Minimally invasive laser procedure for early stages of stress urinary incontinence (SUI)

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ABSTRACT

The objective of this labeled, prospective, single-center pilot study study was to assess the efficacy and safety of a novel minimally invasive, non-ablative laser treatment in the early stages of SUI.

A total of 39 patients suffering from mild-to-moderate stress urinary incontinence underwent treatment with an Er:YAG (2940 nm) laser in non-ablative fractional mode. Assessment tools included the ICIQ-UI SF questionnaire for assessing the degree of incontinence and its impact on the quality of life, the Q-tip test for evaluating the mobility of the urethra and bladder neck, PISQ-12 for assessing quality of life in the area of sexuality, and perineometry for the measurement of muscle strength. Follow-ups were scheduled after 1 month for 39 patients, after 3 months for 22 patients and after 6 months for 6 patients.

Preliminary results of post-treatment evaluation showed significant improvement ($p < 0.05$) in all the domains tested: ICIQ-UI scores decreased by more than 3 points at all follow-ups. A mean duration of muscle contraction measured with perineometry at 1 month increased by 4.7 s, at 3 months by 11.8 s and at 6 months by 22.8 s. Q-tip angle decreased by 14.7° at 1 month follow-up, by 15.9° at 3 months and by 22.5° at 6 months. PISQ-12 scores increased after 1 month by 5.4 points, after 3 months by 5.9 points and after 6 months by 6.6 points.

The preliminary results confirm that a minimally invasive, non-ablative fractional laser treatment (IncontiLaseTM) is an effective, safe and comfortable treatment option for symptom relief in patients with mild and moderate SUI.

Key words: Er:YAG laser; stress urinary incontinence (SUI), Smooth mode, non-ablative laser treatment, collagen remodeling, collagen synthesis

I. INTRODUCTION

The ICS (International Continence Society) defines urinary incontinence (UI) as the involuntary loss of urine, which is objectively demonstrable and with such a degree of severity that it is a social or hygienic problem [1]. UI is one of the manifestations of pelvic floor dysfunction (PFD) [2]. Stress urinary incontinence (SUI) is the most common form of UI in women; it is defined as the involuntary loss of urine during coughing, sneezing, or physical exertion such as sporting activities or sudden change in position [1], and is estimated to affect between 4% to 14% of younger women and 12% to 35% of older women [3].

The etiology of stress-incontinence is not completely understood, although it is known that identifiable risk factors for the condition include pregnancy, childbirth, menopause, cognitive impairment, obesity, and advanced age [4]. Dietz and Clarke [5] proposed that the causes of SUI were relaxation of the anatomical structure that supports the periuretral tissue and impairment of the uretral sphincter. Damage to the pelvic floor neuromusculature during vaginal delivery may lead to loss of pelvic muscle strength and nerve function, resulting in both stress urinary incontinence (SUI) and pelvic floor support defects.

PFD can also lead to pelvic organ prolapse - a condition where organs, such as the uterus, fall down or slip out of place. Pelvic organ prolapse and stress urinary incontinence coexists in 15 to 80 percent of women with pelvic floor dysfunction [6]. While these

conditions are often concurrent, one may be mild or asymptomatic. Also, pelvic floor surgery may expose previously asymptomatic conditions; specifically, in previously continent women with pelvic organ prolapse, stress urinary incontinence may develop or worsen after prolapse repair [7].

Researchers have suggested that the ligaments of women with stress urinary incontinence have decreased collagen content or qualitative alternations in collagen composition. Women with stress urinary incontinence have an altered connective tissue metabolism causing decreased collagen production, which may result in insufficient support of the urogenital tract [8]. A study by Wong et al. [9] showed that cervical collagen content is significantly decreased in women who have pelvic organ prolapse with and without stress urinary incontinence. The pubocervical fasciae of incontinent women show a diminished content of collagen which may contribute to the weakening of support of the bladder neck [10].

Despite the prevalence of SUI and its accompanying embarrassment and diminished quality of life, many women who experience symptoms of SUI do not seek medical treatment. A recent survey found that only 15% of women aged 40 years or older with SUI sought medical treatment for their symptoms [11].

