

A NOVEL REGENERATIVE TREATMENT FOR FEMALE STRESS URINARY INCONTINENCE: SHORT-TERM OUTCOME OF THREE PATIENTS UNDERGOING PERIURETHRAL INJECTION OF AUTOLOGOUS ADIPOSE-DERIVED REGENERATIVE CELLS

Hypothesis / aims of study

We created a novel treatment strategy to regenerate the urethral sphincter function, using autologous adipose-derived regenerative cells (ADRCs) without the need of cell culture (Fig.1). We previously demonstrated the safety and favourable long-term efficacy of periurethral injection of autologous ADRCs for the treatment of male stress urinary incontinence (SUI) following prostatectomy [1]. In the present study, we report the short-term outcome of the first three female patients with SUI undergoing periurethral injection of autologous ADRCs.

Study design, materials and methods

Three female patients with SUI were included in this preliminary clinical trial. No patients had urgency incontinence. After liposuction of 250 mL of adipose tissue from the abdomen, we isolated ADRCs by using the Celution™ system. Subsequently, these ADRCs and a mixture of ADRCs and adipose tissue were transurethraly injected into the rhabdosphincter and submucosal space of the urethra, respectively. Unlike other cell therapies, this treatment is entirely autologous, does not require cell culture, and is performed as a single surgical procedure. In the protocol, the primary outcome is assessed at by a 24-hour pad test, at baseline, 2 weeks, 1 month, and every 3 months thereafter until 36 months after treatment. Secondary outcomes included a validated patient questionnaire (the International Consultation on Incontinence Questionnaire-Short Form; ICIQ-SF), urethral pressure profile, contrast-enhanced transvaginal ultrasonography, and magnetic resonance imaging (MRI). Here, we report the short-term outcomes of treatment efficacy and safety at the 6-month follow-up in these three cases.

Results

After injection, urinary incontinence progressively improved in two (cases 2 and 3) of the three patients during the 6-month follow-up, i.e., decreased leakage volume was observed in a 24-hour pad test (Table 1). In the two patients who showed improvement, the mean daily leakage for 4 days of consecutive measurements gradually improved from 19.4 to 2.5 g and from 25.8 to 0.8 g at 6 months after injection, respectively. The ICIQ-SF total score improved from 15 to 6 and from 14 to 8, respectively. In the urethral pressure profile, the maximum urethral closing pressure (MUCP) and functional profile length (FPL) increased from 42 to 55 cmH₂O and 26 to 30 mm, and from 23 to 47 cmH₂O and 24 to 28 mm, respectively. In one patient (case 1) without improvement in leakage volume (from 70 to 95 g), total ICIQ-SF score, MUCP, and FPL changed from 14 to 19, 23 to 31 cmH₂O, and 25 to 35 mm, respectively. MRI showed sustained presence of the injected adipose tissue in all patients. Enhanced ultrasonography showed a progressive increase in blood flow to the injected area up to 6 months after the injection in all patients. No significant adverse events were observed peri- or postoperatively. On uroflowmetry, there was no significant decrease in maximum flow rate and no significant increase in residual urine volume.

Interpretation of results

The periurethral injection of ADRCs gradually improved SUI over time in two patients. The results of the present clinical trial and a previous experimental study [2] suggest the mechanisms involved in the improvement of the sphincteric function to be bulking effect, regeneration of the smooth muscle, and increased blood flow caused by ADRCs injection.

Concluding message

This is a report of the short-term outcomes of only three cases, and long-term data of a larger number of patients are necessary to confirm treatment safety and efficacy. The results of this preliminary study showed that periurethral injection of autologous ADRCs is a safe and feasible treatment modality for female patients with SUI caused by urethral sphincter deficiency.

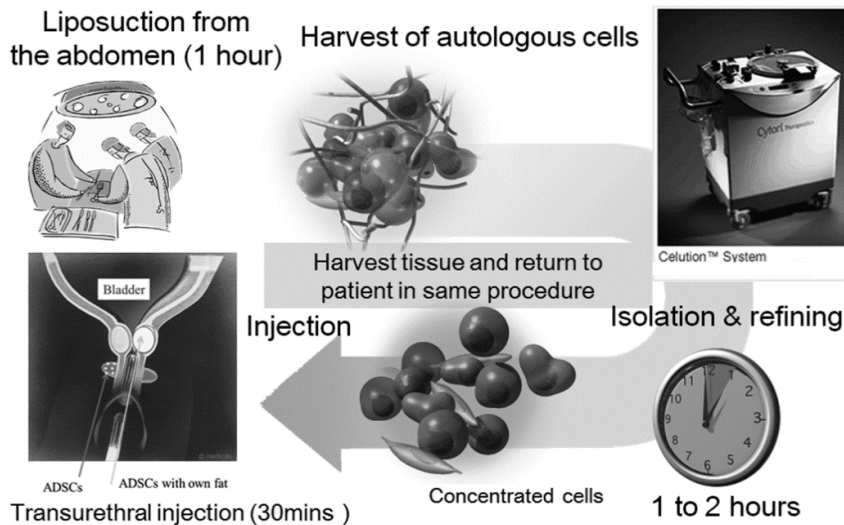


Fig.1: Flow diagram of the periurethral injection of autologous ADRCs

Case	Leakage volume, 24 h	ICIQ-SF, total score	ICIQ-SF, leakage frequency	ICIQ-SF, leakage volume	ICIQ-SF, QOL	MUCP	FPL
1	70	14	4	2	8	23	25
	95	19	5	4	10	31	35
2	19.4	15	4	4	7	42	26
	2.5	6	2	2	2	55	30
3	25.8	14	4	4	5	23	24
	0.8	8	3	2	3	47	28

Upper raw data points: at baseline; Lower raw data points: at 6 months after treatment

Leakage volume, 24 h: mean daily leakage for 4 days of consecutive measurements

ICIQ-SF: International Consultation on Incontinence Questionnaire-Short Form

MUCP: maximum urethral closing pressure on urethral pressure profile

FPL: functional profile length on urethral pressure profile

Table 1: Change in each parameter from baseline to 6 months after treatment

References

1. Gotoh M, Yamamoto T, Kato M, et al.: Regenerative treatment of male stress urinary incontinence by periurethral injection of autologous adipose-derived regenerative cells: 1-year outcomes in 11 patients. *Int J Urol*, Aug 29. doi: 10.1111/iju.12266. Epub ahead of print, 2013.
2. Watanabe T, Maruyama S, Gotoh M, et al.: Increased urethral resistance by periurethral

Disclosures

Funding: none **Clinical Trial:** Yes **Registration Number:** UMINID:UMIN000006116 **RCT:** No **Subjects:** HUMAN **Ethics Committee:** Nagoya University Ethics Committee **Helsinki:** Yes **Informed Consent:** Yes