Periurethral muscle-derived mononuclear cell injection improves urethral sphincter restoration in rats

Abstract
Aims Investigate the effect of a novel cell-based therapy with skeletal muscle-derived mononuclear cells (SMDMCs) in a rat model of stress urinary incontinence. Methods Male Wistar-Kyoto rats' hind limb muscles were enzymatically dissociated, and SMDMCs were isolated without needing expansion. The cell population was characterized. Twenty female rats underwent urethrolysis. One week later, 10 rats received periurethral injection of 10⁶ cells (SMDMC group), and 10 rats received saline injections (Saline group). Ten rats underwent sham surgery (Sham group). Four weeks after injection, animals were euthanized and the urethra was removed. The incorporation of SMDMCs in the female urethra was evaluated with fluorescence in situ hybridization for the detection of Y-chromosomes. Hematoxylin and eosin, Masson's trichrome staining, and immunohistochemistry for actin and myosin were performed. The muscle/connective tissue, actin and myosin ratios were calculated. Morphological evaluation of the urethral diameters and fractional areas of the lumen, mucosa, and muscular layer was performed. Results SMDMCs population was consistent with the presence of muscle cells, muscle satellite cells, perivascular cells, muscle progenitor cells, and endothelial cells. SMDMCs were incorporated into the urethra. A significant decrease in the muscle/connective tissue ratio was observed in the Saline group compared with the SMDMC and Sham groups. The proportions of actin and myosin were significantly decreased in the Saline group. No differences were observed in the morphometric parameters. Conclusions SMDMCs were incorporated into the rat urethra and promoted histological recovery of the damaged urethral sphincter, resulting in decreased connective tissue deposition and increased muscle content. (AU)