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Non-ablative vaginal erbium YAG laser for the treatment of cystocele

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ABSTRACT

Purpose: the aim of the study was to evaluate the effects of Vaginal Erbium Laser (VEL), a non-ablative solid state erbium-doped yttrium-aluminum-garnet crystal (Er:YAG) laser treatment for reduction of prolapses.

Methods: in this prospective cohort study, 61 patients with cystoceles of grades II–IV were submitted to 2-5 treatments with a nonablative VEL laser at 2-month intervals. At baseline and 2, 6 and 12-month follow-ups, prolapses were photographed and graded using the Baden-Walker scale during a physical examination. Patients were interviewed at each follow-up about adverse effects and their satisfaction. Pain during treatment was measured on a 10-point visual analog scale (VAS).

Results: at baseline 40 patients presented with grade II cystoceles, 15 with grade III and 6 with grade IV cystoceles. At the final follow-up, the grade of prolapse was reduced by at least one grade in 95% of patients, with 85% of patients presenting with grade 0 or I prolapses and the remaining 15% of patients with grade II prolapses. Most patients were either very satisfied (57%) or satisfied (33%) with the treatment. Treatment discomfort was low (0.5 VAS). No major adverse effects were reported.

Conclusions: the results of this pilot study show that the non-ablative VEL treatment may improve cystoceles with minimal patient discomfort and no adverse effects. If these preliminary results will be confirmed in a properly designed, controlled study, then VEL could be considered in selected cases as a minimally-invasive alternative to surgery.

Keywords: pelvic organ prolapse, cystocele, Er:YAG, non-ablative laser, non-surgical treatment

SOMMARIO

Scopo dello studio: scopo dello studio è stato quello di valutare gli effetti del trattamento con laser vaginale non ablativo Erbium (Vaginal Erbium Laser, VEL) nella riduzione del prolasso genitale.

Metodi: in questo studio di coorte, prospettico, non controllato, 61 pazienti con cistocele di II–IV grado sono state sottoposte a trattamento con VEL, eseguendo da 2 a 5 trattamenti, ad intervalli di 2 mesi. La valutazione del grado di prolasso è stata eseguita secondo la classificazione di Baden-Walker, sia in condizioni basali che dopo 2, 6 e 12 mesi, registrando le immagini fotografiche durante la visita, valutando anche l'incidenza degli effetti collaterali e la soddisfazione delle pazienti. Il dolore riferito dalle pazienti durante il trattamento è stato valutato attraverso una scala visuo-analogica da 0 a 10 (VAS).

Risultati: in condizioni basali 40 pazienti presentavano un cistocele di II grado, 15 di III grado e 6 di IV grado. Al follow-up finale, il 95% delle pazienti presentava una riduzione del prolasso di almeno 1 grado; l'85% delle pazienti presentava un prolasso di grado 0 o I, e il rimanente 15% delle pazienti presentavano un prolasso di II grado. Il dolore indotto dal trattamento è stato basso (0.5 VAS). La maggior parte delle pazienti è risultata molto soddisfatta (57%) o soddisfatta (33%) del trattamento. Non sono stati riscontrati eventi avversi durante lo studio.

Conclusioni: i risultati di questo studio pilota suggeriscono che il trattamento con VEL possa determinare un miglioramento del grado di cistocele, inducendo minimi effetti collaterali. Se questi risultati fossero confermati in studi controllati, il trattamento laser potrebbe essere considerato in casi selezionati una valida alternativa non invasiva alla chirurgia.

