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PERSPECTIVE

Neural regeneration after spinal cord injury treatment by lavandula angustifolia and human umbilical mesanchymal stem cell transplantation

Spinal cord injury (SCI) is one of the most common causes of paralysis worldwide because the loss of neurons and axons causes permanent neurological deficits which could have influences on quality of life of patients, their family, and society. The complex pathophysiology of SCI, especially the secondary injury cascade, blocks complete recovery after SCI (Dumont et al., 2001).

The severity of spinal cord injury depends on the width, spinal level, and extent of the injury. The primary trauma is initial tissue disruption, followed by the initiation of a series of secondary cellular processes that can lead to long-term functional spinal deficits. Because spinal cord injury is associated with increased oxidative stress and induction of inflammatory genes at the site of the injury and in the adjacent regions, neuroprotective agents could be effective to diminish the injury after SCI-hence, therapeutic strategies for spinal cord injury include both neuroprotective and neurotrophic techniques. Acute neuroprotection could inhibit functional damage of neurons after injury and preserve behavioral output. Additionally, decreasing excitotoxicity by reduction in production of nitric oxide (NO), apoptosis, and inflammation could be a main cellular strategy to alleviate injury (Satake et al., 2000; Schumacher et al., 2000).

It has been shown that the more antioxidant protection, the better the result of SCI improvement. On the other hand, it has been demonstrated that increased oxidative stress can lead to direct DNA damage, which leads to damaged secondary processes, such as an impaired activity of membrane enzymes. Therefore, it appears that inhibiting the progression of secondary injury to spinal cord neurons is one of the most effective therapeutic strategies in limiting tissue injury of an injured spinal cord (Dumont et al., 2002).

In the past ten years, the first cell therapies (ProCord, OEGs, Schwann cells) have started using engineered biomolecules and antibodies. New trials of neuroprotection are underway and several thousand SCI patients have received a variety of cell therapies, bone marrow stromal cells (BMSCs), and cord blood. The rate of progress has been remarkable (Richard et al., 2002), but until today there are no demonstrated treatments for spinal cord injury (Yamaji et al., 2008). Thus, the best course of action is to decrease inflammation and oxidative stress around the damaged neurons and to increase neuroprotective agents.

Therefore, we selected two important tenets to choose the best treatments after an assessment of efficacy in order to reach the best result: good accessibility of selected treatments and that the selected treatments should be affordable. Our two selected treatments were lavender, or Lavandula angustifolia (L. angustifolia) and human umbilical mesenchymal stem cells (HUMSCs) derived from umbilical cord Wharton's jelly. HUMSCs and L. angustifolia are very accessible in Iran and are inexpensive. L. angustifolia is a neuroprotective agent which has diverse therapeutic effects on nervous system disorders (Yaghoobi et al., 2016). HUMSCs play a important role as a neuroregenerative source, and also could have a neuroprotective role. The umbilical cord is a waste product in Iran, so converting a waste product into a valuable neuroregenerative drug could be beneficial. On the other hand, because stem cell therapy has not been as successful as expected yet (Richard et al. , 2002), we need a safe and accessible agent to promote neural regeneration in SCI patients and to potentiate the HUMSCs; for this reason we selected L. angustifolia to potentiate the HUMSCs transplantation results for neural regeneration.

It has been shown that systemic delivery of mesenchymal stem cells (MSCs) have therapeutic benefits in a number of experimental treatments for central nervous system disorders. These cells are multipotent stem cells present in adults, and when cultured they have the ability to differentiate into a variety of lineages, including neurons and glial cells. Moreover, the systemic injection of MSCs prepared from adult bone marrow has therapeutic benefits after cerebral artery occlusion (Dumont et al., 2001). BMSCs ares a reliable source of producing neural-like cells after SCI and are more similar to neural stem cells (Yamaji et al., 2008). HUMSCs from Wharton's jelly are a low-cost source of stem cells that can be easily obtained and propagated in culture without invasive medical procedures or ethical issues (Yaghoobi et al., 2016), possess stem cell properties, are immunotolerable (Yaghoobi et al., 2016), and can be induced to form other cell lineages, such as neurons and glial cells (Mitchell et al., 2003).

The initial observation of our studies was that a single injection of HUMSCs 48 hours after trauma markedly decreased inflammation in the injured region and improved the locomotion of rats. Although extract of L. angustifolia potentiated the effects of HUMSCs transplantation, on its own it was found to significantly decrease damage and inflammation as well as improve locomotion.