There are many possible nonsurgical and surgical therapies for SUI. Initial treatment should include nonsurgical therapies - behavioral changes and pelvic floor muscle exercises [4]. Electrical stimulation, weighted vaginal cones and drug therapy also may reduce stress incontinence. Bulking agents reduce leakage, but effectiveness generally decreases after 1–2 years. Surgical procedures are more likely to cure stress urinary incontinence than nonsurgical procedures but are associated with more adverse events [12].

Many women with SUI do not seek care for their condition because of embarrassment, lack of knowledge about possible treatments or fear that treatment will require surgery. Several studies have shown that if less-invasive treatments become more widely available, more patients may be willing to seek care without the fear of surgery [3]. Many researchers are therefore searching for a minimally invasive treatment that offers good efficacy, safety and a short recovery period.

The medical effects of lasers are well established in terms of biochemical, ablative and thermal effects. Thermal energy from the laser source, especially in moist environments, not only effectively enhances collagen structure but also stimulates neocolagenesis. As a result of laser irradiation the intermolecular cross-links of the triple helix of collagen shorten, which leads to the immediate tightening of collagen fibrils by two-thirds of their length in comparison to the pre-intervention state [13].

Previous experimental and clinical studies have shown significant effects in the treatment of various diseases and conditions deriving from collagen damage. Most of the references are from the field of dermatology and aesthetic medicine. Facial ptosis, relaxation of the uvula and soft palate in snorers and the ligaments in orthopedic trauma are just some of the areas in which the application of heat from a pulsed laser beam has confirmed the scientific effectiveness of thermal laser treatments [14,15,16].

Among minimally invasive laser techniques that enable collagen remodeling, there is a novel laser treatment known as IncontiLaseTM. In a preliminary pilot study, we have showed that this laser treatment for the early stages of SUI, with or without prolapse, effectively improves the symptoms of SUI as well as relevant parameters of pelvic floor muscle strength and quality of life, thus avoiding or postponing the need for possible surgical interventions.

II. METHODS

In this open-labeled, prospective, single-center pilot study, 39 patients suffering from stress urinary incontinence underwent treatment with a 2940 nm Er:YAG laser (XS Dynamis, Fotona, Slovenia). A study was approved by the ethics committee of the University of Rijeka School of Medicine, Croatia. The approval of the ethics committee was obtained according to the principles of the Nuernberg Codex and latest version of the Helsinki declaration [17,18].

a) Inclusion and exclusion criteria:

Between April 2011 and October 2011, a total of 39 patients were recruited with mild-to-moderate SUI with or without prolapse. At the initial consultation the patients were examined to determine the suitability according to the inclusion and exclusion criteria. All patients submitted to treatment had passed the inclusion criteria and had provided a written informed consent form.

The patients were between 30 and 61 years of age (average age 42.6 years) with an average body mass index of 23.5 and parous status from 1-4 (on average 2.2). The birth weight of the children was between

2650 and 4350 g (on average 3340g). All of the patients had delivered vaginally.

The inclusion criteria were: mild and moderate stress urinary incontinence as measured by the ICIQ questionnaire with or without mild prolapse, normal cell cytology (PAP smear), negative urine culture and a vaginal canal, introitus and vestibule free of injuries and bleeding.

The exclusion criteria were: severe stress urinary incontinence with severe prolapse and damage to the recto-vaginal fascia, age 70 years, pregnancy, intake of photosensitive drugs, injury or/and active infection in the treatment area, undiagnosed vaginal bleeding and active menstrual period.

The degree of incontinence and its impact on the quality of life was assessed with the Inernational Consultation on Incontinence Questionnaire - Urinary Incontinence Short Form (ICIQ-UI SF) [19]. The questionnaire allows the assessment of the prevalence, frequency, and perceived cause of urinary incontinence, and its impact on everyday life [20].

Quality of life in the area of sexuality was examined with the validated Pelvic Organ Prolapse / Urinary Incontinence Sexual Questionnaire (PISQ-12) with a maximum score of 48 points. Many recent publications examining the impact of urinary incontinence (UI), fecal incontinence, and pelvic organ prolapse (POP) using validated generalized and disease-specific questionnaires have reported poorer sexual function in women with pelvic floor disfunction (PFD). The PISQ has been used most commonly to evaluate sexual function after surgery for PFD, with increased PISQ scores in approximately 70% [21].

