Transplantation of muscle-derived stem cells plus biodegradable fibrin glue restores the urethral sphincter in a pudendal nerve-transected rat model.

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Abstract:

We investigated whether fibrin glue (FG) could promote urethral sphincter restoration in muscle-derived stem cell (MDSC)-based injection therapies in a pudendal nerve-transected (PNT) rat, which was used as a stress urinary incontinence (SUI) model. MDSCs were purified from the gastrocnemius muscles of 4-week-old inbred female SPF Wistar rats and labeled with green fluorescent protein. Animals were divided into five groups (N = 15): Sham (S), PNT (D), PNT+FG injection (F), PNT+MDSC injection (M), and PNT+MDSC+FG injection (FM). Each group was subdivided into 1- and 4-week groups. One and 4 weeks after injection into the proximal urethra, leak point pressure (LPP) was measured to assess urethral resistance function. Histology and immunohistochemistry were performed 4 weeks after injection. LPP was increased significantly in FM and M animals after implantation compared to group D ($P < 0.01$), but was not different from group S. LPP was slightly higher in the FM group than in the M group but there was no significant difference between them at different times. Histological and immunohistochemical examination demonstrated increased numbers of surviving MDSCs (109 +/- 19 vs 82 +/- 11/hpf, $P = 0.026$), increased muscle/ collagen ratio (0.40 +/- 0.02 vs 0.34 +/- 0.02, $P = 0.044$), as well as increased microvessel density (16.9 +/- 0.6 vs 14.1 +/- 0.4/hpf, $P = 0.001$) at the injection sites in FM compared to M animals. Fibrin glue may potentially improve the action of transplanted MDSCs to restore the histology and function of the urethral sphincter in a SUI rat model. Injection of MDSCs with fibrin glue may provide a novel cellular therapy method for SUI.