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ORIGINAL ARTICLE

The efficacy and feasibility of fractional CO_2 laser therapy for the treatment of urinary incontinence: a multicentric case-control study

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ABSTRACT

BACKGROUND: Female urinary incontinence is a significant public health problem. Conservative treatments require high patient compliance, while surgery often leads to more complications and recovery time. Our aim is to evaluate the efficacy of microablative fractional CO_2 laser (CO_2-laser) therapy in women with urinary incontinence (UI).

METHODS: This is a retrospective analysis of prospectively collected data on women with stress urinary incontinence (SUI) and mixed urinary incontinence (MUI) with predominant SUI subjected to four sessions of CO_2-laser therapy performed once a month, between February 2017 and October 2017, with a 12-month follow-up. The subjective Visual Analogue Scale (VAS) 0-10 was used to score and variables were evaluated at baseline and at one, six and 12 months after initiation of therapy. Finally, results were compared to a control group.

RESULTS: The cohort consisted of 42 women. The proportion of patients with vaginal atrophy among those younger than 55 years was substantially lower (3/23; 13%) than among those older than 55 years (15/19; 78.9%). CO_2 laser treatment was associated with a significant improvement in VAS scores recorded one-month, six-months, and one-year, after conclusion of therapy ($P<0.001$). VAS scores improved significantly in patients with either SUI (26/42; 61.9%) or mixed UI (16/42; 38.1%). No major post treatment complications were registered. Women with vaginal atrophy demonstrated significantly better results ($P<0.001$).

CONCLUSIONS: Results confirm the efficacy and a good safety profile, for CO_2 laser treatment in SUI, mostly in women with postmenopausal vaginal atrophy and should be considered as a treatment option for female patients with concomitant SUI and vaginal atrophy.

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KEY WORDS: Urinary incontinence; Laser therapy; Atrophy; Urinary incontinence, stress; Urinary tract.

Female stress urinary incontinence (SUI) is a significant public health problem, with estimated prevalence rates of 4-35% of adult women, with a considerable social impact that affects millions of women worldwide.[1, 2]

It is related to pelvic floor dysfunction and is caused by relaxation of the anatomical structure that supports the periurethral tissue and impairment of the urethral sphincter, which is responsible for intrinsic and extrinsic continence. This relaxation is caused by hormonal deprivation that impedes collagen production and depletes collagen reserve, resulting in a weakened urogenital tract.[3]

The conservative treatment, as International Continence Society Recommendations indicates, should be the first approach for SUI and includes lifestyle changes as a weight loss if indicated, pelvic floor muscle training considered the standard of care for mild UI,[4] bladder training, electrical stimulation, pharmacotherapy and a combinations of these individual therapies.[5, 6]

However, these strategies require a high patient compliance, thus, even if surgery is more invasive including complications and recovery time, it still remains a more attractive and useful option for the treatment of SUI.[5, 7, 8]

Because of surgical procedures can be associated to adverse and severe events with a rate from 2% to 12% of cases according to the literature,[7, 9] scientific and technological progress has led to better clinical outcomes with less invasive procedures, preserving this type of treatment only when conservative treatment fails.[5] In this sense, recent evidence supports laser treatment as an alternative and effective intervention for SUI.[10]

In fact, in the last decade, the medical use of thermal energy was introduced as a promising alternative potential strategy for the treatment of SUI and genito-urinary syndrome of menopause (GSM) and during puerperium and breastfeeding.[11-15] Some studies have adopted laser therapy for SUI based on the notion that the laser-mediated heating of the pelvic floor tissue could improve the support structures, ensure that the tension developed by the active contraction of the pelvic floor muscles (PFM) is smoothly transmitted, and represent an effective non-surgical method for treating female SUI and other disorders resulting from diminished pelvic floor support,[16] reporting also a beneficial effect on pelvic organ prolapse (POP).[17]

According to literature data the beneficial effect of laser therapy in postmenopausal women with GSM has been amply provided (significant improvement in dyspareunia, dryness, burning, itching, dysuria, urgency, urinary symptoms and decreased UI scores), confirming that laser treatment is a good, painless outpatient procedure with no side effects in postmenopausal women.[15, 18-21] Erbium YAG (Er:YAG) laser has been more widely studied for SUI.[6, 16, 22-32]

Nalewczynska *et al.* and Isaza *et al.* reported about the application of CO_2 laser and provided evidence that Laser CO_2 therapy can be a valid alternative treatment in women with SUI. In addition, no major adverse events were observed throughout the course of laser treatment and the follow-up period, with an improvement rates ranging from 62% to 78%.[6, 33, 34]

In view of this, we analyzed 42 women with the main aim to present the evidence-based subjective and objective medical data computed after transvaginal thermo-ablative fractional CO_2 laser treatment in women with SUI treated in an outpatient setting; secondary aims are to collect possible adverse events and the positive effect of laser CO_2 on vaginal atrophy.