Q-tip measurement was used [22] for the quantification of urethrovesical junction mobility and the urethral axis. The Q-tip test evaluates the mobility of the urethra and bladder neck. This is done by inserting a sterile, lubricated cotton-bud into the urethra to the level of the bladder neck. The patient is then asked to strain. The resting and straining angles are measured, and the difference between the two angles is calculated. Urethral hypermobility was defined as being present when the Q-tip angle was ≥ 30°, while Q-tip movement < 30° was declared as normal. Q-tip angle was measured during Valsalva maneuver before the treatment and compared with the results at the follow-up visits after the intervention in order to assess bladder and urethral support.

For the measurement of muscle strength and the vaginal pelvic diaphragm, an Apimeds perineometer (EXTT-101, Korea) was used. The measurement has showed the maximum clamping pressure (mm Hg), the average contraction pressure (mm Hg) and mean duration of contractions (seconds).

b) Treatment procedure:

The anterior vaginal wall and intoitus were treated by Er:YAG laser (2940 nm) (XS Dynamis, Fotona, Slovenia) in a non-ablative thermal mode according to the manufacturer's proprietary sequence (Fotona, Slovenia), producing a precisely controlled, non-ablative thermal-only effect on the tissue.

The IncontiLaseTM procedure treatment consisted of two phases:

Immediately before the laser treatment the patient's vagina (vestibule, introitus and vaginal canal) was thoroughly washed and the disinfecting solution carefully dried off and removed from the mucosa. Next, a specially designed laser speculum was introduced into the patient's vagina to serve as a guide for the laser beam delivery system – a fractional Er:YAG handpiece with an angular adapter which enables a precise irradiation of the anterior wall of the vagina. Laser energy is applied along the anterior vaginal wall in several longitudinal passes, deposited successively along the vaginal canal without overlapping, by simple step-by-step withdrawal of laser handpiece outwards from the laser speculum. Laser energy of approximately 30 J is delivered to each irradiation location according to the manufacturer's proprietary sequence (Fotona, Slovenija), producing thermal effect on the mucosa tissue and endopelvic fascia of the vaginal wall that causes shrinkage of collagen in the vaginal mucosa.
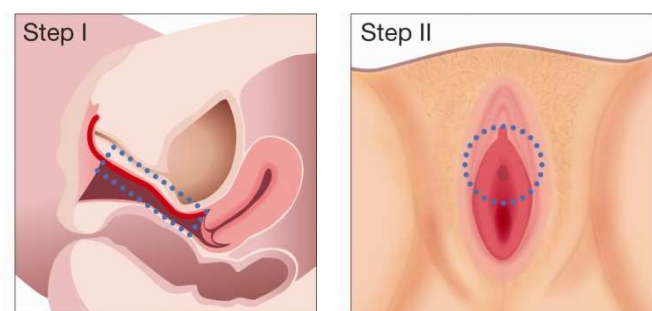

Fig.1: The two step IncontiLaseTM procedure

The second phase of the IncontiLase™ procedure is performed on the vestibule and introitus area using a straight- shooting fractional laser handpiece. The whole area has to be thoroughly covered with laser energy to achieve sufficient level of thermal impact to collagen in treated mucosa.
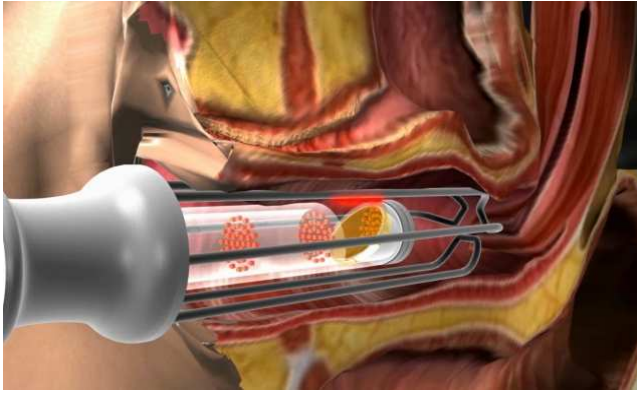
Fig.2: IncontiLaseTM fractional non-ablative laser treatment of the anterior vaginal wall.

