Open Peer Review on Qeios

The Role of Platelet Rich Plasma Injections in Cases of Stress Incontinence

Ahmed Samy Tahoon[1], Hossam El-Din Hussein Salem[1], Assem Anwar Abdo Mousa[1]

1 Al Azhar University

Funding: The author(s) received no specific funding for this work.

Potential competing interests: The author(s) declared that no potential competing interests exist.

Abstract

Background: Stress urinary incontinence is extremely bothersome and can lead to significant interference in the quality of life in the female.

Aim of the Work: to assess the role of platelet-rich plasma in treatment of Stress urinary incontinence as a non-invasive method.

Patients and Methods: Prospective Interventional study was conducted on 20 patients attended the clinic or were admitted and seeking treatment for urinary stress incontinence, the study was carried out at Sayed Galal hospital.

Results: Among the 20 patients enrolled, Treatment efficacy assessed by International Consultation on Incontinence Questionnaire-Short Form, Urogenital Distress Inventory, Incontinence Impact Questionnaire and Overactive Bladder Symptom Scores showed significant incontinence improvement at both 1 month and 3 months post treatment.

Conclusion: Local injection of autologous platelet rich plasma is an effective, affordable, minimally invasive procedure, safe with somewhat satisfactory response in treating female SUI.

Recommendations: PRP is a safe, effective, and noninvasive technique as a line for treating women with SUI.

Ahmed Samy Tahoon[1], Hossam El-Din Hussein Salem[1], Assem Anwar Abdo Mousa[1].

[1]Department of Obstetrics and Gynecology, Faculty of Medicine, Al Azhar University

Corresponding author:

Ahmed Samy Tahoon

Mobile: 01010111841

Email: dactara90@yahoo.com

Key words: platelet-rich plasma; stress urinary incontinence; noninvasive technique.

Introduction

Urinary incontinence can impact on one's social, physical, mental and sexual wellbeing, and lead to depression and

social isolation (A.J. Sinclair, et al; 2011).

Stress urinary incontinence (SUI) refers to the involuntary leakage of urine accompanying physical exertion (i.e. coughing, exercise, and sneezing). It is commonly acquired after pregnancy and childbirth due to weakening of the pelvic floor muscles that support the urethra against the anterior vaginal wall (B.S. Buckley, et al; 2010).

Current SUI treatment includes surgery to re-establish sufficient urethral resistance in order to prevent urine leakage during increased intra-abdominal pressure (J. Han, et al; 2012).

The mid-urethral sling (MUS) has become the preferred procedure, as it is less invasive than the Burch colposuspension. However, the MUS procedure has a 5–20% failure rate and carries risks such as infection, voiding dysfunction, hemorrhage, pain, bladder or urethral injury, and mesh erosion (V.W. Nitti, et al; 2012).

Hence, there is a need for alternative efficacious, outpatient SUI treatments.

Platelet-derived therapies are a growing trend across multiple medical and surgical specialties. Evidence suggests that platelets play an important role in tissue repair, vascular remodeling and inflammatory and immune responses through secretion of growth factors, cytokines and chemokines (Banihashemi M, et al; 2014).These biologically active proteins include transforming growth factor-β, platelet-derived growth factor, platelet-derived epithelial growth factor, insulin-like growth factor, vascular endothelial growth factor. These growth factors are implicated in many aspects of natural wound healing, including chemotaxis, cell proliferation, and cell differentiation. The key role of platelets in these processes makes them an attractive candidate for therapies aimed at accelerating natural healing (Runels C, et al; 2014).

One of the most well described platelet-based therapies is autologous platelet-rich plasma (PRP). PRP is derived from the centrifugation of whole blood with a separator gel to remove the red and white blood cells. The resulting supernatant has a greater than four-fold increase in platelets and other plasma proteins. This concentrate is then administered via injection (Maher CF, et al; 2005).

Aim of the Work

To assess the role of platelet-rich plasma in treatment of SUI as a non-invasive method.

Patients and Methods

Study design: Prospective Interventional (Clinical Trial).

Study setting: The study was carried out at Sayed Galal hospital.

Study duration: One year (February 2021- January 2022).

