THE EFFECT OF SEVERITY OF DEGENERATION ON INTERVERTEBRAL DISC REGENERATION BY USE OF MESENCHYMAL STEM CELLS

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Introduction:

Degenerative disc disease (DDD) is a consequence of alterations in the extracellular matrix composition of the intervertebral disc (IVD). Studies suggest that mesenchymal stem cells (MSCs) have the ability to arrest degeneration but not regenerate it. We hypothesize that this is related to the severity of degeneration. This study investigates the effect of different severity of degeneration on the ability of MSCs to halt or regenerate the IVD.

Methods:

Disc degeneration was induced in 9 New Zealand white rabbits at 4 consecutive lumbar levels by annular puncture. The degeneration was allowed to progress for 1 month (early group, n=5) or 7 months (late group, n=4). Autologous MSCs were then isolated, expanded ex vivo and labeled with bromo-deoxyuridine (BrdU). 1×10^5 MSCs were injected into 2 of 4 punctured discs per rabbit. The other 2 levels were used as control levels that were either sham (punctured but no further treatment) or injected with culture medium only. Serial radiographs of the spine were taken every 2 weeks. All rabbits were sacrificed at 16 weeks post-injection, the discs were retrieved for histological and immunohistochemical examination. Disc heights on radiographs were measured. A histological grading was used to assess the severity of degeneration.

Results:

MSCs could be detected in all IVDs 16 weeks post-injection. For the early group, there were no significant differences in disc height among the normal discs, the control discs or the MSCs-injected discs. For the late group, the medium-injected and MSCs-injected discs had significantly lower disc heights (p<0.05) than the normal discs and the sham discs. Histological grading of annular degeneration revealed that MSCs injection had no effect on the progression of disc degeneration in the early group. However in the late group, the MSCs injected discs were significantly (p<0.05) less degenerated than the control discs. This finding was further supported by the recovery of a near normal proteoglycan level in some areas of the MSCs-injected discs in both early and late groups.

Discussions and conclusions:

Contrary to intuitive belief, MSCs injection has a more significant effect when introduced into more severely degenerated discs. Although evidence of halting progression of degeneration can be demonstrated, they do not have the ability to regenerate the disc or restore disc space height. It is not possible to conclude from the current study whether this failure to regenerate the disc is a problem of the model itself, an insufficient number of cells, a lack of a scaffold material, or that MSCs lack this ability. Nevertheless, this is the first study to demonstrate that severity of degeneration has a significant effect on MSCs ability to regenerate the IVD, and forms the basis for further investigations. Future investigations will need to carefully control for the severity of degeneration when studying intervertebral disc regeneration.