During the execution of the procedure patient discomfort and treatment tolerability, as well as potential adverse events where monitored. No anesthesia was used before or during the first session.

At 1, 3 and 6 month post-treatment follow-ups, as well as at pre-treatment visits, patients were assessed by physical exam (including vital signs, vaginal examination), perineometry measurements, Q-tip measurements as well as by self-reported questionnaires: ICIQ-UI and PISQ-12.

III. RESULTS

A total of 39 patients with mild-to-moderate SUI, with or without mild prolapse, were recruited. All 39 patients underwent the IncontiLaseTM treatment. Before the treatment, ICIQ-UI, PISQ-12, Q-tip tests and perineometry were performed. At the 1-month follow-up, ICIQ-UI, PISQ-12, Q-tip tests and perineometry were performed with all 39 patients. A total of 22 patients underwent a 3-month follow-up and 6 patients underwent a 6-month follow-up.

All IncontiLaseTM procedures were successfully completed in the practitioner's office. The average treatment time was 25 minutes. The sensation of pain and discomfort was monitored during the treatment. Less than half of the patients assessed the IncontiLaseTM treatment as totally painless, while the others reported very mild pain or a burning sensation during the treatment of the introitus area. The discomfort disappeared if the practitioner paused between the train of laser pulses. Patients returned to their routine activities immediately after treatment, and no adverse effects were reported.

a) Perineometry measurements

The measurement of muscle strength with an Apimeds

perineometer (EXTT-101, Korea) show the maximum clamping pressure (mm Hg), the average contraction pressure (mm Hg) and mean duration of contractions (s). The maximum pressure before the treatment was 15.9 mm Hg, which increased one month after the treatment to 18.4 ($p < 0.05$). Also the mean pressure after the treatment was greater than before. Before the treatment the mean pressure was 7.1 mm Hg, after 1 month it was 10.7 mmHg, and after 6 months 12.2 mmHg ($p < 0.05$). The mean duration of contractions is presented in Figure 3. Before the treatment it was 13.7 s, after 1 month 18.4 s, after 3 months 25.5 s, and after 6 months 36.5 s ($p < 0.05$).
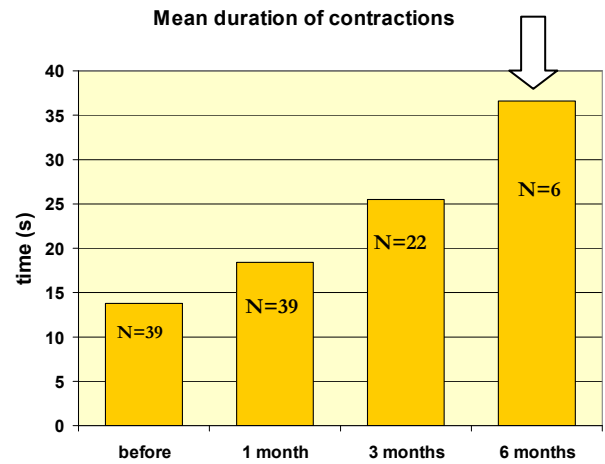

Fig.3: Perineometry measurements – mean duration of contractions before the treatment and after 1, 3 and 6 months. A prolonged duration after the treatment is evident and statistically significant ($p < 0.05$).
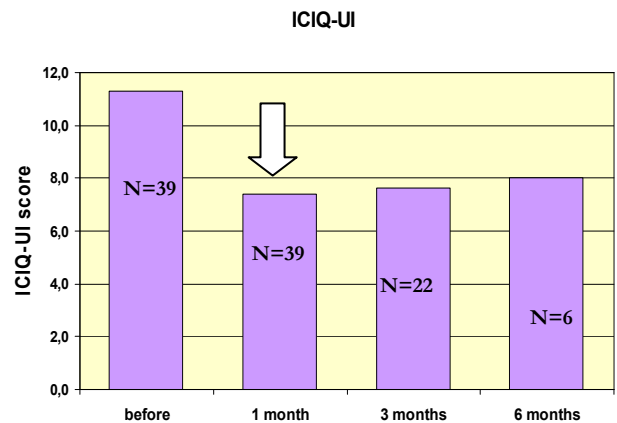