Study population: The study included 20 patients attending the clinic or were admitted and seeking treatment for urinary stress incontinence.

Inclusion criteria: Female patient with mild to moderate SUI above 35 years old.

Exclusion criteria:

- Under anti-platelet agent treatment
- Platelet dysfunction syndrome
- Critical thrombocytopenia

- Acute and chronic infections
- Anti-coagulation therapy
- History of malignancy

Detailed Description:

A total number of 20 consecutive patients consented to enter the trial with full awareness of the experimental nature and treatment process without compensations in any form.

All patients work up:

- Detailed history
  - Personal history (Name, Age)
  - Present history.
  - Obstetric history (Number of parity, Mode of delivery)
  - Medical history (Any chronic disease)
  - Surgical history (Any surgery such as: Hysterectomy)
  - Allergic history.
  - Drug usage.
- Complete physical examination
  - General examination (including height, weight and BMI)
  - Abdominal examination (including scar of any operation)
  - Local examination (inspection, vaginal examination, speculum and bimanual examination)
- Investigation (CBC, urine analysis, urine C&S, LFT, KFT,U/S and urodynamicss)
- Questionnaires (International Consultation on Incontinence Questionnaire-Short Form, Urogenital Distress Inventory, Incontinence Impact Questionnaire, Overactive Bladder Symptom Scores and Female Sexual Function Index)

Equipment's used for the procedure include

- 5 cc syringes, Centrifuge
- 30 G ½ needles,
- Golden VAC PRP tube with separator gel,
- Numbing cream (topic anesthesia).

Technique

The study employed commercialized PRP kit (golden VAC),PRP was prepared according to the standardized procedures instructed by the kit. The tube was used to collect individual patient's whole blood, 15 cc blood sample was aspirated from the patient's peripheral vein in vacuum collection tube with separator gel, which is centrifuged separating red and white cells at 3000 RPM for 10 minutes. Platelet cells were on top of the tube and the 4 cc of cells suspension are called Platelet Rich Plasma.

The patients were placed in a dorsal lithotomy position then disinfection was applied with betadine at the sites of injections. Approximately 5 minutes before the procedure a topical anesthetic was applied in the anterior vaginal wall covering the urethral meatus, paraurethral, suburethral, and lateral urethrovaginal areas.

After isolation of the PRP injection by a 5 cc syringe with 30 G needle into anterior vaginal wall, near external urethral sphincter. While performing the maneuvers and 24 hours after the ending, patients were evaluated for pain using the visual analog scale (VAS) and numerical rating scale (NRS) for assessing pain intensity.

There were no adverse effects or complications associated with the procedures. The assessment of pain was negative, none of the patients complain of pain during the procedure or up to 24 hours after it. Clinical examination after treatment revealed no functional alterations or hypertrophic scarring. The average procedure time was 15 minutes and no prophylaxis antibiotics were used.

Data Analysis

Data were collected, recorded, coded, organized and then entered to a Microsoft Excel sheet then analyzed to give final study results using the IBM Corp. Released 2013. IBM Statistical Package for Social Sciences (SPSS) Statistics, Version 28th (2021).

Normally distributed continuous data was expressed as mean + standard deviation. Categorical data was displayed as frequency and percentage. Data were presented as tables and graphs.

Statistical analysis was performed using Student's t-test and paired t-test.

Results were considered statistically significant at a p-value of less than 0.05.

Ethical Considerations

1. Approval of faculty's ethical committee:

   This study was only carried out after getting approval of the ethical committee in Faculty of Medicine, Al Azhar University as the study aims, methodology and measurements were politically accepted and also to facilitate any problem.
2. Socially acceptable methodology and measurements.
3. Confidentiality of the collected data:
   - Only for research use.
   - No other tests or DNA analysis were done by serum samples.
   - Serum samples were discarded at the end of research.
4. Good communication channel between researchers and target population.
5. Acceptance of all the participants was obtained by written informed consent in an easy understandable language.

Result

Among the 20 patients enrolled, the average age was 48.65 years old with averaged parity of 4.65 times, body mass index 29.4 mg/m2.

