



Original Article

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Therapeutic Efficacy of Urethral Sphincter Injections of Platelet-Rich Plasma for the Treatment of Stress Urinary Incontinence due to Intrinsic Sphincter Deficiency: A Proof-of-Concept Clinical Trial

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Purpose: The aim of this study was to investigate the efficacy of autologous platelet-rich plasma (PRP) in the treatment of stress urinary incontinence (SUI) due to intrinsic sphincter deficiency (ISD) refractory to medical treatment.

Methods: Thirty-five patients with SUI due to urodynamically proven ISD were prospectively enrolled. Five milliliters of PRP (2.5–5 times the platelet concentration in peripheral blood) was injected into the external sphincter at 5 sites; all patients received 4 injections at monthly intervals. The primary end-point was the change in SUI severity as assessed by a visual analogue scale (VAS of SUI). The secondary-endpoints were the Global Response Assessment score and changes in urodynamic parameters from baseline to 3 months after treatment.

Results: The mean age of patients was 68.7 ± 12 years; the median duration of SUI was 4 years. Five patients had neurogenic SUI, while 30 had nonneurogenic SUI (21 with postprostatectomy incontinence, 6 with previous radical cystectomy, and 3 with other etiologies). Complete dryness was achieved in 7 patients (20.0%) while moderate improvement was observed in 14 (40.0%). The mean VAS of SUI score decreased significantly from 6.57 ± 1.89 to 3.77 ± 2.41 after treatment. The abdominal leak point pressure (ALPP) increased significantly from 98.3 ± 55.8 to 157.3 ± 79.3 cm H₂O. There was no increase of ALPP in neurogenic SUI and less increase of ALPP in patients with failed treatment outcomes. No perioperative adverse events or severe complications occurred.

Conclusions: Urethral PRP injection is safe and effective in increasing urethral resistance and improving SUI. PRP could be an alternative treatment modality for male and female patients with moderate SUI due to nonneurogenic causes.

Keywords: Incontinence; Platelet-rich plasma; Minimally invasive therapy

- **Research Ethics:** This study was approved by the Institutional Review Board (IRB) and Ethics Committee (IRB No. 107-231-A). All patients were informed about the study rationale and procedures; written informed consent was obtained prior to enrollment and treatment.
- **Conflict of Interest:** No potential conflict of interest relevant to this article was reported.

INTRODUCTION

Stress urinary incontinence (SUI) is defined by the International Continence Society as involuntary leakage of urine on effort

or exertion, such as during sneezing or coughing [1]. In woman, SUI typically occurs after multiple child births and menopause; in men, SUI may occur after radical prostatectomy or, occasionally, after transurethral prostatectomy [2]. Intrinsic

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sphincter deficiency (ISD) may also result from neurological lesions such as spinal cord injury, myelomeningocele, or spinal bifida, and due to complicated urethral rupture associated with pelvic fracture [3].

SUI impairs the quality of life of the afflicted individual owing to the shame and embarrassment caused by incontinence. Conservative management includes the use of pads, external appliances for urine collection, penile clamps, behavioral modifications, and pelvic floor exercises [4,5]. Suburethral sling procedures are commonly performed to treat SUI in women; the reported success rate is approximately 90% at 3 years and 60% at 20 years [6]. Surgical procedures for male SUI include periurethral injections of bulking agents, suburethral sling procedures, artificial urinary sphincter implantation, periurethral constrictors, and stem cell therapy [7-10]. Many patients with SUI require a surgical intervention for incontinence since non-surgical modalities for postprostatectomy incontinence (PPI) offer limited and unsatisfactory improvement [9,11]. However, patients with mild urinary incontinence may not accept invasive surgical management. Injection therapy with urethral bulking agents or stem cell formulations have been developed as minimally invasive alternatives [10]. Currently, there is no simple treatment modality to cure this distressing disorder in male incontinent patients.