Parole chiave: prolasso genitale, cistocele, Er:YAG, laser non-ablativo, trattamento non invasivo

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INTRODUCTION

Pelvic organ prolapse (POP) affects a large proportion of middle-aged and older women, with a prevalence of any degree of POP ranging in different studies from 32% to 98%[1–3]. POP is a complex condition of pelvic floor dysfunction, with many contributing factors such as vaginal childbirth, aging, congenital conditions (e.g. collagen defects), raised intra-abdominal pressure, etc.[4]. Many women with lower stage POP are asymptomatic, with only 4-10% of women reporting POP-related symptoms[5–7]. Women with symptomatic POP experience a sensation of vaginal bulging or a visible bulge protrusion in higher POP grades, with difficulties in sitting, walking, sexual intercourse and many other everyday activities[4]. Although POP is not a life-threatening condition, its symptoms have a severe impact on patients' quality of life and wellbeing. POP also represents a significant public health expense, being a frequent cause for major gynecological surgery[4]. Current management options for POP include conservative management, such as physical therapy and vaginal pessaries, as well as various surgical procedures. Vaginal pessaries have been in use for a long time because of their low invasiveness[8,9]. However, their use is characterized by a high discontinuation rate, mainly due to difficulties with inserting/removing the pessary and side-effects, such as infections, bleeding and pain[8,9].

Many patients with POP symptoms ultimately undergo surgical treatment. The lifetime risk of having prolapse surgery before the age of 80 is 11%, with almost a third of patients needing repeated procedures[10]. Different surgical techniques are currently used to treat POP[11]. The methods of choice depend on the type and the severity of prolapse. In recent decades, transvaginal insertion of polypropylene mesh implants has been one of the most popular options, although they are associated with a high rate of side effects[12].

Prolapse of the bladder into the anterior vaginal compartment, or cystocele, is the most frequent type of POP - roughly one third of POP patients suffer from cystoceles[3]. The anterior wall of the vagina is a very important structure for pelvic floor support, which provides a hammock-like support to the upper-lying urethra and the bladder[13]. According to the integral theory of Petros and Ulmsten, the connective tissue in the anterior vaginal wall has an important role in supporting the bladder. Vaginal laxity resulting from childbirth trauma and aging-related collagen degradation can cause the loss of support and contractile strength of the pelvic floor muscles that attach to the anterior vaginal wall. As a consequence, stress urinary incontinence and/or POP arise as typical symptoms of this pelvic floor dysfunction[14,15].

Collagen is the connective tissue component that is most responsible for robustness, stability and plasticity of the vagina. Pulses of laser energy that temporarily increase the temperature of collagen can initiate neocollagenesis and improve collagen structure[16,17]. As a result of the laser-induced temperature increase, intermolecular cross-links that stabilize the collagen triple-helix structure are broken, which leads to the shrinkage of collagen fibrils and an improvement in tissue firmness, followed by neocollagenesis. VEL treatment was recently used in different studies in order to achieve strengthening of the vaginal wall for the treatment of SUI[18–21] and vaginal relaxation[18,22].

In the present pilot study, we evaluated the effects of VEL as a noninvasive, non-surgical treatment for cystoceles.

MATERIALS AND METHODS

This was a prospective, single-center, uncontrolled cohort pilot study. It was conducted between March 2012 and November 2013 and included 61 women older than 18 years of age. The study was approved by the Ethical committee of the Republic of Slovenia and was conducted in accordance with the Declaration of Helsinki. No financial incentives were proposed to the participants.

During the first visit, the eligibility of the patient was verified, a written informed consent was obtained and sociodemographic and clinical characteristics were collected. Inclusion criteria for participation in the study were: the presence of POP symptoms, diagnosis of cystocele of grade II to IV according to the Baden-Walker scale, normal PAP smear, negative urine culture and integrity of the vaginal mucosa (without injuries or bleeding) and voluntary informed consent. Exclusion criteria were: previous POP surgery, pregnancy, intake of photosensitive drugs, vaginal bleeding injuries or infection in the treated area. All the consecutive patients who presented at our clinic during the recruitment period and met the inclusion criteria (and did not meet the exclusion criteria) were included in the study.