Treatment efficacy assessed by International Consultation on Incontinence Questionnaire-Short Form, Urogenital Distress

Inventory , Incontinence Impact Questionnaire and Overactive Bladder Symptom Scores showed significant incontinence improvement at both 1 month and 3 months post treatment (Table 1).

Table 1 - Questionnaire results at baseline and 1, 6 months post-treatment.

N = 20	Baseline	1 months post-Tx	3 months post-Tx	P value*	
				1 month	3 month
ICIQ-SF	12 ± 2.9	7 ± 1.8	5 ± 1.4	0.012*	0.002*
UDI-6	35 ± 6.9	24 ± 5.3	16 ± 4.6	0.005*	0.004*
IIQ-7	24 ± 5.3	12 ± 2.9	10 ± 1.3	0.001*	0.016*
OABSS	6 ± 1.2	3 ± 0.5	4 ± 0.5	0.034*	0.044*

Changes in grades of SUI following treatment of PRP injection were shown in Fig. 1.

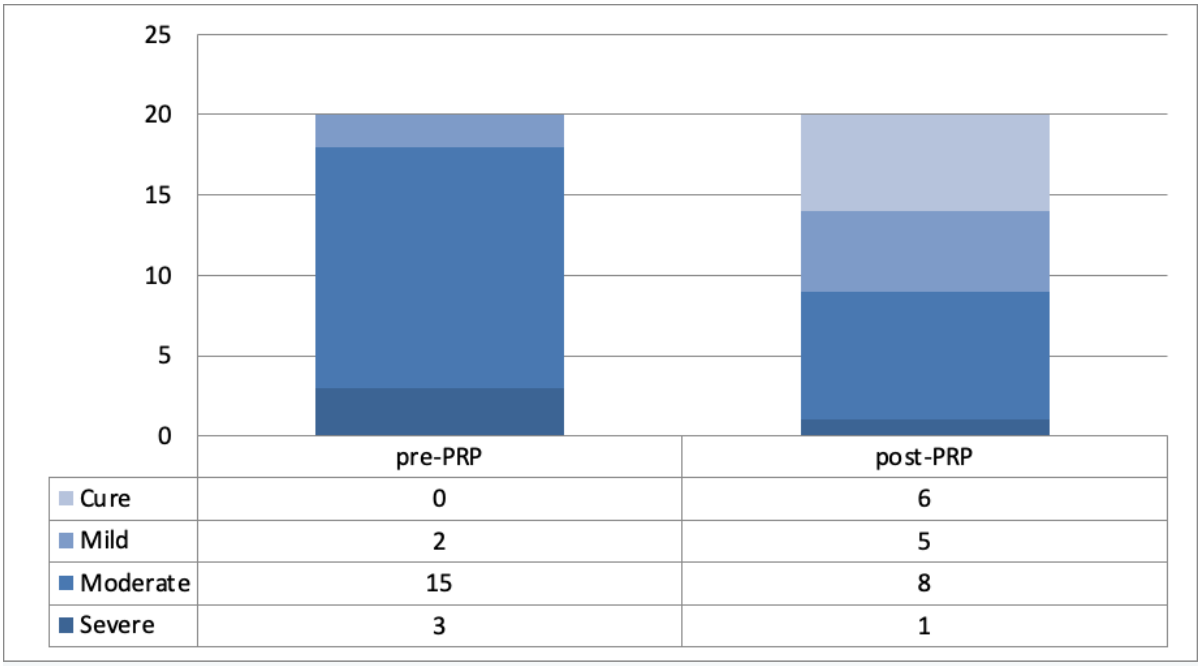

Figure 1 - Changes in grades of stress urinary incontinence following treatment of PRP injection.

However, it seems to have a trend that treatment success rate with cured and improved symptoms was slightly higher in the younger group (70%) compared to that of the older group (60%), although it did not reach statistical significance (P=0.07).