Autologous platelet-rich plasma (PRP) is growing in popularity as a therapy to augment wound healing and hasten recovery after muscle and joint injuries and surgical repair [12]. PRP is extremely rich in growth factors and cytokines that regulate tissue reconstruction; the use of PRP has been extensively studied in trauma patients and trauma experimental models [13-16]. The local application of autologous bone marrow-derived progenitor cells and PRP was shown to improve tissue regeneration [15]. PRP is an easily produced and relatively inexpensive biological material. It is produced directly from the patient's blood, and is thus superior to synthetic materials in terms of potential adverse effects such as foreign body reaction.

During wound healing, biologically active molecules are released from platelets. Platelets play an essential role in promoting tissue regeneration and wound healing [12]. Recent studies have demonstrated the immunomodulatory effect of PRP on the inflammatory response [15,16]. Platelet-rich concentrates are used as a source of growth factors to improve the healing process. PRP can also eliminate neuropathic pain by the direct effect of some factors acting directly on neurons to promote axonal regeneration [16]. Preliminary studies have also shown

that repeated PRP injections into the suburothelium improved bladder pain and decreased frequency urgency episodes in patients with interstitial cystitis/bladder pain syndrome [17,18].

Owing to the potential regenerative effect of PRP, it seems rational to inject PRP into the urethral sphincter to increase the sphincter muscle bulk and urethral resistance. Because autologous PRP does not have antigenicity to the patient's own tissue and has been proven safe for facilitating wound healing and in the treatment of interstitial cystitis [15-18], we performed a clinical trial to investigate the use of autologous PRP for treatment of SUI due to ISD of neurogenic or nonneurogenic etiology. Our results may provide clinical evidence for a novel therapeutic regimen for the treatment of ISD and SUI.

MATERIALS AND METHODS

A total of 35 patients with SUI with urodynamically proven ISD who did not respond to conventional treatments were enrolled in this study. All these patients had been treated with an oral medication (e.g., methylephedrine, imipramine, or duloxetine) or surgical treatment with a suburethral sling or artificial sphincter device, but treatment had failed for at least 1 year. The diagnosis of ISD was established based on the characteristic symptoms and video urodynamic findings. All patients had urinary incontinence and required pad protection. All patients were investigated thoroughly at enrollment and were excluded if they did not satisfy the study-selection criteria (Supplementary material 1).

The severity of SUI was reported by the patient's self-assessment using a 10-point visual analogue scale (VAS) score (0 indicating no incontinence and 10 indicating severe incontinence) (Table 1). The SUI VAS system was validated in the first 10 patients; the Cronbach alpha for test-retest reliability was 0.929, confirming the reproducibility of the reported grading of SUI. Patients were requested to maintain a 3-day voiding diary prior to treatment to record the functional bladder capacity, urinary frequency, nocturia, and daily urinary leakage episodes. Videourodynamic studies were performed by standard procedures using a 6F dual channel catheter and an 8F rectal balloon catheter [19]. Videourodynamic studies, abdominal leak point pressure (ALPP) measurements, and urethral pressure profilometry (UPP) were routinely performed at baseline and after PRP treatment. ALPP measurements were performed at full bladder to measure the smallest ALPP during cough and abdominal straining maneuvers. If there was no leak in response

Table 1. The visual analogue scale for assessment of stress urinary incontinence

VAS of SUI	Stamey SUI grade	Situation of SUI	Frequency of SUI (per situation)	Pad protection
0	0	Complete dryness	Zero	No
1	1	Heavy straining	1 episode/per days to weeks	No/yes
2			1 episode/day	
3		Coughing/sneezing/laughing or nighttime		
4		Heavy straining	> 1 episode/day	
5		Coughing/sneezing/laughing or nighttime		
6	2	Walking	< 50% of situations (every day)	Yes
7		Very mild movement/change in position		
8		Walking	≥ 50% of situations (every day)	
9		Very mild movement/change in position		
10	3	Any condition; persistent	All the time	Absolute

VAS, visual analogue scale; SUI, stress urinary incontinence.

to coughing or the Valsalva maneuver, the highest abdominal pressure was used to represent the ALPP. UPP parameters included maximum urethral closing pressure (MUCP) and functional profile length (FPL). All descriptions and terminology in this report are in accordance with the recommendations of the International Continence Society [1]. In this study, all patients were proven not to have urodynamic ISD or detrusor overactivity.

