major sensory-motor impairments. Symptoms of Spinal cord injury (SCI) may include the loss of muscle function, sensation, or autonomic function in the body parts served by the spinal cord below the level of the injury. The medicinal therapy of Spinal cord injury (SCI) complications is still a clinical challenge one. Understanding the molecular pathways and underlying the progress of damage will help us to find new therapeutic candidates. The Spinal cord injury (SCI) experience significantly shows the impairments in various aspects of their life. The goals of rehabilitation and other treatment approaches in Spinal cord injury (SCI) are to improve the functional level, decrease secondary morbidity and enhance the health-related quality of life. There are two medical complications that are common in patients with Spinal cord injury (SCI) they are Acute and long-term secondary medical complications. There are some common secondary long-term complications after Spinal Cord Injury (SCI) that includes respiratory complications, cardiovascular complications, urinary and bowel complications, spasticity, pain syndromes, pressure ulcers, osteoporosis and bone fractures. However, chronic complications shows further negatively impact on patient's functional independence and also quality of life.

The Prevention, early diagnosis and treatment of chronic secondary complications in patients with Spinal cord injury (SCI) is critical for limiting these complications, improving survival, and community participation. Cell therapy in combination with pharmacological agents can be a promising approach to attenuate spinal cord injury (SCI) damages. Nevertheless, the ideal treatment has not found for spinal cord injury (SCI). Since the spinal cord injury (SCI) is a complex, multifaceted disease process so, the combinatorial treatments can be a promising approach. Epidermal neural crest stem cells (EPI-NCSCs) are unique candidates which is isolated from bulge hair follicles in adults due to the possibility of autologous transplantation.

Objective:

We evaluated whether combination of a potent antioxidant such as Astaxanthin (AST), potent antioxidant and (EPI-NCSCs) transplantation could affect spinal cord injury (SCI).

Astaxanthin (AST) is a ketocarotenoid and it is a strong antioxidant, anti-inflammatory and anti-apoptotic agent. Astaxanthin (AST) showed the anti-inflammatory effects in models of traumatic brain injury. The benefit of Astaxanthin (AST) shoes the decreased post- Spinal cord injury (SCI) tissue damage and preserved neurons after Spinal cord injury (SCI). At present it was tested in SCI model with emphasis on sensory-motor outcomes, signaling pathways, along with other complications also. The sever spinal cord injury (SCI) induced by dropping a metal rod onto the exposed dorsal surface of the spinal cord on male rats which treated by Ast (0.2mM) and EPI-NCSCs (106/10µl PBS) alone and combined together after SCI contusion. The Basso, Beattie and Bresnahan (BBB) test on days 1, 3, 7, 14, 21, 28, 35 and 42 post-injury was used for assessing of Motor function. The Motor neurons number and the myelin level were investigated on days 14 and 42 using Nissl and Luxol Fast Blue staining. All treatments improved the motor function on days 7, 14, 21, 28, 35 and 42 compared to spinal cord injury (SCI). However combination therapy was more effective than Astaxanthin (Ast) or Epidermal neural crest stem cells (EPI-NCSCs) individually in behavioral improvement. Decreased the motor neurons number following

spinal cord injury (SCI), increased by Ast, Cell and Ast+Cell, but combination therapy significantly had better effects. Although all treatment increased white matter compared to SCI, treatment with Ast+Cell had increased myelin levels. We observed the reduction in PGC1α, NRF1, and TFAM expression in spinal tissue after the spinal cord injury (SCI), and the treatment with Cell and Ast + Cell significantly restored NRF1 and TFAM mRNA levels. These results show that Ast in combination with EPI-NCSCs has shown the better effects on behavioral dysfunction, motor neuron loss and demyelination after spinal cord injury (SCI). These protective effects may be attributed to the mitochondrial biogenesis activation.

Methods:
The sever SCI induced by dropping a metal rod onto the exposed dorsal surface of the spinal cord on male rats witch treated by Ast (0.2mM) and EPI-NCSCs (106/10µl PBS) alone and combined.

Results:
The Basso, Beattie and Bresnahan (BBB) test on days 1, 3, 7, 14, 21, 28, 35 and 42 post-injury was used for assessing of Motor function. The Motor neurons number and the myelin level were investigated on days 14 and 42 using Nissl and Luxol Fast Blue staining. All treatments improved motor function on days 7, 14, 21, 28, 35 and 42 compared to SCI.

Significance:
The Spinal cord injury (SCI) damages the sensory-motor function and also causes the complications. The astaxanthin (AST) has the potential to be used as a treatment for it. The present study investigates the effects of Astaxanthin (AST) in a compression model of Spinal cord injury (SCI) with emphasis on sensory-motor outcomes alongs with other complications also. The histopathological damage and also related signalling pathways.

Conclusion:
However combination therapy was more effective than Ast or EPI-NCSCs individually in behavioral improvement. Decreased the motor neurons number following SCI, increased by Ast, Cell and Ast+Cell, but combination therapy significantly had better effect. Although all treatment increased white matter compared to SCI, treatment with Ast+Cell had increased myelin levels. The suggest is that it had a strong therapeutic agent towards the clinical applications.