In our studies, we found that the effective dose of L. angustifolia hydro-alcoholic extract was 400 mg/kg and the lethal dose of L. angustifolia hydro-alcoholic extract was 800 mg/kg.

Our studies showed that L. angustifolia significantly improved behavioral results; such as the Basso, Beattie, and Bresnahan (BBB), sensory test, and electrophysiological evaluation results. L. angustifolia also increased the number of the ventral horn motor neurons and decreased the number of astrocytes and therefore decreased astrogliosis. The result of intraspinal transplantation of HUMSCs to the injured spinal cord was similar to L. angustifolia, and when we used a combination of L. angustifolia and HUMSCs, the results were stronger. The results of behavioral tests significantly increased improvement; for example, the blood-brain barrier, sensory test, and electrophysiological evaluation results were improved in comparison with either single treatment (Kaka et al., 2016; Yaghoobi et al., 2016). The increase of the number of ventral horn motor neurons and decrease of the number of astrocytes were better than either single treatment. In our study, we strongly demonstrated that extract of L. angustifolia could have neuroprotective effects (Yaghoobi et al., 2016) to diminish cavity area of gray and white matter in injured spinal cord (Kaka et al., 2016; Yaghoobi et al., 2016) (**Figure 1**).

These findings may have significant implications for elucidation of the cellular and molecular mechanisms involved in L. angustifolia and HUMSCs neuroprotection and may constitute as an attractive therapeutic target in injured area after SCI.

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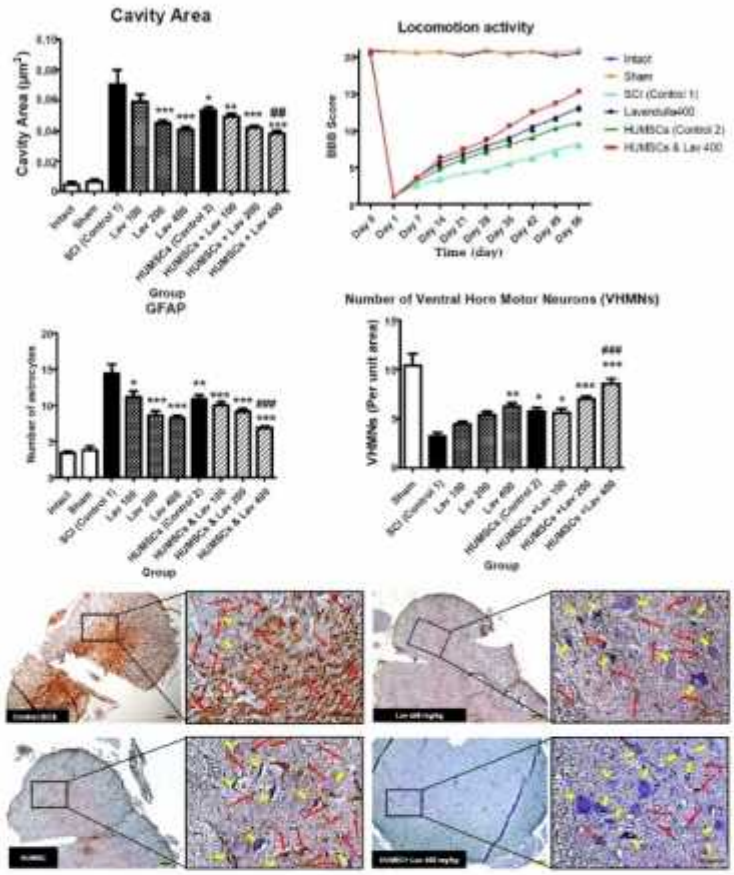

Figure 1 Effects of L. angustifolia and HUMSCs treatment on SCI.