This study was approved by the Institutional Review Board (IRB) and Ethics Committee (IRB No. 107-231-A). All patients were informed about the study rationale and procedures; written informed consent was obtained prior to enrollment and treatment. Eligible patients were admitted for PRP treatment. All subjects received a urethral sphincter injection of 5 mL of PRP (extracted from 50 mL of the patient’s own whole blood) under intravenous general anesthesia in the operating room. The procedure was repeated every 1 month for a total of 4 treatments within 3 months. Patients were informed of the possible complications of urethral sphincter injection, such as hematuria, micturition pain, difficulty urinating, transient urinary retention, and urinary tract infection (UTI).

The procedure of preparing PRP was described in a previous report and is presented in Supplement material 2 [18]. In brief, a 50-mL whole blood specimen was withdrawn and subjected to centrifugation twice. The concentration of platelets in the PRP was 2.5–5 times that in the peripheral blood. Then, 5 mL of PRP in saline was sent to the operating room in a sterile test tube for urethral sphincter injection. The urethral sphincter PRP injections were administered at 5 sites via an injecting cys-

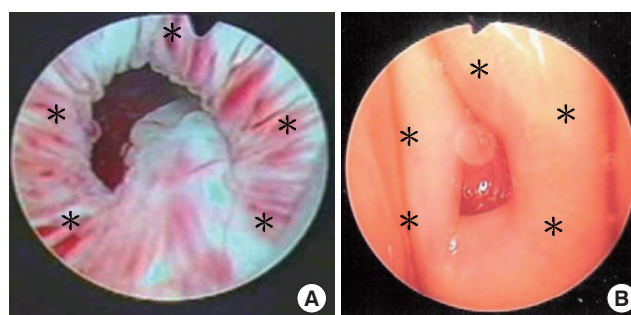


Fig. 1. Urethral sphincter platelet-rich plasma injections were administered at 5 sites (asterisks) via an injecting cystoscope for male patients (A), and from the perineum around the urethral meatus in female patients (B).

toscope for male patients and from the perineum around the urethral meatus in female patients (Fig. 1). At each site, 1 mL of PRP was injected at each site. After the PRP injections, patients were followed up at the outpatient clinic every month, and at 3 and 6 months after the 4 PRP injection.

The treatment outcome was assessed by the Global Response Assessment (GRA). The treatment result was considered excellent (GRA = 3) when patients reported complete dryness at the end of the study. A GRA score of 2 was considered indicative of moderate improvement. Excellent and moderately improved results were considered indicative of successful treatment. A GRA score of 1 or a reduction of 2 points in the VAS score was considered indicative of mild improvement. GRA improvement ≤ 1 was considered indicative of treatment failure.

The results of the voiding diary, urodynamic studies, and VAS scores were compared between baseline and the primary

end-point at 6 months; urodynamic parameters were compared between baseline and after the PRP treatment. Data were compared between different patient groups and between baseline and post-PRP treatment. Continuous variables are expressed as mean ± standard deviation, while categorical variables are presented as frequency (percentage). The paired t-test was used to analyze the data between baseline and posttreatment status, and the Wilcoxon rank-sum test was used for statistical comparisons of variables in the between-subgroup analysis. All statistical analyses were conducted using SPSS ver. 12 (SPSS Inc., Chicago, IL, USA). Two-sided P-values < 0.05 were considered indicative of statistical significance.

RESULTS

In total, 35 patients with SUI were enrolled in this study. The mean age of patients was 68.7 ± 12.0 years (range, 35–87 years); the median duration of SUI was 4 years (range, 1–10 years). The underlying diseases in the study population are listed in Table 2. Neurogenic SUI was noted in 5 patients, while 30 patients had nonneurogenic SUI (21 with PPI, 6 with previous radical cystectomy for bladder carcinoma, and 3 with other etiologies of ISD).