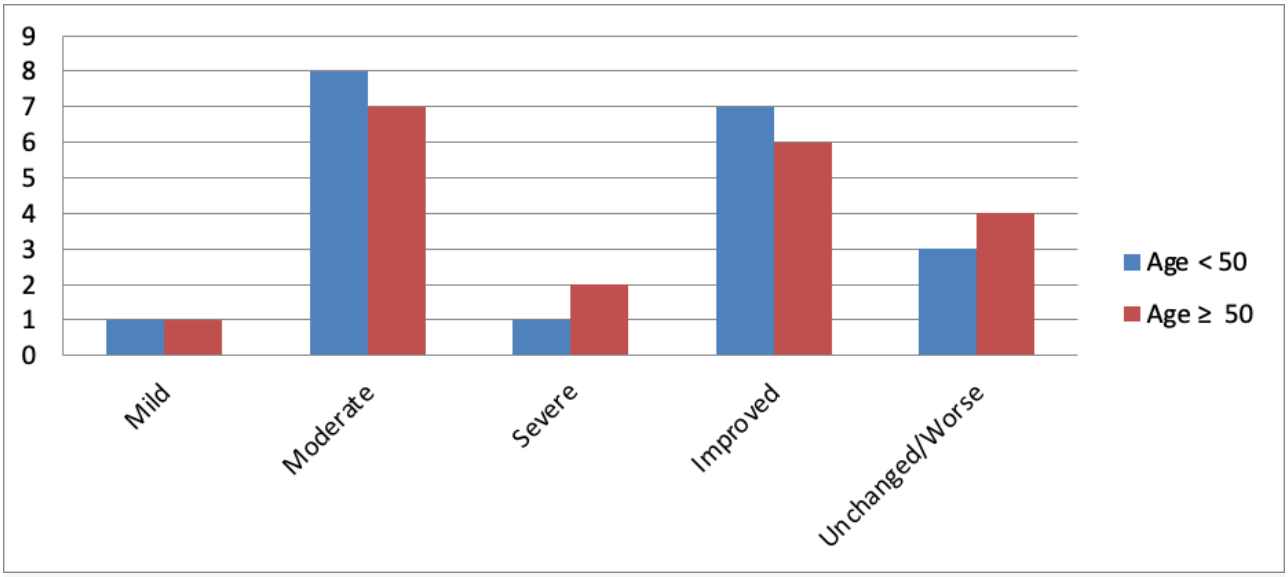

Figure 2 - Changes in grades of stress urinary incontinence following treatment of PRP injection with patients' age.

The treatment efficacy is also demonstrated by disease severity distribution pre-PRP and 3 months post-PRP (Table 2), with a shift of the majority reporting moderate and severe diseases to moderate and milder diseases.

Table 2 - Treatment efficacy of PRP injection.

Pre-op	Post-op						
	Cure	Mild	Moderate	Severe	Improved	Unchanged/Worse	Efficacy
Mild(n=2)	2	0	0	0	2	0	100%
Moderate (n=15)	4	5	6	0	9	6	60%
Severe (n=3)	0	0	2	1	2	1	66.6%
All(n=20)	6	5	8	1	13	7	65%

The influence of PRP injection on sexual function was investigated by Female Sexual Function Index (FSFI) questionnaire.

No significant changes before and after the treatment were reported by the patients. (Table 3).

Table 3 - Changes Female Sexual Function Index (FSFI) scores at baseline and 3 months post-treatment with PRP injection.

	Pre-treatment	3 months post-treatment	P value
Desire	2.7±1.3	3.9±2.4	0.79
Arousal	2.6±1.8	2.9±0.9	0.46
Lubrication	3.2±2.1	3.5±2.1	0.34
Orgasm	3.0±1.9	3.4±2.1	0.35
Satisfaction	3.2±2.0	3.8±2.3	0.13
Pain	3.2±2.0	3.9±2.4	0.11
FSFI total scores	17.9±10.2	20.3±11.0	0.25

Discussion

Urinary incontinence can impact on one's social, physical, mental and sexual wellbeing, and lead to depression and social isolation (A.J. Sinclair, et al; 2011).Stress urinary incontinence (SUI) refers to the involuntary leakage of urine accompanying physical exertion (i.e. coughing, exercise, and sneezing). It is commonly acquired due to weakening of the pelvic floor muscles that support the urethra against the anterior vaginal wall (B.S. Buckley, et al; 2010).

Platelet-derived therapies are a growing trend across multiple medical and surgical specialties. Evidence suggests that platelets play an important role in tissue repair, vascular remodeling and inflammatory and immune responses through secretion of growth factors, cytokines and chemokines (Banihashemi M, et al; 2014).

