# Abstract

Vertebral body fractures together with the spinal cord injury (SCI) remain a challenging medical condition. While management of the thoracic-lumbar (Th-L) vertebral fractures belongs to basic neurosurgical procedures with a usually excellent outcome, treatment of the severe spinal cord injury has mostly unsatisfactory results and thus novel approaches are highly in demand. In this study, experimental treatment of the SCI in a rat model using human mesenchymal stem cells derived from Wharton´s jelly (WJ-MSCs) and a novel highly water soluble, nano-formulated curcumin is evaluated. Furthermore, a novel method of mini-invasive percutaneous posterior stabilisation (MIS) of Th-L vertebral fractures is retrospectively compared with classical open posterior (OPEN) procedure.

To assess the effectivity of hWJ-MSCs treatment in the ischemic-compression model of SCI in rats, different dosages (0.5 or 1.5 million cells) and repeated applications were compared. Cells or saline were applied intrathecally by lumbar puncture once, or in three consecutive weeks after injury. Nanocurcumin and a vehicle nanocarrier as a control were delivered both locally, immediately after the spinal cord injury, and subcutaneously during the four consecutive weeks after SCI. Rats were assessed for locomotor skills (BBB, flat beam, motoRater) for 9 weeks. Spinal cord tissue was morphometrically analysed for axonal sprouting, sparing of grey and white matter and astrogliosis. The expression of endogenous genes (*Gfap, Casp3, Irf5, Cd86, Mrc1, Cd163, Sort1, Fgf2, Olig2, Gap43, Vegf, Nfkβ*) and interleukins (IL-1β, TNF-α, IL-6, IL-12, CCL-5, IL-11, IL-10, IL-13) was studied with qRT PCR.

Significant recovery of functional outcome was observed in all of the hWJ-MSCs treated groups except for the single application of the lowest number of cells (0.5 M). Histochemical analyses revealed a gradually increasing effect of grafted cells, resulting in a significant increase in the number of $GAP43^{+}$ fibers, a higher amount of spared grey matter and reduced astrogliosis. mRNA expression of macrophage markers and apoptosis was downregulated after the repeated application of 1.5 million cells. We conclude that the effect of hWJ-MSCs on spinal cord regeneration is dose-dependent, and potentiated by repeated application.

The behavioural tests revealed a significant improvement of the biomechanics of hind limbs with a better weight-carrying ability in the nanocurcumin treated group, compared to the

nanocarrier control. An immunohistochemical and histological analysis confirmed a significant sparing of the white matter tissue, a reduced area of glial scaring and a higher amount of newly sprouted axons in the nanocurcumin treated group. The mRNA expression of endogenous genes and interleukins showed changes in the expression of the inflammatory cytokines in the first two weeks after SCI.

Retrospective clinical analysis of the patients who suffered traumatic vertebral fracture(s) of the lower thoracic and lumbar spine and were operated by classical open posterior stabilisation (group OPEN) or by mini-invasive percutaneous posterior stabilisation (group MIS) was performed. The precise position of the pedicular screws, Cobb´s angle, vertebral body angulation (VBA), vertebral body index (VBI), duration of the surgery and exposition to the X-ray was evaluated. In the period 2015-2018 totally 147 patients were analysed. We found no significant difference in number of pedicle screw malpositions, Cobb´s angle, VBI and VBA between the groups. While duration of the operation was significantly shorter in the MIS group, exposition time to the X-ray was in the same group significantly higher. MIS procedure was found as a safe and comparable to the classical OPEN surgical procedure.

**Key words**: spinal cord injury - human mesenchymal stem cells derived from Wharton´s jelly (hWJ-MSCs) - nanocurcumin - inflammatory response - neuroregeneration - astrogliosis - axonal sprouting - open stabilisation - mini-invasive percutaneous stabilisation - traumatic vertebral fractures - pedicular screw