Three months after the fourth PRP injection, 7 patients (20.0%) reported complete dryness, while moderate improvement was observed in 14 patients (40.0%); thus, the overall success rate was 60.0%. Among the 30 patients with nonneurogenic SUI, 28 patients (93.3%) had a GRA ≥ 1, while 20 patients (66.7%) had a GRA ≥ 2. However, only 1 out of the 5 patients (20%) with neurogenic SUI had a GRA ≥ 2 (P = 0.044) (Table 2). There was no significant difference between patients with successful treatment outcomes and those with failed treatment outcomes with

respect to the baseline demographics and urodynamic variables (Table 3).

Table 4 shows the changes in the SUI VAS score and urodynamic variables from baseline to the primary end-point in the overall patients. The SUI VAS score significantly decreased after PRP treatment. No significant difference was noted in any of the urodynamic measures after PRP treatment, with the exception of ALPP (98.3 ± 55.8 cm H₂O vs. 157.3 ± 79.3 cm H₂O, P = 0.000) and FPL length (26.2 ± 6.59 mm vs. 28.7 ± 7.46 mm, P = 0.037). The mean SUI VAS score improved from 6.57 ± 1.90 at baseline to 5.57 ± 1.99 at 1 month, 4.74 ± 2.19 at 2 months, 4.24 ± 2.02 at 3 months, 3.9 ± 2.20 at 3 months after the fourth PRP injection, and 3.77 ± 2.41 at 6 months after the fourth PRP injection (P < 0.05 for all, compared with baseline) (Fig. 2). There was a significant difference between the successful and failed treatment groups with respect to changes in the SUI VAS score (−4.0 ± 1.92 vs. −1.36 ± 1.50, P = 0.000) and ALPP (74.0 ± 69.7 vs. 28.1 ± 61.1, P = 0.050). There was no urodynamic DO at baseline or *de novo* DO in the follow-up urodynamic study. The other urodynamic parameters showed no significant difference between groups.

During the video urodynamic study, no urine leakage while performing the Valsalva maneuver was noted in 20 of 30 patients (66.7%) with nonneurogenic SUI; however, all patients with neurogenic SUI showed urine leakage during the stress test. We compared changes in urodynamic variables between patients with neurogenic and those with nonneurogenic SUI; the change in ALPP after PRP injection in nonneurogenic SUI patients (64.7 ± 65.9 cm H₂O) was greater than that in neurogenic SUI patients (1.0 ± 71.0 cm H₂O) (P = 0.056). The change in the SUI VAS score from baseline to 6 months was 3.0 ± 2.23 in the nonneurogenic SUI group and 2.60 ± 2.07 in the neuro-

Table 2. Treatment outcomes of platelet-rich plasma urethral sphincter injections in different patient subgroups

Variable	Neurogenic ISD (n = 5)	PPI (n = 21)	Cystectomy ISD (n = 6)	Other ISD (n = 3)	Total (n = 35)
Sex, male : female	3 : 2	21 : 0	5 : 1	1 : 2	30 : 5
Age (yr)	51.6 ± 15.4	74.2 ± 7.15	62.4 ± 9.42	67.3 ± 9.45	68.7 ± 2.0
Complete dryness	0	5	1	1	7 (20.0)
GRA = 2	1	8	4	1	14 (40.0)
GRA = 1	2	6	1	1	10 (28.6)
GRA ≤ 0	2	2	0	0	4 (11.4)
Total success rate (GRA ≥ 2)	1/5 (20)	13/21 (61.9)	5/6 (83.3)	2/3 (66.7)	21 (60)

Values are presented as mean ± standard deviation or number (%).

ISD, intrinsic sphincter deficiency; PPI, postprostatectomy incontinence; GRA, Global Response Assessment.

genic SUI group ($P=0.614$). On further analysis of the effect of baseline demographics and urodynamic measures on the treatment outcomes, patients with PPI who had successful treatment outcomes had significantly higher ALPP at baseline (123.0 ± 51.0 cm H₂O) than those with failed treatment outcomes (56.1 ± 20.1 cm H₂O, $P=0.001$).

