

HUMAN MESENCHYMAL STEM CELLS ENCAPSULATED IN A DITYRAMINE CROSS-LINKED HYDROGEL RECONSTITUTE URINARY CONTINENCE IN A PUBOURETHRAL LIGAMENT TRANSECTED RAT MODEL

Hypothesis / aims of study

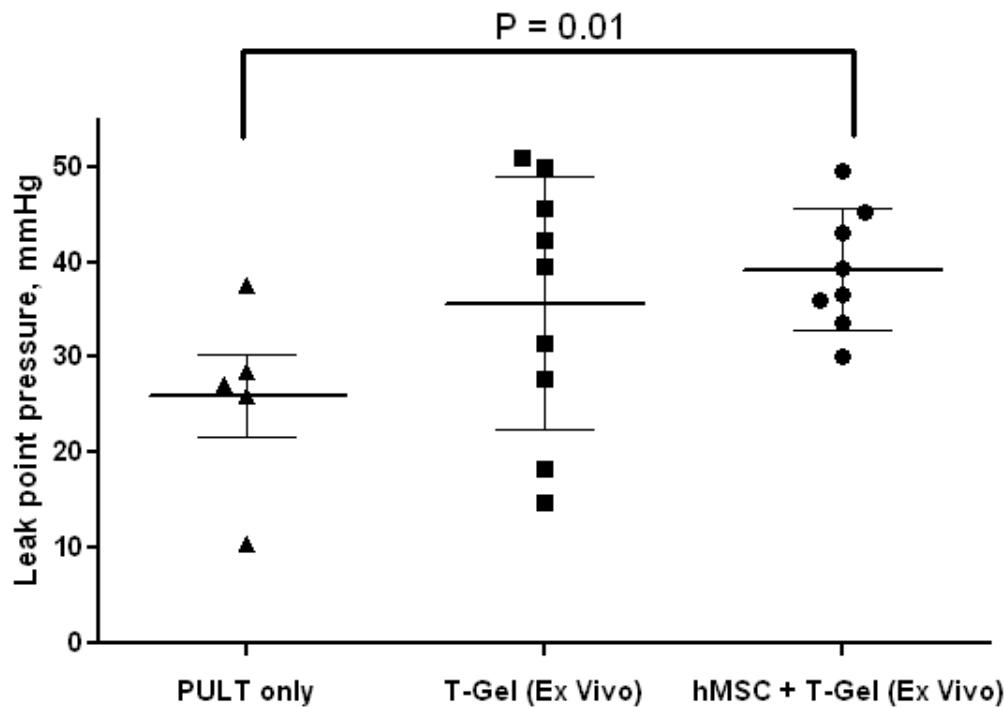
The integral theory of stress urinary incontinence (SUI) implicates a deficient pubourethral ligament (PUL) as a major contributor to SUI in women. Mid-urethral slings have been developed based on this theory to treat SUI in more than 2 million women worldwide. The aim of this study was to examine the efficacy of bone marrow derived human mesenchymal stem cells (hMSCs) and a patented dityramine cross-linked porcine collagen-based hydrogel (T-gel) to restore continence in a previously described model of PUL deficiency.

Study design, materials and methods

Female Sprague-Dawley rats received pubourethral ligament transection (PULT) (n=8), bilateral pudendal nerve transection (PNT) (n=8), or sham surgery (n=8). Additional rats undergoing PULT received treatment immediately post-operatively with hMSCs and T-gel cross-linked ex vivo and injected in situ (n=12), T-gel cross-linked ex vivo and injected in situ (n=12), hMSCs injected in situ (n=12), or hMSCs injected systemically (n=12). Four weeks after surgery, leak point pressure (LPP) was measured in animals via an implanted suprapubic tube. The mean of 9-10 LPP measurements was calculated per rat, and the level of significance between groups was determined using a two-tailed unpaired t-test assuming equal variance.

Results

Mean LPP was significantly decreased in untreated rats undergoing PULT compared to sham, and no difference was detected compared to PNT group. When treated with hMSCs encapsulated in T-gel cross-linked ex vivo and injected at the PUL in situ, treated animals demonstrated statistically significant improvement in mean LPP compared to PULT alone (39.14 vs. 25.91 mmHg, p=0.01) (figure). PULT rats treated with only T-gel, systemic hMSCs, or locally injected hMSCs showed an improved but statistically insignificant difference in mean LPP compared to control.



Interpretation of results

Human mesenchymal stem cells encapsulated in T-gel cross-linked ex vivo and injected at the PUL in situ restored continence in a rat model of SUI.

Concluding message

This patented material could be used in clinical trials for treatment of SUI in women.

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| Specify source of funding or grant | This research was funded by departmental funding from Case Western Reserve University School of Medicine Department of Urology. |
| Is this a clinical trial? | No |
| What were the subjects in the study? | ANIMAL |
| Were guidelines for care and use of laboratory animals followed or ethical committee approval obtained? | Yes |
| Name of ethics committee | IACUC #2010-0029 |