One of the most well described platelet-based therapies is autologous platelet-rich plasma.

This study aims to assess the role of platelet-rich plasma in treatment of SUI as a non-invasive method.

The current study demonstrates A-PRP is effective in treating women with SUI for as long as 3 months post treatment.

Among the 20 patients enrolled, the average age was 48.65 years old with averaged parity of 4.65 times, body mass index 29.4 mg/m2.

Primary end-point is the change of the objective assessment of urinary incontinence severity by visual analog scale.

Secondary end-points include:

1. Net change of daily pad use.
2. Net change of the following parameters from baseline to 3 months after the treatment day: maximum flow rate; residual urine; first sensation to void; maximum cystometric capacity and detrusor pressure at peak flow.
3. International Consultation on Incontinence Questionnaire-Short Form, Urogenital Distress Inventory, Incontinence Impact Questionnaire, Overactive Bladder Symptom Scores and Female Sexual Function Index are the questionnaires used to assess the impact of urinary incontinence on the quality of life from baseline to 1 and 3 months after the treatment day.

Prior to the PRP treatment, the average pad test was 5.35 g. Two patient (10%) reported mild symptom while 15 patient (75%) and 3 patient (15%) reported moderate and severe diseases, respectively by International Consultation on Incontinence Questionnaire-Short Form score.

After the PRP treatment, the average pad test was 2.55 g; 6 patient (30%) cured, 5 patient (25%) reported mild symptom while 8 (40%) reported moderate and only one patient (5%) severe diseases, by (ICIQ-SF) score.

Treatment efficacy assessed by ICIQ-SF, UDI, IIQ and OABSS showed significant incontinence improvement at both 1 month and 3 months post treatment.

The mean value of ICIQ-SF before treatment was 12 and 3 months post treatment was 5; with significant change (p value 0.002), Improvement occurred in 13 patients with no change in 7 patients.

A secondary analysis of this study observed a superior treatment outcome in the patient group younger than 50 years old. However, it seems to have a trend that treatment success rate with cured and improved symptoms was slightly higher in the younger group (70%) compared to that of the older group (60%), although it did not reach statistical significance (P=0.07). It is postulated that being younger might pose better rejuvenating abilities, and thus better treatment effect of A-PRP.

Also, aged patients are likely to be impacted with additional variables such as menopausal state, more severe SUI symptoms and more underlying systemic conditions such as diabetes mellitus, hypertension, and history of hysterectomy, abdominal surgeries and previous anti-continence treatments.

These potential confounding factors are demonstrated by a trend in our small study groups, although not reaching statistical significance.

Further study with greater patient number and variable-adjusted analysis is required to validate the assertion. If proven, these factors would be very helpful for patient selection that will benefit the most from PRP treatment.

Sexual function is intimately related to urinary incontinence, thus warranting a secondary analysis in the treatment of SUI with A-PRP.

The current study utilizes FSFI questionnaires pre- and post-PRP treatment but failed to reveal significantly improved composite sexual function score, regardless the length of follow up.

The mean value of FSFI before treatment was 17.9 and 3 months post-treatment was 20.3; with a non-significant change (p value 0.25).

Stress urinary incontinence impacts the patient's self-image, confidence and fear of embarrassment when it comes to sexual functions. Therefore, an improvement in SUI symptoms readily enhances sexual desire. Interestingly, our finding is in contrary to that.

The results of this study are in agreement with those of (João Brito Jaenisch Neto, et al) which measure the response of women with stress incontinence, overactive bladder, lubrication and sexual dysfunction (libido, arousal, dyspareunia) to evaluate the safety, tolerability and clinical efficacy of "O-Shot" Platelets Rich Plasma (PRP) of the vulvo vaginal field.

The Results of this study show that about sixty-eight women in the age ranging from 32 to 97 (average: 62.8 years old) were enrolled in this study. Of the sixty-eight patients, 94% of them were satisfied, only 6% of them with overactive bladder did not have any improvement with this treatment.