After the fourth PRP injection, 3 patients were converted to a suburethral sling procedure and 2 received artificial sphincter implantation due to failed outcomes. The other 30 patients were followed up with a stable condition at 6 months after the fourth PRP injection. The median follow-up duration was 13 months (range, 6–24 months). Adverse events following PRP injection

Table 3. Comparison of the baseline parameters between patients with successful and failed treatment outcomes

Variable	Successful outcomes (n = 21)	Failed outcomes (n = 14)	P-value
Age (yr)	71.4 ± 9.0	64.6 ± 14.0	0.104
Sex, male : female	19 : 2	11 : 3	
Neurogenic ISD	1 (20.0)	4 (80.0)	
Nonneurogenic ISD	20 (66.7)	10 (33.3)	
Baseline SUI VAS score	6.14 ± 1.82	7.21 ± 1.89	0.103
CBC (mL)	323.9 ± 118.6	260.6 ± 155.6	0.188
Volume (mL)	254.4 ± 138.4	209.9 ± 136.2	0.360
Qmax (mL/sec)	10.4 ± 5.81	9.29 ± 5.0	0.578
Pdet (cm H ₂ O)	12.1 ± 10.3	15.9 ± 13.6	0.359
PVR (mL)	66.2 ± 113.1	75.7 ± 114.6	0.810
ALPP (cm H ₂ O)	111.0 ± 48.8	83.8 ± 62.5	0.164
BOO index	-8.75 ± 13.1	-2.71 ± 18.2	0.268
MUCP (cm H ₂ O)	36.6 ± 16.8	31.6 ± 15.3	0.433
FPL (mm)	25.9 ± 7.15	26.6 ± 5.80	0.801

Values are presented as mean ± standard deviation or number (%).

ISD, intrinsic sphincter deficiency; SUI, stress urinary incontinence; VAS, visual analogue scale; CBC, cystometric bladder capacity; Qmax, maximum flow rate; Pdet, detrusor pressure; PVR, postvoid residual; ALPP, abdominal leak point pressure; BOO, bladder outlet obstruction; MUCP, maximum urethral closure pressure; FPL, functional profile length.

Table 4. Changes in urodynamic variables from baseline to 3 months after the fourth platelet-rich plasma (PRP) injection

Variable	Baseline	After PRP	P-value
SUI VAS score	6.57 ± 1.89	3.77 ± 2.41	0.001
CBC (mL)	293.6 ± 136.3	315.5 ± 177.1	0.478
Volume (mL)	230.0 ± 134.4	256.1 ± 164.7	0.293
Qmax (mL/sec)	10.0 ± 5.69	10.7 ± 6.04	0.606
Pdet (cm H ₂ O)	13.4 ± 11.9	12.0 ± 11.1	0.503
PVR (mL)	74.2 ± 114.2	68.5 ± 157.9	0.820
ALPP (cm H ₂ O)	98.3 ± 55.8	157.3 ± 79.3	0.000
BOO index	-6.16 ± 15.5	-8.91 ± 14.0	0.338
MUCP (cm H ₂ O)	34.3 ± 16.3	32.5 ± 15.7	0.406
FPL (mm)	26.2 ± 6.59	28.7 ± 7.46	0.037

Values are presented as mean ± standard deviation.

SUI, stress urinary incontinence; VAS, visual analogue scale; CBC, cystometric bladder capacity; Qmax, maximum flow rate; Pdet, detrusor pressure; PVR, postvoid residual; ALPP, abdominal leak point pressure; BOO, bladder outlet obstruction; MUCP, maximum urethral closure pressure; FPL, functional profile length.