The efficacy of L. angustifolia 400 mg/kg to improve SCI, potentiated the improvement after intraspinal transplantation of HUMSCs. *, **, and *** show significant differences between *Cavity Area* of all groups and SCI (Control 1) ($P < 0.05$, $P < 0.001$, and $P < 0.0001$, resp.); moreover ## show significant differences between *Cavity Area* of HUMSCs+Lav400 and HUMSCs (Control 2) ($P < 0.001$). *, **, and *** show significant differences between *Number of* GFAP$^+$ *astrocytes* of all groups and SCI (Control 1) ($P < 0.05$, $P < 0.001$, and $P < 0.0001$, resp.); moreover ### show significant differences between *Number of* GFAP$^+$ *astrocytes* of HUMSCs+Lav400 and HUMSCs (Control 2) ($P < 0.0001$). *, **, and *** show significant differences between *Number of ventral Horn Motor Neurons* of all groups and SCI (Control 1) ($P < 0.05$, $P < 0.001$, and $P < 0.0001$, resp.); moreover ### show significant differences between *Number of ventral Horn Motor Neurons* of HUMSCs+Lav400 and HUMSCs (Control 2) ($P < 0.0001$). Transverse section of spinal cord showing the ventral horn gray matter at the T_{12}–L_1 level for all groups on day 56 GFAP-stained images. Yellow arrows indicate VHMNs. Red arrows indicate the GFAP$^+$ astrocytes. Decreased GFAP$^+$ astrocytes and increased VHMNs are evident. The lesion area including the cavity and surrounding damaged tissue in area of 3,562,500 mm^2, was then measured by using an image analyzing software (Motic 2.1, Italy, Cagli); in addition, the number of lower motor neurons in area of 5,700 mm^2, the number of GFAP-positive astrocyte perikaryon in ventral horn, and area of 33,625 mm^2 were measured. Only those cells that showed clearly discernible nucleus were counted. GFAP: Glial fibrillary acid protein; HUMSCs: human umbilical mesenchymal stem cells; Lav: lavandula angustifolia; SCI: spinal cord injury; VHMNs: ventral horn motor neurons. Bar in 40× = 100 micrometer and bar in 200× = 50 micrometer (ECLIPSE 50i microscope).

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References

Dumont AS, Dumont RJ, Oskouian RJ (2002) Will improved understanding of the pathophysiological mechanisms involved in acute spinal cord injury improve the potential for therapeutic intervention? Curr Opin Neurol 15:713-720.

Dumont RJ, Okonkwo DO, Verma S, Hurlbert RJ, Boulos PT, Ellegala DB, Dumont AS (2001) Acute spinal cord injury, part I: pathophysiologic mechanisms. Clin Neuropharmacol 24:254-264.

Kaka G, Yaghoobi K, Davoodi S, Hosseini SR, Sadraie SH, Mansouri K (2016) Assessment of the neuroprotective effects of lavandula angustifolia extract on the contusive model of spinal cord injury in wistar rats. Front Neurosci 10:23.

Mitchell KE, Weiss ML, Mitchell BM, Martin P, Davis D, Morales L, Helwig B, Beerenstrauch M, Abou-Easa K, Hildreth T, Troyer D, Medicetty S (2003) Matrix cells from Wharton's jelly form neurons and glia. Stem Cells 21:50-60.

Richard WH, Volker CIS, Sonntag KH, Voll DG (2012) Spine. YOUMANS Neurological Surgery. pp2719-2729. Saunders/Elsevier.

Satake K, Matsuyama Y, Kamiya M, Kawakami H, Iwata H, Adachi K, Kiuchi K (2000) Nitric oxide via macrophage iNOS induces apoptosis following traumatic spinal cord injury. Brain Res Mol Brain Res 85:114-122.

Schumacher PA, Siman RG, Fehlings MG (2000) Pretreatment with calpain inhibitor CEP-4143 inhibits calpain I activation and cytoskeletal degradation, improves neurological function, and enhances axonal survival after traumatic spinal cord injury. J Neurochem 74:1646-1655.

Yaghoobi K, Kaka GR, Davoodi S, Ashayeri H (2016) Therapeutic effects of Lavandula angustifolia. J Gorgan Uni Med Sci 17:1-9.

Yaghoobi K, Kaka G, Mansouri K, Davoodi S, Sadraie SH, Hosseini SR (2016) Lavandula angustifolia extract improves the result of human umbilical mesenchymal Wharton's jelly stem cell transplantation after contusive spinal cord injury in wistar rata. Stem Cells Int 2016:5328689.

Yamaji T, Yamazaki S, Li J, Price RD, Matsuoka N, Mutoh S (2008) FK1706, a novel non-immunosuppressant neurophilin ligand, ameliorates motor dysfunction following spinal cord injury through its neuroregenerative action. Eur J Pharmacol 591:147-152.