Materials and methods

We performed a retrospective analysis of prospectively collected data on women with SUI or mixed UI (MUI) who were subjected to four of CO_2-laser therapy sessions, once a month for four months and had 12 months minimum follow-up, was undertaken. The study was approved by local research board (IRB).

Women with primary SUI or MUI with SUI predominance who met the inclusion criteria were enrolled. Patients underwent microablative fractional CO_2 laser procedures between February 2017 to October 2017 at the Departments of Gynecology of University Campus Bio-Medico, via Alvaro del Portillo 200, Rome and Department of Gynecology San Raffaele Hospital in Milan. All participants signed informed consent forms.

Inclusion criteria included: a normal citology, age >18 years, presence of involuntary loss of urine due to any events which put pressure on bladder (coughing, laughing, sneezing, running, heavy lifting) or mixed urinary incontinence (stress and urgency), Eastern Cooperative Oncology Group performance status <2 and a negative urine culture.

Exclusion criteria included: age younger than 18 years old or older than 75, pregnancy, symptomatic genital or urinary infections, hematuria, presence of abscess, fistula, or any anatomical abnormality that could interfere with

treatment, use of local therapy 15 days prior to enrolment, prolapse stage higher than 2 according to the Pelvic Organ Prolapse Quantification System (Baden-Walker grading system), stenosis, trauma or necrosis of the urethra; alcohol or drug addictions, uncontrolled psychiatric disorders and Eastern Cooperative Oncology Group performance status (ECOG)[35] of more than two. Intravaginal Laser CO_2 applications were instituted once a month for four consecutive months. Women then underwent periodic checks one, six and 12 after the initiation of treatment.

Pre-treatment evaluation included medical history, menopausal status, gynecological examination with assessment of vaginal atrophy, urodynamic testing (included post-void residual volume, uroflowmetry, cystometry) repeats after 12 months and cough stress test repeated after 6 months. The subjective Visual Analogue Scale 0-10 (VAS) was used to score for the presence and the degree of SUI: scoring from 0 (no discomfort) to 10 (maximum discomfort), vaginal atrophy was analyzed with the Vaginal Health Index Score (VHI) through 5 parameters: vaginal elasticity, vaginal secretions, pH, epithelial mucous membrane, vaginal hydration; these scores were used at the beginning of treatment (before first session), and if the VHI<15 patient was affected also by vaginal atrophy. At the end of entire treatment patients repeated the urodynamic testing and cough stress test and completed also the questionnaire of QoL (EORTC QLQ – CX24).

The presence or absence of adverse events was noted. The nature of study was retrospective and all the procedures being performed were part of the routine care. We also retrospectively compared results of this group of patients with a control group in which patients were underwent to the standard treatment of pelvic floor muscle training. This treatment was recommended for 2 consecutive months (once weekly session for a total of 8 sessions) and finally we asked to patients to perform regular pelvic floor exercises at home during the follow-up period.

The side effects were evaluated as a pain greater than VAS>6 during the treatment, a deterioration in urinary function after and during the treatment, and/or the presence of vaginal or vulvar abrasions or ulcerations after the laser treatment.

Microablative fractional CO_2 laser procedure

CO2 laser system MonaLisa Touch (SmartXide2V2LR, Deka m.e.l.a., Florence, Italy) was used with a vulvovaginal Laser Reshaping (V2LR) scanning system and appropriate hand pieces for the vaginal area. Patients were treated with a 360° vaginal probe, in order to cover all the vaginal canal, once a month for four consecutive months.

Our group, according to bio-engineer, has applicated a protocol with power 40 watts, scan time 1000ms, spacing 1000mm, smart stack 1 (the same protocol for vaginal atrophy), re-treated along the entire anterior wall of the vagina with a 90° vaginal probe to reinforce the effect of treatment on the peri-urethral tissue with the same protocol as before but with smart stack 2 in order to have a deeper effect in the tissue in the anterior wall.