Laser therapy was performed using a 2940 nm VEL (SP Spectro, Fotona, Slovenia) with SMOOTH

mode setting, which enables non-ablative, thermal-only operation[18]. The parameters were selected based on extensive preclinical and clinical studies[23–26]. Briefly, Variable Square Pulse (VSP) technology controls the energy and time duration (or pulse width) simultaneously, reducing the power and increasing the pulse duration. The SMOOTH™ mode, with its sequence of low-fluence longer-shaped Erbium pulses, distributes the heat into the mucosa surface, achieving a controlled, deep thermal effect without ablation. Therefore, the Erbium SMOOTH™ mode pulses allow controlled tissue heating in a safe and harmless ambulatory procedure without ablation or carbonization of the tissues, practically avoiding the risk of perforation with accidental lesions of the urethra, bladder or rectum. Each laser treatment session consisted of a full vaginal canal irradiation (using a 360° circular adapter), followed by additional irradiation of the prolapsed anterior wall (using a 90° angular adaptor) and concluded with irradiation of the vestibule area. Depending on the prolapse severity, multiple passes of laser irradiation were applied, with emphasis on the anterior wall irradiation. On average, we used a total of 8 passes per session, delivering in this manner around 1500 J of laser energy to the vaginal mucosa. The VEL procedures were performed in an outpatient clinical setting, without any specific preparation, anesthesia, or post-treatment medications. The treatment time was approximately 15 minutes and the procedure did not require any consumables.

Patients received 2-5 treatment sessions with intervals of 2 months in between the sessions. This time interval is sufficient to allow the neocollagenesis initiated by the previous laser session to proceed[27], and similar intervals were used in previous studies using VEL[26]. The effect of the previous session can thus be seen and the need for additional sessions correctly evaluated. At least two treatments are deemed necessary to provide long-term results. The total number of sessions was dependent on the patients' satisfaction with the result (lack of symptoms) and the physical examination after the 2nd session.

At baseline and at each follow-up visit, a physical examination was conducted, prolapses were photographed, and the prolapse stage was determined in a restful and straining (achieved by coughing) dorsal lithotomy by 2 physicians according to the Baden-Walker scale[28]. The Baden-Walker scale is fast, simple, and has been used widely in recent studies on cystocele repair, with which we wished to compare our results[29]. Follow-up visits were performed at 2, 6 and 12 months after the last VEL procedure.

At each follow up the patients were interviewed about post-op adverse effects and their level of satisfaction. Patient satisfaction with the outcome of treatment was measured on a 4-point scale: not satisfied, partially satisfied, satisfied or very satisfied. Pain during the treatment was measured for every session with a 10-point VAS pain scale.

All the results are reported as the Mean ± SD of absolute values. Statistical significance (α=0.05) was calculated with Crosstabs and the Chi-square test, as well as with one-way ANOVA and Bonferroni tests in SPSS 17.0 (SPSS Science, Chicago, IL, USA) and GraphPad Prism (GraphPad, La Jolla, CA, USA).

RESULTS

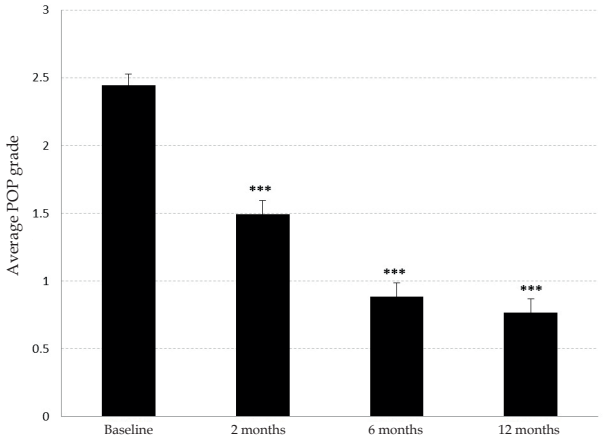
In this study 61 patients suffering from pelvic organ prolapse were included. Their average age was 54.9 ± 9.1years (range: 29-78 years). Mean parity was 2.2 ± 0.8: 42 patients had 2 children (69%), 8 patients had 1 child (13%), 6 patients 3 children (10%), and 3 patients 4 children (5%). Only 2 patients (3%) were nulliparous. The average BMI was 25.5 ± 3.1 (range: 19-32). Distribution of cystocele stages according to the Baden-Walker (BW) scale at baseline is reported in Table 1. Twenty patients (33%) had had a hysterectomy, 40 patients (66%) had a concurrent rectocele and 8 patients (13%) had a concurrent uterine prolapse. No patient had had previous POP surgery. 7% of the patients underwent two procedures, 60% three, 26% four and 7% underwent five procedures.