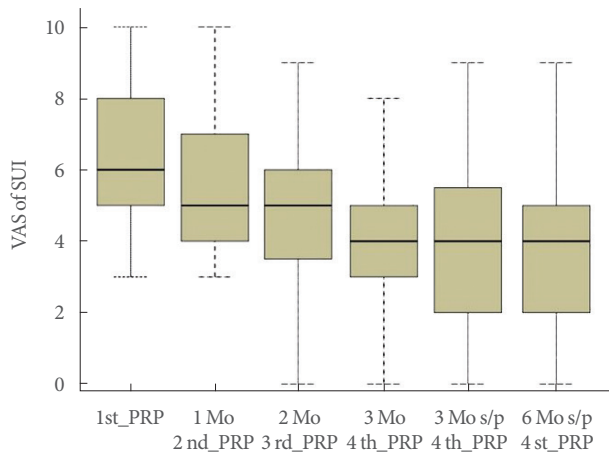


Fig. 2. Changes in visual analogue scale (VAS) score of stress urinary incontinence (SUI) from baseline to the end-point of platelet-rich plasma (PRP) treatment. s/p, status post.

(mild hematuria and pain during micturition) were reported by 10 patients (28.6%). These adverse events resolved after conservative medical treatment. None of the patients developed UTI, difficult urination, or urinary retention after treatment.

DISCUSSION

This is the first study to demonstrate the efficacy of urethral sphincter PRP injections in alleviating SUI in patients with ISD caused by surgical trauma or nonneurogenic diseases. Twenty-one out of 35 patients (60.0%) showed moderate to excellent improvement; among these, 7 (20%) patients became dry after 4 injections of PRP. However, this treatment was not very effective in patients with neurogenic SUI. The therapeutic efficacy lasted for up to 1 year and no severe adverse events were reported.

Since the 1990s, platelet-derived products have been widely used in regenerative medicine. PRP has been applied to hasten healing of macular holes, dental implants, ulcers, burns, bone diseases, as well as for muscle repair and to enhance postoperative tissue recovery [20-22]. In our previous study, PRP injections into the bladder suburothelium were found to decrease tissue inflammation and improve urothelial barrier function in patients with interstitial cystitis [17,18]. Therefore, it is plausible that the deficient urethral sphincter in SUI may regain its innervation or striated muscle cells through repeat PRP injections.

In our study, 4 urethral sphincter injections of PRP effectively alleviated the severity of SUI by 3.0 points on the VAS in patients with nonneurogenic SUI; 66.7% of nonneurogenic patients were satisfied with this treatment. Although only 7 pa-

tients achieved complete dryness after PRP injections, our results demonstrate the efficacy of this novel minimally invasive therapeutic modality for SUI. However, the effects of PRP depend on the release of growth factors from the alpha-granules of platelets [12], as well as on the response of the progenitor cells in the damaged tissue; therefore, patients with neuropathic urethral sphincter deficiency or those with severe intrinsic sphincter damage may not show an adequate response to 4 injections of autologous PRP. Therefore, PRP treatment should not be recommended to patients with severe ISD or neurogenic SUI.

The therapeutic effect of PRP on ISD was demonstrated by both the subjective improvement in symptoms and the objective increase in ALPP and FPL in urodynamic studies. Patients with successful treatment outcomes showed a greater increase in ALPP than those with failed outcomes. Higher ALPP indicates an increase in the urethral resistance, while a longer FPL suggests increased external sphincter volume. Most patients experienced a lesser degree of SUI immediately after the first PRP injection; this was likely attributable to the bulking effect of the injection. However, most patients perceived improvement before the next PRP injection. The wound healing process usually takes 1 month; therefore, an interval of 1 month between successive injections is rational to achieve further improvement in urethral tissue and an increase in urethral resistance.

In this study, the treatment success rate in patients with previous radical cystectomy and neobladder formation was 83.3%. These patients had lost bladder urethral sphincter coordination during bladder storage, and therefore, may experience SUI at an extremely full bladder. PRP injection increases the resistance of the urethral sphincter, and patients were educated to urinate at regular time intervals; this helped to improve the success rate. Among 21 men with radical prostatectomy, the success rate was 60.0%. The only variable associated with successful or failed treatment outcomes was a higher baseline ALPP; this suggests that a higher grade of SUI due to low urethral resistance may result in less effective treatment outcomes in this patient group. However, age and bladder condition were not associated with treatment outcomes.