Every pulse consisted of constant high-energy peak power to produce rapid micro-ablation of the epithelial component of the mucosa followed by longer emission times that allow the CO_2 laser to penetrate further into the mucosa. The pulses were distributed over the vaginal wall and spaced (DOT spacing) to cover the entire treatment area. To treat the vaginal area completely, many laser spots were emitted while progressively extracting the hand-piece from the vaginal fundus followed by another treatment of the anterior vaginal wall as described.

During all treatment sessions, the following two-phase protocol was followed; initial positioning of the speculum and observation of the vagina, then careful introduction of the hand-piece deep into the vaginal canal before starting the procedure. Each session took 6 minutes on average. No local therapy was recommended during and after the vaginal laser sessions. The procedure is usually performed in an outpatient setting and does not require any anesthesia. It is recommended to avoid vaginal sexual intercourse for at least 48 hours after the laser application in order to prevent an inflammatory.

Statistical analysis

Categorical variables were reported as frequency and percentage. Continuous variables were evaluated for normal distribution using histogram and reported as median and interquartile range. Association between age and VAS was evaluated using Spearman's rank correlation coefficient. Comparison of VAS between the different time points was performed using Wilcoxon signed-rank test. VAS was compared between patients with and without atrophy and patients with SUI or MUI using Mann-Whitney Test. All statistical tests were two sided and $P<0.05$ was considered as statistically significant. SPSS software was used for all statistical analyses (IBM SPSS Statistics for Windows, Version 26, IBM Corp., Armonk, NY, USA, 2019).

Results

The cohort consisted of a total 42 women referred to University Campus Bio Medico of Rome and San Raffaele Institute in Milan, with a median age of 55.9 years (interquartile range (IQR) 49 to 63 years) (Table I). Participants were diagnosed with either of SUI (26/42; 61,9%) or MUI with predominant stress component (16/42; 38,1%). Eighteen participants had vaginal atrophy at the beginning of treatment with a VHI<15 (18/42; 42.9%) and 24 participants had no signs of vaginal atrophy (24/42; 57.1%). Patients with vaginal atrophy were substantially older (median age 65.5 years (IQR 55.75 to 68.25) than patients with no signs of vaginal atrophy who had a median age of 50 years (IQR 48.25 to 51.75 years). The proportion of patients with vaginal atrophy among those younger than 55 years was substantially lower (3/23; 13%) than among those older than 55 years (15/19; 78.9%).

Table I.—*Main demographic characteristics: laser Co_2 group* vs. *control group.*

	Laser CO_2	Pelvic floor training
N. patients	42	42
Age (median)	55.9	58
Vaginal atrophy	18/42	17/42
SUI	26/42	24/42
MUI	16/42	15/42
VAS baseline	8	7
VAS 1 months	2	4
VAS 6 months	1	3
VAS 12 months	2	5.5

Treatment protocol included 4 monthly laser therapies applied at monthly intervals: from the first to the second Co_2 Laser therapy mean calculated interval was 31 days (range 21 to 40 days); from the second to the third Laser therapy mean calculated interval was 33 days (range 28 to 42 days); from the third to the fourth Laser therapy mean calculated interval was 31 days (range 21 to 35 days). Total interval from first to the fourth Laser therapy was 93.5 days (range 73 to 107 days).

One month after initiation of therapy significant improvement in VAS scores was observed in all 42 patients. The same improvement was observed six-months and at one-year follow-up ($P<0.001$). Complete resolution of SUI was reported by 17 (40%) patients at six months follow-up, yet eight of them regained a mild elevation of VAS Score at 12 months follow-up. Women with vaginal atrophy demonstrated significantly better scores ($P<0.001$) and women older than 55 years also saw a major positive response to the CO_2 laser treatment (Table II).

Vaginal laser treatment was associated with a significant decrease in VAS scores as early as one month after the initiation of therapy ($P<0.001$), maintained during the follow-up period of 12 months.

In our 42 patients' cohort, median VAS Score of 8 at baseline, significantly decreased to 2.25 (IQR 0-4) at one month, to 1 (IQR 0-3) at six months, rising again to 2 (IQR 0-4) at 12 months ($P<0.001$) follow-up visit.