There was a significant improvement in BW grade already after the first laser treatment ($p<0.001$). At the time of first follow-up, 48% of the patients improved to BW grades 0 or 1 (**Table 1**).

Table 1.
Distribution of cystocele stages according to the Baden-Walker scale (BW Grade) at baseline and at three follow-ups

BW Grade	Baseline (n=61)	FU-1 (n=61; 2 months)	FU-2 (n=61; 6 months)	FU-3 (n=52; 12 months)
0		7 (12%)	21 (35%)	20 (39%)
I		22 (36%)	28 (46%)	24 (46%)
II	40 (66%)	27 (44%)	10 (16%)	8 (15%)
III	15 (24%)	5 (8%)	2 (3%)	
IV	6 (10%)			
Average grade	2.4	1.5	0.9	0.8

The differences between average prolapse grades at baseline and at each follow-up were highly statistically significant (p<0.001, **Fig. 1**).



*** -statistical significance, p<0.001

Figure 1.
Average cystocele stages before VEL treatment and at 3 follow-ups. The bars show mean POP grade value ± SEM

Additional laser treatments brought additional improvement in BW grade. By the second follow-up, 81% of patients had improved to a grade 0 or 1 cystocele (Table 1). At the third follow-up, there were no longer any patients with a cystocele stage above 2 (Table 1). 39% had normal organ position (grade 0 cystocele) and a further 46% of the patients were asymptomatic with a grade 1 cystocele (Table 1).

On average, cystoceles improved by 1.6 grades (**Fig. 2**) and 95% of cystoceles improved by at least one grade. After the final treatment 57% of the patients were very satisfied with the outcome, 33% were satisfied and 8% were partially satisfied. Only 1 patient was not satisfied with the outcome (2%).

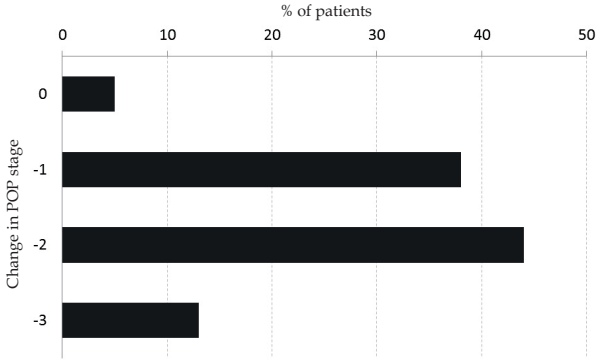


Figure 2.
Cystocele grade reduction after VEL treatment from baseline to the last follow-up. Bars present mean values. 13% improved by 3 grades, 44% by 2 grades and 38% by one grade. 5% did not improve. The average improvement was 1.6 grades

Treatment discomfort was very low; the average pain level on a 10-point VAS scale was 0.49 during the first procedure, 0.22 during the second and 0.17 during the third procedure. There were no adverse effects reported.

Many of the patients had concurrent rectoceles or uterine prolapses at baseline. These prolapses also improved after the laser treatment of cystoceles, but as the treatment of cystoceles was the main objective of our study, these improvements are not described here.