Patients with SUI due to radical hysterectomy or radical prostatectomy may have detrusor underactivity in addition to ISD [23]. The SUI in these patients can be treated with a suburethral sling or artificial sphincter implantation. However, difficulty urinating might be a *de novo* issue that bothers patients after surgical treatment of SUI [24]. If repeated PRP injections

can improve the degree of SUI, these patients can be adequately treated with a balance between SUI and spontaneous urination. For patients with normal detrusor contractility and ISD, a trial of PRP urethral injection may also be performed prior to conducting a definitive surgical procedure such as a sling or artificial sphincter.

There are several limitations of this study. The first is the small case number and lack of a placebo control arm. However, because this is a proof-of-concept clinical trial, we should determine the safety and efficacy for this novel treatment before further investigation. Second, although this study demonstrated the clinical efficacy of PRP injections for ISD, the underlying mechanism remains to be elucidated. PRP contains several platelet-derived growth factors and cytokines, which promote revascularization, migration of fibroblasts, and regeneration of mesenchymal cells in the striated muscles [25]. In this study, we did not observe an increase in the real urethral sphincter volume after PRP injection; however, there was a significant increase in the ALPP and FPL in patients with nonneurogenic SUI. Further imaging studies or electromyographic studies of the external sphincter may provide evidence of the true effect of PRP on urethral sphincter regeneration.

In conclusion, our results demonstrate the safety and efficacy of repeated urethral sphincter injections of autologous PRP in increasing urethral sphincter resistance and alleviating urinary incontinence in patients with SUI due to ISD. However, patients with neurogenic SUI and those with very low urethral resistance may not be good candidates for this treatment.

SUPPLEMENTARY MATERIALS

Supplementary materials can be found via <https://doi.org/10.5213/inj.2040272.136>.

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AUTHOR CONTRIBUTION STATEMENT

- Conceptualization: HK
- Data curation: HK
- Formal analysis: YJ, PL, HK

- Methodology: YJ
- Project administration: PL
- Visualization: YJ
- Writing-original draft: YJ, PL, HK
- Writing-review & editing: HK

REFERENCES

1. Abrams P, Cardozo L, Fall M, Griffiths D, Rosier P, Ulmsten U, et al. The standardisation of terminology of lower urinary tract function: report from the Standardisation Sub-committee of the International Continence Society. *Neurourol Urodyn* 2002;21:167-78.
2. Radadia KD, Farber NJ, Shinder B, Polotti CF, Milas LJ, Tunuguntla HSGR, et al. Management of postradical prostatectomy urinary incontinence: a review. *Urology* 2018;113:13-9.
3. Myers JB, Mayer EN, Lenherr S; Neurogenic Bladder Research Group (NBRG.org). Management options for sphincteric deficiency in adults with neurogenic bladder. *Transl Androl Urol* 2016;5: 145-57.
4. Lukacz ES, Santiago-Lastra Y, Albo ME, Brubaker L. Urinary incontinence in women: a review. *JAMA* 2017 24;318:1592-604.
5. Kretschmer A, Hübner W, Sandhu JS, Bauer RM. Evaluation and management of postprostatectomy incontinence: a systematic review of current literature. *Eur Urol Focus* 2016;2:245-59.
6. Liu HH, Kuo HC. Durability of retropubic suburethral sling procedure and predictors for successful treatment outcome in women with stress urinary incontinence. *Urology* 2019;131:83-8.
7. Angulo JC, Schönburg S, Giammò A, Abellán FJ, Arance I, Lora D. Systematic review and meta-analysis comparing Adjustable Transobturator Male System (ATOMS) and Adjustable Continence Therapy (ProACT) for male stress incontinence. *PLoS One* 2019; 14:e0225762.
8. Tutolo M, Cornu JN, Bauer RM, Ahyai S, Bozzini G, Heesakkers J, et al. Efficacy and safety of artificial urinary sphincter (AUS): Results of a large multi-institutional cohort of patients with mid-term follow-up. *Neurourol Urodyn* 2019;38:710-8.
9. Kretschmer A, Nitti V. Surgical treatment of male postprostatectomy incontinence: current concepts. *Eur Urol Focus* 2017;3:364-76.
10. Hillary CJ, Roman S, MacNeil S, Aicher WK, Stenzl A, Chapple CR. Regenerative medicine and injection therapies in stress urinary incontinence. *Nat Rev Urol* 2020;17:151-61.
11. Ireneusz O, Emil Ś, Janusz C, Tomasz G, Jakub B, Mikolaj P, et al. Current interventional management of male stress urinary incontinence following urological procedures. *Cent European J Urol* 2015; 68:340-7.