Decrease in VAS scores was constantly significant at each follow-up relative to pretreatment scores, with 85% decrease in VAS scores after six months and an overall 75% decrease in VAS scores at the last follow-up ($P<0.001$).

All 42 patients reported marked improvement throughout one year follow-up period and 40.5% (N.=17) reported complete absence of UI at six month follow-up confirmed by cough stress test, however, in eight of them a mild non-significant increase in VAS Score at 12 months follow-up was recorded, confirmed by the urodynamic test.

In the subgroup analysis of patients with and without vaginal or vulvar atrophy, although both

TABLE II.—*VAS scores at diagnosis and among treatment with microablative fractional Co_2 laser therapy for urinary incontinence.*

	VAS Score				Improvement (DELTA)					
					After 1 month		After 6 months		After 12 months	
	Pre-treatment	After 1 month	After 6 months	After 12 months	Delta VAS	%	Delta VAS	%	Delta VAS	%
Median (N.=42)	8 (8-10)	2.25 (0-4)	1 (0-3)	2 (1-4)	6 (5-8)	75	7 (6-8)	87.5	6 (5-8)	75
Under 55 (N.=22)	9 (8-10)	2.5 (1-3)	1 (0-3)	3 (2-4)	6 (5-8)	66.6	7.5 (7-10)	83.3	6 (5-7)	66.6
55 and older (N.=20)	8 (8-9)	2 (0-4)	1 (0-3)	1 (0-4)	7 (5-8)	77.7	7 (6-8)	77.7	7 (6-8)	87.5
Significance	0.509	0.737	0.785	0.077	0.979		0.264		0.127	
No atrophy	9 (8-10)	2.75 (1-3.75)	1 (0-3)	3 (2-4)	6 (5-8)	66.6	7 (5-9)	77.7	5.5 (4-6)	66.6
Atrophy	8 (8-9)	1.5 (0-4)	0.5 (0-2)	1 (0-1.25)	6.5 (5-8)	81.2	7.5 (6-8)	93.7	7 (6-8)	87.5
Significance	0.150	0.406	0.142	0.000	0.835		0.640		0.001	
SUI (N.=26)	9 (8-10)	2 (0-3.25)	0.5 (0-3)	3 (0-4)	7 (5-8)	77.7	7.5 (6-8)	83.3	6 (5-8)	66.6
Mixed (N.=16)	8 (8-9)	2.75 (1.25-4)	1 (0-2)	2 (1-3.75)	6 (5-6.75)	75	7 (6-9)	87.5	6 (5-7)	75
Significance	0.194	0.191	0.724	0.627	0.076		0.690		0.393	

groups scored a comparable VAS Score prior to treatment, patients who suffered from atrophy had a significant better VAS Score at 12 months (P<0.001), while the VHI Score was improved >15 in all patients with atrophy at beginning of the treatment.

The type of UI, whether SUI or mixed with predominant SUI, was equally distributed in all subgroups (younger *vs.* elder patients; with/without vaginal atrophy). Patients with either SUI or MUI with predominant SUI component responded equally well to laser treatment. Questionnaires about QoL (EORTC QLQ – CX24) showed a good quality of life in patients submitted to the treatment: no abnormal bleeding from vagina, no pain or problems vagina, with a real improvement in sexual function and reduction in number of pass urine especially in the night time (urge component).

We also retrospectively analyzed a same group of 42 patients with SUI: women underwent to pelvic floor muscle training. Median age in this subgroup was 58 years (IQR 49.7 to 67.2). The proportion of patients without vaginal atrophy was 40% (17/42) and with atrophy 60% (25/42) (Table I).

In this cohort of patients median VAS Score was 7 at baseline, significantly decreased to 4 at one month (<0.05), to 3 after two months (>0.001), this result was maintained at six months, but went back to 5.5 at 12 months (P>0.1) follow-up visit.

No major side effects were observed in any of the CO_2 laser sessions. Nobody reported a pain with a VAS>6 during the treatment. Patients did not report any deterioration in urinary function after and during the treatment, and/or the presence of vaginal or vulvar abrasions or ulcerations throughout the course of laser treatment and the follow-up period, other than mild discomfort during the procedure.