Baseline cystocele grade had a significant (p=0.007) effect on the reduction in BW grade at the final follow-up. The majority of patients with grade 2 cystoceles at baseline improved to grade 0 (50%) or grade 1 (43%) after laser treatment, but some 7% remained at grade 2. 20% of the patients with grade 3 cystoceles at baseline improved to grade 0 after treatment, 40% improved to grade 1 and the remaining 40% to grade 2. Of all the patients diagnosed with the severest POP (grade 4), a full 83% improved to grade 1 and the remaining 17% to grade 2. All the patients diagnosed with either grade 3 or 4 cystoceles therefore showed improvement after treatment.

There were no statistically significant differences in improvement between patients with or without a hysterectomy. For patients that had undergone hysterectomy, the treatment was a full success (grade 0 cystocele) in 40% of the cases. The final diagnosis was grade 1 for 35% and grade 2 for the remaining 25%. Patients without a hysterectomy procedure were diagnosed at the end of treatment with grade 1 cystocele in 51% of the cases, grade 2 in 12%, while 37% were grade 0.

DISCUSSION

The results of this preliminary pilot study suggest that the nonablative VEL is an effective and safe tool for the treatment of cystoceles. In most of the patients the improvement occurred after the first treatment, with patients reporting better prolapse containment inside of the vaginal canal and less frequent occurrence of the prolapse falling out of vaginal canal. Further treatments induced additional improvement in up to 85% of patients to grade 0 or 1 cystocele. In comparison, 3 years after POP surgery 93% of patients had grade 0 or 1 cystocele[29]. However, VEL has none of the side effects of POP surgery (fever, urinary retention, de novo urinary incontinence, mesh extrusion, mesh retraction, dyspareunia, chronic pelvic pain)[29].

A typical example of prolapse improvement after laser therapy is shown in **Fig. 3**, while **Fig. 4** presents the improvement of a large (grade 4) prolapse in a 66-year-old patient.

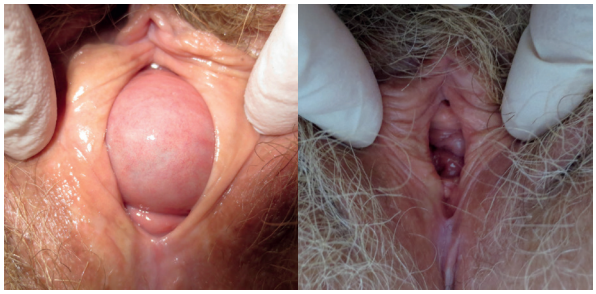


Figure 3.
Pelvic organ prolapse in a 63 year old woman (a) before and (b) after 3 laser treatments

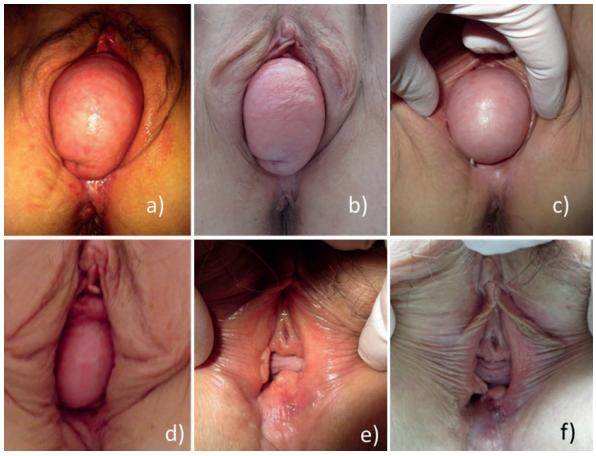


Figure 4.
Reduction of grade 4 prolapse in a 66 year old woman with 4 vaginal deliveries after the laser therapy: (a) before the therapy, (b) one month after the first session, (c) one month after the second session, (d) one month after the third session, (e) 3 months and (f) 6 months after the last (fourth) session.treatments

There were no significant differences in prolapse improvement with respect to the patients' ages or with respect to the number of procedures applied. The decision about the number of treatments was based on the level of improvement observed after the second procedure. The patients with lower rates of improvement received additional treatments. The largest group of patients (60%) received three procedures; the second largest group (26%) received four procedures.