12. Mussano F, Genova T, Munaron L, Petrillo S, Erovigni F, Carossa S. Cytokine, chemokine, and growth factor profile of platelet-rich plasma. *Platelets* 2016;27:467-71.
13. Etulain J. Platelets in wound healing and regenerative medicine. *Platelets* 2018;29:556-8.
14. Roy S, Driggs J, Elgharably H, Biswas S, Findley M, Khanna S, et al. Platelet-rich fibrin matrix improves wound angiogenesis via inducing endothelial cell proliferation. *Wound Repair Regen* 2011;19:753-66.
15. Wu Y, Wang J, Scott PG, Tredget EE. Bone marrow-derived stem cells in wound healing: a review. *Wound Repair Regen* 2007;15(Suppl 1):S18-26.
16. Kuffler DP. Platelet-rich plasma and the elimination of neuropathic pain. *Mol Neurobiol* 2013;48:315-32.
17. Jhang JF, Wu SY, Lin TY, Kuo HC. Repeated intravesical injections of platelet-rich plasma are effective in the treatment of interstitial cystitis: a case control pilot study. *Low Urin Tract Symptoms* 2019;11:O42-7.
18. Jhang JF, Lin TY, Kuo HC. Intravesical injections of platelet-rich plasma is effective and safe in treatment of interstitial cystitis refractory to conventional treatment-A prospective clinical trial. *Neurourol Urodyn* 2019;38:703-9.
19. Jiang YH, Wang CC, Kuo HC. Videourodynamic findings of lower urinary tract dysfunctions in men with persistent storage lower urinary tract symptoms after medical treatment. *PLoS One* 2018;13:e0190704.
20. Liggett PE, Skolik DS, Horio B, Saito Y, Alfaro V, Mieler W. Human autologous serum for the treatment of full-thickness macular holes. A preliminary study. *Ophthalmology* 1995;102:1071-6.
21. Anitua E. Plasma rich in growth factors: preliminary results of use in the preparation of future sites for implants. *Int J Oral Maxillofac Implants* 1999;14:529-35.
22. Burnouf T, Strunk D, Koh MB, Schallmoser K. Human platelet lysate: replacing fetal bovine serum as a gold standard for human cell propagation? *Biomaterials* 2016;76:371-87.
23. Chuang FC, Kuo HC. Management of lower urinary tract dysfunction after radical hysterectomy with or without radiotherapy for uterine cervical cancer. *J Formosan Med Assoc* 2009;108:619-26.
24. Chen CJ, Yeoh SC, Yeh HT, Hsiao SM, Kuo HC, Chen CJ, et al. Surgical results in women with detrusor underactivity and stress urinary incontinence undergoing suburethral sling procedure-Predictive factors for successful outcome. *Low Urin Tract Symptoms* 2020;12:143-9.
25. Chellini F, Tani A, Zecchi-Orlandini S, Sassoli C. Influence of platelet-rich and platelet-poor plasma on endogenous mechanisms of skeletal muscle repair/regeneration. *Int J Mol Sci* 2019;20:683.