Discussion

Urinary incontinence constitutes one of the major reasons for gynecological surgery. Surgical procedures are associated with adverse events such as urethral obstruction, vaginal, bladder and/or urethral erosion, refractory chronic pain, hemorrhage and onset of dyspareunia due to excessive scarring with a complication rate from 2% to 12% of cases according to the literature.[7, 9] Scientific and technological progress has led to better clinical outcomes with less invasive procedures and surgical treatment should be used when only conservative treatment fails.[5] In this sense, recent evidence supports non-invasive treatment like laser treatment as an alternative and effective intervention for SUI.[10]

Moreover, the pelvic floor muscle training could be a valid option for SUI, but the fractional CO_2 laser is a well tolerated approach and safe procedure for the treatment of GSM with a relevant increase in Vaginal Health Index (VHI) scores and a good level of satisfaction for the procedure,[8, 9, 13, 16, 20, 25-28, 34] may materialize as the promising minimally invasive safe treatment alternative for patients who suffer from SUI. Ac-

cording to literature data a non-systematic review by Conté *et al.*[6] asserts that laser treatment for female SUI is associated with improvement rates ranging from 62% to 78%, with no major adverse events noted, other than minor side effects such as increased vaginal discharge and transient urge urinary incontinence.

The first pilot study regarding Er:YAG laser in the treatment of female SUI started on September 2009,[24] in 2015 Ogrinc BU *et al.*[33] published a study on 175 women with newly diagnosed SUI (66%) and mixed urinary incontinence (MUI, 34%), treated according Er:YAG laser protocol. The results showed one year after laser treatment only 34% of the MUI remained continent and no difference in the efficacy was noted between pre- and postmenopausal patients. In 2018, Gambacciani *et al.*[36] published the first results of VELAS study (Vaginal Erbium Laser Academy Study) in 1500 postmenopausal women including eleven centers in Italy using the same Er:YAG laser technology. They showed that this laser treatment significantly improved GSM at 12 months after the last laser application, whereas the effects decreased afterward.

CO_2 laser has been used for GSM treatment,[11-15, 21] but very few studies regarding CO_2 laser treatment of SUI have been published. Pitsouni *et al.* evaluated the significant improvement in terms of dyspareunia, dryness, burning, itching, dysuria, urgency, and SUI scores in a prospective observational study including postmenopausal women with moderate to severe clinical signs of GSM, As a secondary outcome, the authors noted that urinary symptoms improved.

In 2016, Perino *et al.* showed that fractionated CO_2 laser vaginal treatment has an important and positive effect in improving overactive bladder (OAB) symptoms in post-menopausal women.[29]

Results of our study are aligned with this data and assert that four laser applications instituted at monthly intervals, provided a beneficial effect noted as early as one month after the first session and sustainable for at least 12 months, without major complications and more effective in older women with vaginal atrophy.

In fact, the beneficial effect of Laser treatment in women without vaginal atrophy was weaker at 12-month follow-up than in patients with vaginal atrophy. Otherwise, enhanced improvement was noted in women older than 55 years compared with women younger than 55 years possibly attributed to the predominance of vaginal atrophy in older women.

CO_2 laser procedure being equally effective for USI and MUI with predominant SUI pares well with the deduction that in women with UI the most consistent measure that predicts the success of CO_2 Laser therapy is the presence of vaginal atrophy. As such, ideal CO_2 laser therapy candidates seem to be older women with vaginal atrophy. This conclusion does not pare well with those reported by others that have determined that the best results, after laser treatment of SUI, should be expected in women younger than 47.5 years.[21, 22]

We think that the link between vaginal atrophy and urinary incontinence may be the deprivation of collagen production, resulting in a weakened urogenital tract that cause a relaxation of the anatomical structure that supports the periurethral tissue, important for continence.

Our results have been computed from existing databases. Data from the retrospective control group showed as patients which used pelvic floor training maintained the result over the full 6 months, but the efficacy decreased after the six months, becoming not statistically significant at 12 months' follow-up visit, without differences between patients affected by SUI and MUI.

Based on our short-term pilot study and those reported previously treatment micro-ablative fractional CO_2 Laser therapy emerges as a well-tolerated, minimally invasive, safe and efficacious treatment for UI. Moreover, the QoL questionnaire completed by patients showed an improvement of nicturia too.

Limitations of the study

We also know that the study has limitations: the characteristic of being a retrospective study in comparison with prospective or randomized studies, the limited follow-up and the small sample.

Surely, other perspective and randomized studies with longer follow-up are necessary to validate the effectiveness and potentialities of this approach.

