Efficacy of Fractional CO_2 Laser for the Treatment of Female Stress Urinary Incontinence Grade I

Puckjira Iaocharoen MD*,
Orawan Lekskulchai MD*, Chamnan Tanprasertkul MD*

** Department of Obstetrics and Gynecology, Faculty of Medicine, Thammasat University, Pathumthani, Thailand*
*** Urogynecology clinic, Department of Obstetrics and Gynecology, Faculty of Medicine, Thammasat University, Pathumthani, Thailand*
**** Center of excellence in Applied Epidemiology, Faculty of Medicine, Thammasat University, Pathumthani, Thailand*

Objective: *To study the efficacy of fractional carbon dioxide (CO_2) laser for treatment of stress urinary incontinence (SUI) grade I.*
Material and Method: *A prospective single arm clinical trial was conducted from December 2015 to February 2016 at Thammasat University hospital, a tertiary care center in Thailand. Women with SUI grade I were recruited and treated with fractional CO_2 laser for 3 episodes, 4-week interval. Pre and post-treatment SUI symptoms, bladder neck descent (BND) and the Q-tip test were compared. The study hypothesis was that fractional CO_2 laser could improve the anatomical changes of the vaginal wall under the bladder neck and help strengthen the bladder neck support.*
Results: *Fifty women of mean age 55.4 years with SUI grade I were recruited. The frequency of SUI grade I and nocturia decreased significantly after laser treatments. The average of pre-treatment BND was 12.03$\pm$7.3 mm and after treatment the average BND was decreased to 8.6$\pm$3.7 mm with statistical significance. The Q-tip test was also significantly decreased. No women had serious complications from the treatment.*
Conclusion: *Fractional CO_2 laser was well tolerated. It seems to improve the anatomical function of the bladder neck which may help improve the bladder neck support and mild stress incontinence. However, further well controlled study need to be done to decrease the confounding factors and biases.*

Keywords: *Stress urinary incontinence, Fractional CO_2 laser, Lower urinary tract symptoms*

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Carbon dioxide (CO_2) laser is one of the most widely used lasers in the field of dermatology[1]. Many studies show that fractional CO_2 laser treatment increased epidermal thickness, collagen and elastic fibers[2-4]. It can induce the dermal extracellular matrix remodeling and provides immediate tissue tightening[3]. The heating effect of fractional CO_2 laser limits to a 100- to 150-µm layer of tissue when use laser pulse at less than 1 millisecond and the laser vaporizes tissue up to 20 to 30 µm per pulse[5].

On gross examination, the thickness of the vaginal wall is about 0.4 mm[6]. The epithelial cell layer comprises of 20 to 30 cell layers; these numbers vary with the menstrual cycle and affect differently in the upper and lower thirds of the vagina[7]. The posterior wall of the urethra is supported by the endo-pelvic connective tissue which consists of collagen, elastin and smooth muscle. It is embedded in the lower third of the anterior vaginal wall and acts as a hammock around urethra and bladder neck[8,9]. Defects in this tissue may result in urethral hypermobility and cause stress urinary incontinence (SUI). In Thailand, the incidence of urinary incontinence in women is approximately 17% with nearly a half having SUI[10]. Among women with SUI, 77.5% reported that their symptoms had an impact on their quality of life. Two thirds of these women had mild symptom which associated with mildly bothersome SUI[11]. The severity of SUI can be evaluated by using Stamey's incontinence scoring system which is based on the patient's history: grade 0 = no incontinence, grade 1 = incontinence with coughing or straining, grade 2 = incontinence with change in position or walking and grade 3 = total incontinence at all times. The anatomical function of the bladder neck can be assessed as urethral mobility by evaluation of the Q-tip test and the bladder neck descent[12].

