Abstract

Spinal cord injury is a serious trauma and despite intensive research there is still no effective treatment for patients. The aim of this thesis is to study new possibilities of spinal cord injury therapy in animal models. We have focused on the use of natural materials, stem cells, gene therapy and the possibility of combining these approaches.

The effect of extracellular matrix (ECM) based materials prepared by decellularization of porcine spinal cord and porcine urinary bladder on tissue regeneration after acute hemisection of the spinal cord was investigated. Another tested material was a hydrogel based on hyaluronic acid modified with RGD adhesion peptide, which was applied acutely and subacutely into the hemisection lesion. We have shown that both types of biomaterials have positive effect on regeneration of the spinal cord tissue by bridging the lesion and promotion of axonal ingrowth. In addition, ECM hydrogels promote the growth of blood vessels into the lesion site. The combination of hydrogels with mesenchymal stem cells derived from human umbilical cord (hWJ-MSCs) had synergistic effect, but since only a limited number of cells could be incorporated into hydrogels, this effect was not associated with improvement in motor skills. The limitation of ECM hydrogels is their rapid degradation, which will not allow full recovery of damaged tissue.

Another part of this work is focused on intrathecal transplantation of hWJ-MSCs into the balloon-induced compression lesion. We have shown that the effect of cells is dose dependent and that 1.5 million transplanted hWJ-MSCs in one dose or in three doses of 0.5 million is the minimum number of hWJ-MSCs, which leads to improvements in behavioural and histological parameters such as axonal ingrowth and reduction of the glial scar. However, only repeated application of 1.5 million hWJ-MSCs led to significant improvement in more demanding behavioural test that requires coordination of movements.

As another possible therapeutic approach, neural cell transfection was chosen. We have shown that gene therapy using vectors with α9 integrin subunit and the integrin activator kindlin 1 combined with the implantation of a biomaterial modified with specific adhesion peptide could be another possible approach how to promote the growth of axons into the lesion site.