Fig.4: The degree of incontinence and its impact on the quality of life was assessed with the ICIQ-UI SF questionnaire before the treatment and at 1, 3 and 6 month follow-ups. The score significantly improved after the IncontiLaseTM treatment.

b) ICIQ-UI questionnaire

All patients responded to the ICIQ-UI questionnaire

before the treatment and at 1, 3 and 6 month follow-ups. In Figure 4 the results of ICIQ-UI before the treatment, at 1, 3 and 6 months are represented. The average ICIQ-UI score before the treatment was 11.3 points (p<0.05), the second measurement at 1 month was 7.4, at 3 months 7.6, and at 6 months 8.0 (p<0.05).

c) PISQ-12 questionnaire

All patients also responded to the PISQ-12 questionnaire before the treatment and at 1, 3 and 6 months. The average PISQ-12 score before the treatment was 32.9 points (p<0.05), the second measurement at 1 month was 38.3, at 3 months 38.8, and at 6 months 39.5 (p<0.05).

d) Q-tip test

Q-tip measurement was used to investigate urethrovesical junction mobility and the urethral axis. An example of Q-tip test measurements before and after IncontiLaseTM treatment is presented in Figure 6

The angle of the Q-tip with the Valsalva maneuver before the treatment was on average 65°. A month after the IncontiLaseTM treatment the angle was on average 50.3° (p<0.05), after 3 months it was 49.1° (p<0.05) and after 6 months 42.5° (p<0.05) as presented in Figure 7.

IV. DISCUSSION

For most patients with SUI, the initial management involves a variety of noninvasive interventions, including behavioral therapy and pelvic floor muscle exercises (PFMEs). These therapies do require patience, motivation and time commitment. There have been several trials that demonstrate improvement and satisfactory cure rates in patients adhering to a strict program of behavior modification and pelvic floor muscle tonus. Patient compliance and motivation, however, are essential to successful results [4]. The questionnaire responses showed that women are unlikely to carry out regular pelvic floor exercises except for a short time after childbirth or when prompted by urinary symptoms [20]. Benefits usually depend on the patient's training, motivation and understanding.

Other nonsurgical techniques include electric stimulation, vaginal cones, occlusive and intravaginal devices and pharmacological treatments. Reports of the efficacy vary [23]. There are few studies that have prospectively evaluated and compared the efficacy of the various nonsurgical therapies.
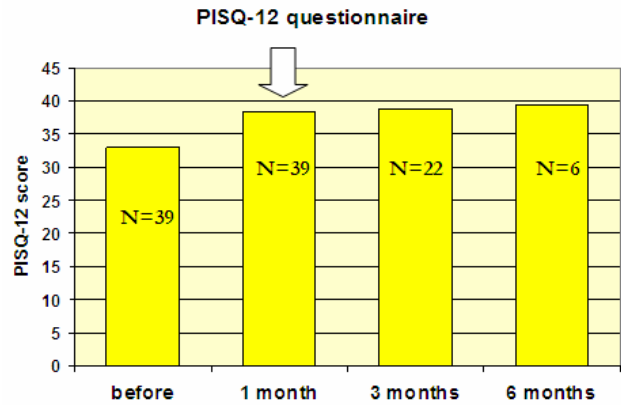

Fig.5: Patients' assessment of improved sexual gratification measured with PISQ-12 questionnaires before the treatment and after 1, 3 and 6 month follow-ups. The improvement after IncontiLaseTM treatment after 6 months was more than 6 score points.
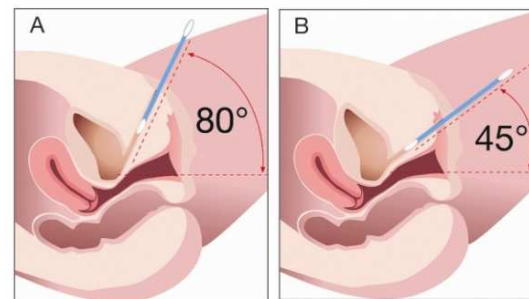

