

Treatment of lower oesophageal sphincter damage with bone marrow derived mesenchymal stem cells

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Background. The incompetence of lower esophageal sphincter (LES) with consequent exposition of the esophageal mucosa to gastric acid leads to gastroesophageal reflux disease. The aim of this study was to evaluate whether intralesional injections of Bone Marrow Mesenchymal Stem Cells (BM-MSC), which proved useful in the treatment of urinary (1) and anal (2) incontinence, could also help muscle regeneration at the site of surgical myotomy of rat LES.

Methods. 24 inbred Wistar Furth rats were divided into three groups: group A underwent a sham operation followed by saline injection; group B LES myotomy plus saline injection; group C LES myotomy followed by an intra-sphincteric injection of culture-expanded syngeneic BM-MSC. At day 30, histological and morphometric analysis were performed on metacrylate embedded samples. GFP positive MSC isolated from transgenic rats were moreover used to track the cells in the injured area in cryostat sections at days 7, 14 and 30 after the lesion. Cryostat sections were also used for immunohistochemical detection of striated and smooth muscular markers (a actinin, a smooth muscle actin, calponin).

Results. At day 30 of surgery, the muscle area fraction (MAF) at the site of LES myotomy was significantly higher in group C compared to group B animals ($p < 0.05$) and contained a high number of small irregularly arranged smooth muscle cells, sometimes grouped in clusters. GFP positive cells could be tracked at the periphery of the lesion at day 7 and also inside the lesion at day 14 of surgery when the damaged area, as evidenced by specific antibodies, was still devoid of smooth or striated muscle cells. At day 30, the lesion was recognizable only as a disorganized area at the periphery of the muscular layer. At this time clusters of GFP positive cells, unstained by muscular specific antibodies, could still be detected at the periphery and sometimes also in the center of the muscular layer.

Conclusions. BM-derived MSC, improving muscle regeneration of surgically myotomized LES in the rat, may represent a valuable tool in the treatment of LES injury.

1) Y.Kinebuchi et al. Int.J.Urol. 2010, 17:359-68

2) B.Lorenzi et al.Dis Colon Rectum 2008, 51:411-20.

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