And this study demonstrates that Platelet Rich Plasma, "O-Shot" is an office treatment that is safe, effective, non-surgical, and non-hormonal option for women having stress incontinence, overactive bladder, lack of lubrication, and sexual dysfunction, such as lack of libido, arousal or dyspareunia. The advantage of this study is more than 90% of patients complaining from stress urinary incontinence improved.

Similar to this study, Ariel Luksenburg, Juan J. Barcia, Roberto Sergio, et al studied "Stress Urinary Incontinence: Treatment with Platelet-Rich-Plasma Injection and Placement of Polydioxanone Threads" A total of 23 patients with mild

urinary incontinence, mean age 46, were evaluated with detailed history, examination, urinary diary, complete laboratory tests, ultrasonography, urodynamics studies, and completion of International Consultation on Incontinence Questionnaire Short Form. Under local anesthesia, PRP was injected through the anterior vaginal wall, PDO threads placed in paraurethral, suburethral, and lateral urethrovaginal spaces, using instruments developed for safe and effective performance. Patients were analyzed at 1, 2, 4, 8 weeks and 6 months posttreatment. A total of 10 patients were biopsied preoperatively and 60 days after treatment.

Symptoms and ICIQ-UI SF score were significantly improved. Postoperative urodynamics studies were normal in all cases.

Biopsies after treatment showed a dense connective tissue tridimensional mesh. The minimally invasive technique presented here results in strengthening of the paraurethral, suburethral, and lateral urethrovaginal spaces and the mucosa of the anterior vaginal wall. The combination of PRP injections and the placement of PDO threads creates a fibrotic and absorbable mesh-like structure, aimed to increase the urethral resistance, so that under effort the intravesical pressure does not overcome the urethral pressure.

Unlike the current study, Charles Runels, Hugh Melnick, et al. examined the Effect of Localized Injections of Autologous Platelet Rich Plasma (PRP) for the Treatment of Female Sexual Dysfunction. Its report demonstrate significantly improved FSFI performance in total scores, desire, arousal, lubrication and orgasm in women receiving PRP injection for sexual disorders. The authors also reported prolonged arousal, ejaculatory orgasm, and spontaneous orgasm in younger women as side effects that resolve in 2 weeks without treatment.

The observation is not revealed by our study that aimed at treating urinary incontinence, which is mainly attributed to disparity in injection sites.

Runels' group, who specifically aimed at treating sexual dysfunctions, injected A-PRP at both clitoris and a spot of anterior vaginal wall.

Conclusion

Local injection of autologous platelet rich plasma is an effective, affordable, minimally invasive procedure, safe with somewhat satisfactory response in treating female SUI.

Until now, how long the treatment effect could sustain remains unknown!

Recommendations

PRP is a safe, effective, and noninvasive technique as a line for treating women with SUI.

Follow up for those patients to detect the time validity of the treatment and if re-injection is recommended.

References

- A.J. Sinclair, I.N. Ramsay. *The psychosocial impact of urinary incontinence in women*. The Obstetrician & Gynaecologist. 2011;13:143–148.
- Alves, Rubina MD; Grimalt, Ramon MD, PhD. *Randomized Placebo-Controlled, Double-Blind, Half-Head Study to*

Assess the Efficacy of Platelet-Rich Plasma on the Treatment of Androgenetic Alopecia. Dermatologic Surgery: April 2016 - Volume 42 - Issue 4 - p 491-497 doi:10.1097/DSS.0000000000000665.