Conclusions

In conclusion, fractional CO_2 laser therapy has a regenerative effect on the vulvovaginal and in lower urinary tract tissue as well and related physiological trophism and may emerge as a standard treatment for post-menopausal women with SUI and vaginal atrophy. In fact, atrophy of the genital tract is one mechanism that predisposes to UI, in line with our observation that older patients with vaginal atrophy respond best to laser therapy with a really regenerative effect.

References

1. Luber KM. The definition, prevalence, and risk factors for stress urinary incontinence. Rev Urol 2004;6(Suppl 3):S3–9.

2. Dumoulin C, Hay-Smith EJ, Mac Habée-Séguin G. Pelvic floor muscle training versus no treatment, or inactive control treatments, for urinary incontinence in women. Cochrane Database Syst Rev 2014;5:CD005654.

3. Han L, Wang L, Wang Q, Li H, Zang H. Association between pelvic organ prolapse and stress urinary incontinence with collagen. Exp Ther Med 2014;7:1337–41.

4. Price N, Dawood R, Jackson SR. Pelvic floor exercise for urinary incontinence: a systematic literature review. Maturitas 2010;67:309–15.

5. Syan R, Brucker BM. Guideline of guidelines: urinary incontinence. BJU Int 2016;117:20–33.

6. González Isaza P, Jaguszewska K, Cardona JL, Lukaszuk M. Long-term effect of thermoablative fractional CO2 laser treatment as a novel approach to urinary incontinence management in women with genitourinary syndrome of menopause. Int Urogynecol J Pelvic Floor Dysfunct 2018;29:211–5.

7. Imamura M, Hudson J, Wallace SA, MacLennan G, Shimonovich M, Omar MI, *et al.* Surgical interventions for women with stress urinary incontinence: systematic review and network meta-analysis of randomised controlled trials. BMJ 2019;365:l1842.

8. Lazarou G, Minis E, Grigorescu B. Outcomes of stress urinary incontinence in women undergoing TOT versus Burch colposuspension with abdominal sacrocolpopexy. Int Urogynecol J Pelvic Floor Dysfunct 2019;30:245–50.

9. Ford AA, Rogerson L, Cody JD, Ogah J. Mid-urethral sling operations for stress urinary incontinence in women. Cochrane Database Syst Rev 2015;(7):CD006375.

10. Bergsland J. Major innovations and trends in the medical device sector. Acta Inform Med 2012;20:44–6.

11. Filippini M, Luvero D, Salvatore S, Pieralli A, Montera R, Plotti F, *et al.* Efficacy of fractional CO2 laser treatment in postmenopausal women with genitourinary syndrome: a multicenter study. Menopause 2020;27:43–9.

12. Angioli R, Stefano S, Filippini M, Pieralli A, Montera R, Plotti F, *et al.* Effectiveness of CO2 laser on urogenital syndrome in women with a previous gynecological neoplasia: a multicentric study. Int J Gynecol Cancer 2020;30:590–5.

13. Athanasiou S, Pitsouni E, Grigoriadis T, Zacharakis D, Falagas ME, Salvatore S, *et al.* Microablative fractional CO2 laser for the genitourinary syndrome of menopause: up to 12-month results. Menopause 2019;26:248–55.

14. Salvatore S, Pitsouni E, Del Deo F, Parma M, Athanasiou S, Candiani M. Sexual Function in Women Suffering From Genitourinary Syndrome of Menopause Treated With Fractionated CO2 Laser. Sex Med Rev 2017;5:486–94.

15. Pitsouni E, Grigoriadis T, Falagas ME, Salvatore S, Athanasiou S. Laser therapy for the genitourinary syndrome of menopause. A systematic review and meta-analysis. Maturitas 2017;103:78–88.

16. Blaganje M, Šćepanović D, Žgur L, Verdenik I, Pajk F, Lukanović A. Non-ablative Er:YAG laser therapy effect on stress urinary incontinence related to quality of life and sexual function: A randomized controlled trial. Eur J Obstet Gynecol Reprod Biol 2018;224:153–8.

17. Mackova K, Van Daele L, Page AS, Geraerts I, Krofta L, Deprest J. Laser therapy for urinary incontinence and pelvic organ prolapse: a systematic review. BJOG 2020;127:1338–46.