Twenty patients included in this study (33%) had previously undergone hysterectomy. Although hysterectomy is recognized as a risk factor for POP[30,31] previous hysterectomy did not significantly affect the outcome of VEL treatment in this study. The laser treatment was successful (post-treatment BW grades 0 or 1) in 75% of post-hysterectomy patients.

There is a well-established connection between collagen deficiency and the occurrence of POP. Lammers et al.[32] compared the incidence of various collagen disorders between POP patients and a control group and found a significantly higher prevalence of other collagen-related disorders, such as varicose veins, joint hypermobility and rectal prolapse, in the POP group. Han et al.[33] have observed abnormal connective tissue architecture, decreased collagen expression and increased frailness of the tissue in patients with POP and SUI. Genetic collagen-associated disorders have also been associated with an increased incidence of POP[34].

In this pilot study, we report a novel approach of treating cystocele using a VEL thermal-only treatment. The idea comes from pilot studies of a laser therapy designed for the treatment of vaginal relaxation syndrome and stress urinary incontinence that reported improvement of POP as an additional effect[18]. The treatment uses innovative low-fluence pulse sequences (SMOOTH™ mode) to achieve precise heating of the tissue up to 65°C without causing ablation or damage to the epithelium. Pulses of heat in the range of 60-65°C have been shown to achieve immediate shrinkage of collagen, while maintaining its structure without destruction[16,17]. Besides the immediate shrinkage of collagen, heat pulsing stimulates the synthesis of new collagen, as the heat induces a heat-shock healing response[17,27]. Stacking of low-fluence pulse sequences has been shown in numerical models[35], as well as animal[36,37] and human studies[38], to be effective in shrinking the collagen in the dermis up to a depth of several hundred micrometers, without causing damage to the epidermis.

The above-mentioned principle was applied in several studies that aimed to treat different conditions arising from pelvic floor dysfunction, such as vaginal relaxation and stress urinary incontinence (SUI)[18,23–26]. Recently, Gambacciani et al.[20,21] have reported a study using the non-ablative VEL for the treatment of genitourinary symptom of menopause, with a significant decrease in symptoms of SUI in a subset of incontinent women[20,21].

The overall success rate (post-treatment BW grade 0 or 1) in our study was 85%. Surgical methods can achieve higher cure rates, but are also associated with higher costs and a higher rate of side effects and re-operation[1,10,29].

The most popular method for cystocele treatment in the past decade has been surgical insertion of polypropylene meshes[11,12,29]. There has been a lot of controversy regarding polypropylene meshes following their reclassification by the FDA into high-risk Class III medical devices due to numerous side effects[39,40]. These developments have emphasized the lack of effective and safe therapies for POP. We believe that the minimally invasive VEL treatment could play an important role in the future as an intermediate step between currently available conservative therapies and surgery. Many of the patients in this study enlisted due to a fear of surgery or because they already had undergone previous surgery (e.g. hysterectomy) and were trying to avoid or postpone re-operation. The large majority of the patients were satisfied with the procedure and the results of the therapy.

The follow-up in this study showed that the results of laser treatment could last at least 12 months. Long-term experiences with the same Er:YAG modality in aesthetics and dermatology suggest that the procedure could be safely repeated several times. Therefore, it can be suggested that for long-term maintenance, patients could be offered repeated treatments when the VEL effects start to fade.

One of the limitations of the present study is the lack of a control group. POP is a dynamic state, and several studies show that with observation alone, POP can progress as well as regress. However, the expected spontaneous regression rate is very low and much lower than natural progression rates[41,42]. Since our results show a regression of cystocele grade in up to 95% patients, this dramatic improvement cannot be explained by natural POP regression.

In conclusion, this pilot study indicates that the non-ablative VEL treatment can improves cystoceles with minimal patient discomfort and no adverse effects. If these preliminary results will be confirmed in further, properly designed, controlled studies, VEL could be offered as a new, safe and effective option to treat cystoceles as a minimally invasive alternative to surgery in properly selected patients.

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