

Mixed treatment for same-severe Mixed Urinary Incontinence: a novel method

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Introduction

International continence society defined mixed urinary incontinence (MUI) as “complaint of involuntary loss of urine associated with urgency and also with effort or physical exertion or on sneezing or coughing”., which include both urgency urinary incontinence (UUI) and stress urinary incontinence (SUI) complaints. Urinary incontinence affects social behaviors, financial burden such as using class of drugs, rehabilitation floor muscles, and psychological suffering such as dissatisfaction in sexual activity. Diagnosis of urinary incontinence is based on history, physical examinations and supplemental evaluations like dye test, cystoscopy, urodynamic study, urine analysis, urine culture, and imaging technics. (1)

At the first, conservative treatments are performed for patient such as biofeedback, pelvic floor muscle exercise, electrical stimulation and drug treatment. In the second step of treatment, surgery is considered. The surgery is usually used to address the failure of normal anatomic support of the bladder neck and proximal urethra, and intrinsic sphincter deficiency, meanwhile its implementation should be approached with caution for carefully. In some cases, surgery intervention also failed and other novel interventions should be considered. (2)

Platelet rich fibrin glue, stem cells, butolonium toxins and TVT separately applied for treatment of patients, but this is the first time that these mixed modalities were used for the treatment of mixed urinary incontinence which did not respond to pharmaceutical and surgical treatment.

Case

A 56 years old multiparous female was referred to the clinic with complaint of mixed urinary incontinence for 7 years back. She had 6 normal vaginal delivery and history of disc surgery and Burch colposuspension. She suffered from nocturia and terminal dribbling. She had the history of 6 natural vaginal delivery, spinal surgery on L4 and L5 vertebrae after several years suffering from lumbar discopathy and she had history of surgery on her gallbladder two years before. Oxybutynin and vesicare(Solifenacin Succinate) and amitriptiline were prescribed which no improvement was seen. Pelvic muscle training and biofeedback method were performed followed by anti-incontinence surgery Burch Colposuspension for patient three years ago. These treatments had not any effect on improvement. The patient did not have burning sensation indicative of urinary tract infection, also no flank or supra-pubic pain. Voiding diary showed frequent episodes of incontinence during day and night. In the physical examination, no vaginal prolapse was detected due to previous Burch Colposuspension. kidney Ultrasound evaluation was normal. Urodynamic study showed high pressure intravesical pressure and episodes of urge incontinence and UPP (Urethral pressure profile) exposed sphincter

deficiency. Abdominal leak point pressure (ALPP) was 62 cm H₂O. In cystoscopy, fixed open internal sphincter with normal capacity and moderate trabeculation in the bladder were exposed.

Informed consent was obtained from patient. At the baseline, 1 and 3 months after intervention, the patient were assessed according to cough test, pad test, urodynamic study, upper tract ultrasonography (UTU), uroflowmetry (UFL), post voiding residue (PVR), International Consultation on Incontinence Questionnaire-Urinary incontinence (ICIQ-UI), and International Consultation on Incontinence Modular Questionnaire-Quality of Life (ICIQ-QOL).

For patient, platelet rich plasma-fibrin glue-stem cells injection, butolonium toxins injection and TVT were applied in one session of surgery under general anesthesia and lithotomy position which took 64 minutes.

Preparation of autologous platelets rich plasma-fibrin glue-stem cell :

Sixty milliliters of peripheral blood were taken in 9mL of citrate phosphate dextrose buffer. PRP: blood was centrifugated at 2000 g for 2 minutes, RBC and plasma was separated and plasma was centrifuged at 4000 g for 8 minutes, and the supernatant plasma was separated and 4mL PRP was separated. Fibrin glue (cryoprecipitation method): the supernatant plasma was freeze at -80°C, thawed and centrifuged at 4000 g for 8 minutes. The supernatant plasma was separated to a final volume of 4 mL. Stem cell: hydroxyethyl starch was added to RBC and left for 45 minutes RBC sedimentation. Supernatant was separated, centrifuged 400g about 10 minutes, and supernatant was removed to final 4 ml volume. (3)

Platelets rich plasma-fibrin glue-stem cell and botulinum injection

In operation room, the patient was under general anesthesia and lithotomy position. PRP, Fibrin glue and stem cell were mixed (12 ml) before injection. The transurethral endoscopic injection of PRP-Fibrin glue-stem cell was carried out by a 21-Fr rigid cystoscope. Under endoscopic vision, a puncture needle was passed through the cystoscope into the urethra at the region of the external urethral sphincter and submucosal injections of PRP-Fibrin glue-stem cell was performed. Initially, 8 ml was injected at a depth of 5 mm into the rhabdosphincter. Subsequently, 4 ml was equally injected into the submucosal spaces at 3 and 9 O'clock positions. Hundred unit of botulinum toxin was injected via cystoscope into vesical detrusor.