18. Shobeiri SA, Kerkhof MH, Minassian VA, Bazi T; IUGA Research and Development Committee. IUGA committee opinion: laser-based vaginal devices for treatment of stress urinary incontinence, genitourinary syndrome of menopause, and vaginal laxity. Int Urogynecol J Pelvic Floor Dysfunct 2019;30:371–6.

19. Okui N. Comparison between erbium-doped yttrium aluminum garnet laser therapy and sling procedures in the treatment of stress and mixed urinary incontinence. World J Urol 2019;37:885–9.

20. Kwon TR, Kim JH, Seok J, Kim JM, Bak DH, Choi MJ, *et al.* Fractional CO2 laser treatment for vaginal laxity: A preclinical study. Lasers Surg Med 2018;50:940–7.

21. Franić D, Fistonić I. Laser Therapy in the Treatment of Female Urinary Incontinence and Genitourinary Syndrome of Menopause: an Update. BioMed Res Int 2019;2019:1576359.

22. Erel CT, Inan D, Mut A. Predictive factors for the efficacy of Er:YAG laser treatment of urinary incontinence. Maturitas 2020;132:1–6.

23. Fistonić I, Fistonić N. Baseline ICIQ-UI score, body mass index, age, average birth weight, and perineometry duration as promising predictors of the short-term efficacy of Er:YAG laser treatment in stress urinary incontinent women: A prospective cohort study. Lasers Surg Med 2018. [Epub ahead of print]

24. Fistonić N, Fistonić I, Lukanovič A, Findri Guštek Š, Sorta Bilajac Turina I, Franić D. First assessment of short-term efficacy of Er:YAG laser treatment on stress urinary incontinence in women: prospective cohort study. Climacteric 2015;18(Suppl 1):37–42.

25. Klovning A, Avery K, Sandvik H, Hunskaar S. Comparison of two questionnaires for assessing the severity of urinary incontinence: the ICIQ-UI SF versus the incontinence severity index. Neurourol Urodyn 2009;28:411–5.

26. Pardo JI, Solà VR, Morales AA. Treatment of female stress urinary incontinence with Erbium-YAG laser in non-ablative mode. Eur J Obstet Gynecol Reprod Biol 2016;204:1–4.

27. Leshunov EV, Martov AG. [Application of laser technologies for treatment of urinary stress incontinence in women of reproductive age]. Urologiia 2015;1:36–40. [Russian].

28. Neimark AI, Yakovleva AY, Lapii GA. [Outcomes of ER:YAG LASER treatment of stress urinary incontinence in women]. Urologiia 2018;2:20–5. [Russian].

29. Perino A, Cucinella G, Gugliotta G, Saitta S, Polito S, Adile B, *et al.* Is vaginal fractional CO2 laser treatment effective in improving overactive bladder symptoms in post-menopausal patients? Preliminary results. Eur Rev Med Pharmacol Sci 2016;20:2491–7.

30. Gaspar A, Brandi H. Non-ablative erbium YAG laser for

the treatment of type III stress urinary incontinence (intrinsic sphincter deficiency). Lasers Med Sci 2017;32:685–91.

31. Conté C, Jauffret T, Vieillefosse S, Hermieu JF, Deffieux X. Laser procedure for female urinary stress incontinence: A review of the literature. Prog Urol 2017;27:1076–83.

32. Zhang L, Lai Y, Pan W, Zhou B, Qiang X, Mao Z, *et al.* Application of ultra pulse CO2 lattice laser in the treatment of female urinary incontinence. Transl Androl Urol 2021;10:2471–7.

33. Ogrinc UB, Senčar S, Lenasi H. Novel minimally invasive laser treatment of urinary incontinence in women. Lasers Surg Med 2015;47:689–97.

34. Nalewczynska AA, Barwijuk M, Kolczewski P, Dmoch-Gajzlerska E. Pixel-CO2 laser for the treatment of stress urinary incontinence. Lasers Med Sci 2022;37:1061–7.

35. Azam F, Latif MF, Farooq A, Tirmazy SH, AlShahrani S, Bashir S, *et al.* Performance Status Assessment by Using ECOG (Eastern Cooperative Oncology Group) Score for Cancer Patients by Oncology Healthcare Professionals. Case Rep Oncol 2019;12:728–36.

36. Gambacciani M, Levancini M, Russo E, Vacca L, Simoncini T, Cervigni M. Long-term effects of vaginal erbium laser in the treatment of genitourinary syndrome of menopause. Climacteric 2018;21:148–52.

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