- Alves R, Grimalt R. *A Review of Platelet-Rich Plasma: History, Biology, Mechanism of Action, and Classification* Skin Appendage Disord. 2018;4:18-24. doi:10.1159/000477353.
- Andia E, Rubio-Azpeitia J, Martin I, Abate M. *Current concepts and translational uses of platelet rich plasma biotechnology*. In Ekinci D (ed.): Biotechnology. InTech, 2015, doi10.5772/59954.
- Anitua E, Sánchez M, Orive G. *The importance of understanding what is platelet-rich growth factor (PRGF) and what is not*. J Shoulder Elbow Surg 2011;20:e23–e24.
- Arshdeep, Kumaran MS. *Platelet-rich plasma in dermatology: boon or a bane?*Indian J Dermatol Venereol Leprol 2014;80:5–14.
- Azam U, Frazer MI, Kozman EL, Ward K, Hilton P, Rane A.*The tension-free vaginal tape procedure in women with previous failed stress incontinence surgery*. J Urol 2001; 166:554-556.
- B.S. Buckley, M.C. Lapitan. *Prevalence of urinary incontinence in men, women, and children-current evidence: findings of the fourth international consultation on incontinence*. Urology, 76 (2010), pp. 265-270.
- Banihashemi M, Nakhaeizadeh S. (2014). *An introduction to application, of PRP in skin rejuvenation* Rev Clin Med 1: 38-43.
- Bright E, Drake MJ, Abrams P. *Urinary diaries: evidence for the development and validation of diary content, format, and duration*. Neurourol Urodyn 2011; 30(3):348-352.
- Brown JS, Wing R, Barrett-Connor E, Nyberg LM, Kusek JW, Orchard TJ, Ma Y, Vittinghoff E, Kanaya AM*Lifestyle intervention is associated with lower prevalence of urinary incontinence: the Diabetes Prevention Program*. Diabetes Care 2006; 29:385-390.
- Busby G, Broome J. *Necrotising fasciitis following unrecognised bladder injury during transobturator sling procedure* BJOG 2007; 114:111-112.
- Castro RA, Arruda RM, Zanetti MR, Santos PD, Sartori MG, Girao MJ.*Single-blind, randomized, controlled trial of pelvic floor muscle training, electrical stimulation, vaginal cones, and no active treatment in the management of stress urinary incontinence*. Clinics (Sao Paulo) 2008; 63:465-472.
- Cheng M., Johnson V. M., Murray M. M.*Effects of age and platelet-rich plasma on ACL cell viability and collagen gene expression*. J Orthop Res. 2012;30:79–85.
- Conde Montero E, Fernández Santos ME, Suárez Fernández R. (2015).*Platelet-Rich Plasma: Applications in Dermatology*. Actas Dermo-Sifiliográficas Engl Ed. 106:104–111. doi:10.1016/j.adengl.2014.12.009
- G. Isom-Batz, P. E. Zimmern. (2009). *Collagen injection for female urinary incontinence after urethral or periurethral surgery*. J Urol. 181:701–704. doi:10.1016/j.juro.2008.10.027.
- J. Han, K. Lee, M. Choo. *Management of Recurrent or Persistent Stress Urinary Incontinence after Mid-urethral Sling* LUTS, 4 (2012), pp. 95-100.
- Maher CF, O'Reilly BA, Dwyer PL, Carey MP, Cornish A, Schluter P.*Pubovaginal sling versus transurethral Macroplastique for stress urinary incontinence and intrinsic sphincter deficiency: a prospective randomised controlled trial*. BJOG 2005;112:797-801.

- Palma P, Riccetto C, Fraga R, Portugal S, Dambros M, Rincón ME, Silveira A, Netto NR Jr.*Three dimensional anatomy and virtual surgery for transobturator approach*. Actas Urol Esp. 2007;31(4):361–5.
- Petros PE, Swash M. *The musculo-elastic theory of anorectal function and dysfunction* Pelviperineology. 2008;27:89–93.
- Runels C, Melnick H, Debourbon E, Roy L. (2014).*A pilot study of the effect of localized injections of autologous Platelet Rich Plasma (PRP) for the treatment of female sexual dysfunction*. J Womens Health 3: 169.
- V.W. Nitti. *Complications of midurethral slings and their management* Can Urol Assoc J, 6 (2012) pp. 120-122.
- Wroblewski AP, Melia HJ, Wright VJ. *Application of Platelet-Rich Plasma to Enhance Tissue Repair* Oper Tech Orthop 2010;20:98– 105.
- Yadav C., Meherda M., Kothiwala R., et al. (2017).*A comparative study of efficacy of micro-needling alone versus micro-needling with autologous platelet rich plasma in facial atrophic acne scars*. IMJ Health 3:268-274.
- Zumbe J, Porres D, Degiorgis PL, Wyler S.*Obturator and thigh abscess after transobturator tape implantation for stress urinary incontinence*. Urol Int 2008; 81:483-485.