Tension free Vaginal Tape

Sixty milliliters of Citanest-Adrenalin (0.25%) were injected in the abdominal skin just above the pubis symphysis and retzius space. After 2 cm long transverse skin incision, 40 ml of 0.25% Citanest-Adrenalin was injected into the vaginal wall sub- and paraurethraly. 1.5 cm long incision in the midline starting approximately 0.5 cm from the outer urethral meatus in the vaginal wall. Laterally a blunt dissection 1.0 cm long each side of the urethra. By needle the sling was placed around the urethra: it was inserted into the prepared paraurethral incision on the right side of the urethra. The urogenital diaphragm was perforated and the tip of the needle was brought up to the abdominal incision by 'shaving' the back of the pubic bone. The procedure was then repeated on the left side. When the sling had been placed in a U shape around the midurethra, owing to the strong adhesive forces (friction) around the sling no fixation is necessary. The vaginal incision is then closed. A foley catheter was inserted. One-gram cephalosporin was injected intravenously.

Outcome:

Results:

No complications were observed after injection. After surgery the patient had compression device for 24 hours and then she was motivated to walk gently. Catheter was removed the following day after surgery. Patient was discharged from hospital while is capable to urinate with acceptable post void residue. In this surgery, the utmost effort was done to minimis the vaginal bleeding in order to not apply the vaginal tampon for preventing the damage to stem cells. After 3 month follow up, patient was completely satisfied and her problem was completely sorted out. At the baseline, cough test and pad test were positive; UTU, UFL and PVR were normal; ICIQ-UI and ICIQ-QOL were 21 and 24, respectively. At 1 and 3 months after intervention, cough test and pad test were negative; UTU, UFL and PVR were normal; ICIQ-UI and ICIQ-QOL were 0 and 104.

After the recovery, she was observed one day in female urology ward and next day was discharged with prescription. After 3 months, the incontinency was completely cured and she had not any urinary complaints.

Discussion:

A single modality may be inadequate for treatment of MUI and multiple treatment modalities are required. There is a controversy about the results of pharmaceutical treatment for MUI and surgical treatment is associated with significant failure rates. It is mentioned that applying of anti-incontinence procedures may be effective in treating both the stress and urge components of MUI. (4)

American urology association (AUA) mentioned “the success rate of TVT surgery is between 51% and 87 %” (5). Labire et al (6) expressed that the pharmacological therapy is less effective in comparison to surgery after 12 months. Surgery is done for those patients who deny conservative managements or symptoms have not been improved inadequately. (1) Kulseng-hanssen et,al (7) mentioned “the TVT objective care was 87.3% after 7 months and 82.7 after 38 months. The subjective care was 60 % and 53.8% after 7 and 38 months”.

Botulinum toxin is a neurotoxin which has been used for various clinical applications for many years, and inhibits the release of the neurotransmitter acetylcholine at the presynaptic nerve terminals. Urologists use it for patients with lower urinary tract symptoms secondary to idiopathic overactive bladder (OAB) and also after initial therapeutic modalities have failed to improve symptoms. Intradetrusor botulinum toxin injection has shown to improve urinary urgency, frequency, nocturia, and urgency urinary incontinence. In the other hand, not all patients can achieve excellent therapeutic outcomes which is leakage associated with a rise in abdominal pressure e.g., due to cough, sneeze and exercise (8). Phelan et al reported that after injection, 67% of patients were able to void smoothly with the PVR decreased by 71% and voiding pressure decreased by 38% (9).

For tissue regeneration of muscles; stem cells, PRP and fibrin glue strongly collaborate together to create new blood vessels and capillaries, extracellular matrix through cell proliferation, chemotaxis, cell differentiation, and angiogenesis. PRP provides the best concentration of growth factors (transforming growth factor- β , platelet-derived growth factor, insulin-like growth factor, fibroblast growth factor, epidermal growth factor, vascular endothelial growth factor, and endothelial cell growth) and bioactive factors (serotonin, histamine, dopamine, calcium, and adenosine). These factors lead to wound healing events by modulating the recruitment, duplication, activation, and differentiation. FG creates a temporary matrix and stimulating the local proliferation of fibroblasts, collagen synthesis, new blood vessels formation and connective tissue (3). The malfunction old cells will be replenished by stem cells which these young workers actively collaborate in vascularization and muscle tissue repairmen. In our previous report, peripheral stem cells and PRP are used for treatment of SUI. (10)

In this case report, PRP-Fibrin Glue- Stem Cell injection, Botox injection, and TVT has been used for treatment of MUI. Further research is need to validate the efficacy of these mixed treatments for recalcitrant MUI.

Conclusion: Mix treatment of PRP-Fibrin Glue- Stem Cell injection, Botox injection, and TVT may be a very good approach for treatment of patients with MUI who have a very open sphincter. Further research is need to validate the efficacy of these mixed treatments for recalcitrant MUI.

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Abbreviation:

(MUI): mixed urinary incontinence

(UUI): urgency urinary incontinence

(SUI): stress urinary incontinence

(UTU): upper tract ultrasonography

(UPP): Urethral pressure profile

(PRP): Platelets rich plasma

(TVT): Tension free Vaginal Tape

(UFL): uroflowmetry

(PVR): post voiding residue

(ICIQ-UI): International Consultation on Incontinence Questionnaire-Urinary incontinence **(ICIQ-QOL):** International Consultation on Incontinence Modular Questionnaire-Quality of Life

Authors' contributions:

Author 1: Writing - original draft, Conceptualization, Project administration

Author 2: Conceptualization, Methodology

Author 3: Supervision, Investigation

Author 4: Data curation, Supervision

Author 4: Data curation, Methodology

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