Fig.6: The cotton-tipped swab (Q-tip) test for assessment of urethral and bladder support. A: Angle of the Q-tip with Valsalva maneuver. The urethrovesical junction descended, causing upward deflection of the Q-tip. B: Q-tip measurements with Valsalva maneuver after IncontiLaseTM treatment.
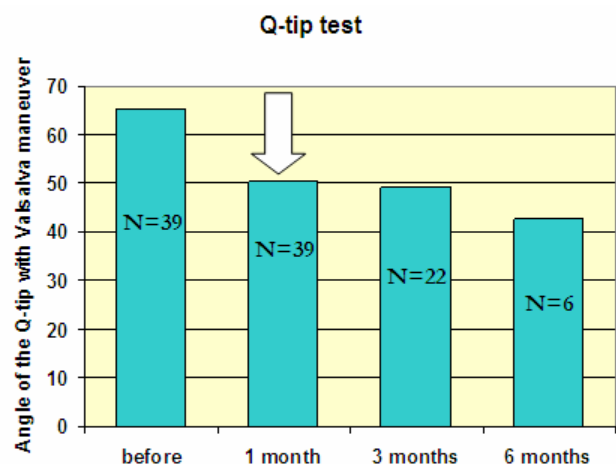

Fig.7: Q-tip measurement was used to investigate the degree of genital prolapse. Angles of the Q-tip with the Valsalva maneuver before the treatment and after 1, 3 and 6 months are represented. The Q-tip angle after the treatment decreased by more than 20°.

In a study of 107 patients with SUI, Bo and colleagues [24] compared the efficacy of electrical stimulation, vaginal cones and a control group, and concluded that pelvic floor exercise is superior to both electrical stimulation and vaginal cones in the treatment of genuine SUI in women. In the nine trials comparing pelvic floor electric stimulation (PFES) to a placebo, only three (Barroso et al., 2004; Yamanishi et al., 2000; Sand et al., 1995) [25-27] found statistically significant results in favor of electrical stimulation. However, each of these trials suffered from methodological flaws. None of the eight trials of PFES vs. behavioral treatment conclusively demonstrated the superiority of PFES [28]. There were also reports of complications such as urinary tract infections [23]. In a study by Davila and colleagues [29] in which 53 patients with SUI or mixed incontinence were fitted with the Introl device, they have proven statistically significant reductions in incontinence, however, 23 patients reported vaginal soreness or irritation.

Surgical techniques are very common, safe and effective option although they are much more invasive, have more complications and require a recovery period of several weeks before the patient can return to normal daily activities [4]. There is insufficient evidence to compare surgery with other interventions, and most experts recommend that patients undergo non-surgical options first [30]. Despite being the most used and a very efficacious minimally-invasive surgical procedure – the TVT sling procedure with studies reporting a 5-year cure rate as high as 84.7% and only a 4.5% failure rate [31], there are reports of complications such as voiding difficulties and detrusor over-activity [32]. In 2008 the FDA issued an alert for mesh devices used to repair POP and SUI. The most frequent complications included erosion through the vaginal epithelium, infection, pain, urinary problems, and recurrence of prolapse and/or incontinence. The alert was updated in 2011 [33].

Despite its prevalence and the associated distress, embarrassment, and diminished quality of life, many women who experience symptoms of SUI choose to delay or do not seek medical treatment because of embarrassment, lack of knowledge about possible treatments or fear that the treatment will require surgery. Public interest in less invasive, efficient, safe and in-office procedures for treatment of SUI is therefore growing.

Following these requirements, the IncontiLaseTM laser treatment was developed. In our pilot study with 6 month follow-up of patients with mild to moderate stress urinary incontinence treated with non-ablative laser, we demonstrated the efficacy and safety of the procedure. To our knowledge, this is the first study using nonsurgical intravaginal laser treatment for SUI.

The stress incontinence was measured by ICIQ-UI SF and showed score improvement after IncontiLaseTM treatment by more than 3 points, also at 6-month follow-ups, indicating significant improvement of stress urinary incontinence symptoms. ICIQ-UI SF was shown in several studies [20,34] to be an effective measurement method for assessment of the impact of symptom severity on the quality of life.

For objective measurements of structural tissue changes, a perineometer was used. Perineometric measurements showed an improvement in muscle strength, especially in the mean duration of contraction that increased by 22.8 seconds 6 months post-treatment. The usefulness of digital assessment of pelvic floor muscle strength by perineometry to identify women with urinary symptoms who have underlying fascia defects was shown in the study by Isherwood et al. [20], as there is a strong correlation between contraction strength and the ability to control urine flow, and defective pelvic floor function, which is an important component of stress urinary incontinence and uterine prolapsed.

Quantification of urethrovesical junction mobility and the urethral axis showed a decrease of the angle by more than 20° at 6 months post IncontiLaseTM treatment. Although by the results of some studies, the Q-tip "cotton swab test" test has poor predictive value for either stress urinary incontinence diagnosis or predicting treatment success [35], it has been successfully used by many clinicians to determine the urethral axis and urethrovesical junction mobility [36].

We have also decided to utilize a PISQ-12 questionnaire that measures quality of life in the area of sexuality. It is known that approximately 25-50% of women with pelvic floor disorders report impaired sexual function [37,38]. Many studies document an improvement in PISQ-12 score after successful treatment of SUI. A study by Handa et al. [39] established that after therapy, successful non-surgical treatment of SUI (continence pessary, behavioral therapy through pelvic floor muscle training and continence strategies, or combination therapy) was associated with greater improvement in PISQ-12 (2.26 ± 3.24 versus 0.48 ± 3.76, p=0.0007). Brubaker and colleagues described PISQ-12 score increases by a mean of 5.8 points after successful surgery (Burch colposuspension or sling surgery) and only 3.8 points for unsuccessful surgery [40]. In our study we have

established a mean improvement of PISQ-12 score after 6 months by more than 6 points.

Regarding safety and tolerability, we have not noticed any adverse events throughout the whole course of treatment and the follow-up period. The discomfort level during the treatment was mild and was gone as soon as the treatment ended. All patients returned to their daily activities immediately after treatment. We have concluded that IncontiLaseTM is a safe treatment and that patients find it comfortable and non invasive.

A positive effect on the symptoms of stress urinary incontinence was ascribed to neocolagenesis and collagen remodeling. The objective of the non-ablative laser treatment is to achieve selective, heat-induced denaturation of dermal collagen that leads to subsequent new collagen deposition with as little damage to the epidermis as possible [41]. The shortening of collagen to the longitudinal axis occurs under the influence of specific temperatures from 61°C to 63°C [13]. In addition to the instantaneous collagen and tissue shrinkage reaction, the processes of collagen remodeling and neocollagenesis start [42-45] and at the end of these processes the treated tissue becomes enriched with new collagen and is tighter and more elastic.

Precisely controlled VSP [46] laser energy pulses delivered to the vaginal canal and introitus area cause a heating of the tissue and the collagen in it, and consequently a contraction and shortening of fibers. Also the process of neocolagenesis is stimulated [42-45]. The irradiated tissue consequently contracts and shrinks, improving support to the bladder and thus reducing the symptoms of stress urinary incontinence.

Effective results for transurethral collagen denaturation treatments have been previously reported [47,48]. Transurethral collagen denaturation resulted in significant improvements in stress leaks and quality of life for at least 18 months in the treatment of nonsurgical radiofrequency collagen denaturation [48]. These treatments, however, were connected to some adverse event effects such as dysurea, urinary retention and post-procedure pain [48]. In a paper describing another minimally invasive laser therapy for vaginal rejuvenation treatments performed with a fractional ablative CO_2 laser, Gaspar et al. [49] reported beneficial effects in the three layers of the vaginal tissue and in sexual function. They also reported several adverse events effects such as bleeding, pain and burning.

V. CONCLUSION

In conclusion, although we are aware that this is a pilot study with a 6-month follow-up for a small number of patients, preliminary results show that the minimally invasive non-surgical IncontiLase™ treatment offers efficacious treatment for SUI, and is associated with high a level of safety and a short recovery period.

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