There is a broad array of treatment options for women with SUI, including lifestyle modification,

Correspondence to:
Iaocharoen P, Department of Obstetrics and Gynecology,Faculty of Medicine, Thammasat University, Patumtani 12120, Thailand.
Phone: +66-93-6416969
E-mail: puckjiraaeocharoen@gmail.com

behavioral intervention, and surgical management. The treatment plan depends on the patient's expectation and the aim of the treatment. For women with SUI grade I, conservative management such as lifestyle and behavioral modification, continent pessary,pelvic floor muscle training, is recommended[13].

In 2013, a CO_2 laser-vaginal probe was developed and a pilot study of its use for treating vulvovaginal atrophy (VVA) was published[14]. Ex vivo and in vivo histological studies showed that fractional CO_2 laser increased and promoted the production of collagen and ground substance and resulted in the restoration of vaginal mucosa[15,16]. The studies of efficacy of fractional CO_2 laser for treatment of vulvovaginal atrophy showed significant improvement of the VVA symptom including sexual function and increasing of vaginal pH. Symptom of SUI was assessed as one of the VVA symptom which seems to be improved after the laser treatment[14].

As there are no data about the laser treatment for SUI in Thai women, we conducted this study to evaluate the efficacy and acceptability of fractional CO_2 laser for treatment of female stress urinary incontinence stage I in Thai women under the hypothesis that the fractional CO_2 laser could help improve the anatomical function of the bladder neck support and improve the mild symptom of SUI.So the BND was used as an objective primary outcome for this study.

Material and Method

Study design

This was a prospective single armed clinical study conducted between December 2015 and February 2016 at Thammasat University Hospital (TUH), a tertiary referral center on the outskirts of Bangkok, Thailand. This study was approved by the TUH ethics committee.

Study population

All women attending the TUH urogynecology clinic with the symptom of stress urinary incontinence grade I, according to Stamey's incontinence scoring system (incontinence with coughing or straining), were asked to join in the study. The exclusion criteria were women with pelvic organ prolapsed more than stage II, severe perineal skin infection, a urinary tract infection, or any clinically significant underlying medical illness that could influence the study outcome e.g. multiple sclerosis, Parkinson's disease, stroke, anomalies of spine and lower back, bleeding disorders, immunocompromising diseases and psychiatric disorders.

Study protocol

After signing the inform consent, all 102 participants were asked to have a mid stream urine analysis. Twenty six women had abnormal urinalysis. They were excluded from the study and sent for appropriated treatment. There were remained 76 women in the study.

On the first visit, the project-assisted nurse did the interview and recorded the general data of these 76 participants including the frequency of the SUI grade I. Then all participants were asked to empty their bladder, change their dresses into the suitable dresses and refer to see the first co-author, an urogynecologist, who could not see any data of the participants. The first co-author did the pelvic organ prolapse assessment and found that 26 women had prolapse more than grade 2. All of these 26 women were excluded from the study. Finally, there were 50 women remaining in the study. The Q-tip testand transperineal ultrasound for evaluating the BND, by the method according to previously published study[17] were done by the first co-author. All measured parameters were recorded in the password locked file.

The fractional CO_2 laser treatment was performed by the author. The SmartXide2V2LR machine (Monalisatouch®, DEKA, Italy) with the setting of dot power 30 watts, dwell time 1,000 µs, dot spacing 1,000 µm and 3 smart stacks was used in this study. During the treatment, the women were asked to slightly bare down for better exposure of the bladder neck (about 3 cm proximal to urethral meatus). Immediately after treatment, all adverse effects occurring during and after the procedure were recorded and any discomfort/ painful was assessed by using the visual analogue scale score (0 = no pain, 10 = extreme pain).

On the second and third visit (4 and 8 weeks after visit 1), all 50 participants come back and were asked for any long term adverse effect and their willing to had another second and third laser treatment before continuing the study by the previous assisting nurse. Then after empting their bladder and changing dresses, they were sent to the laser room and received the second or third laser treatment with the same setting as previously mentioned by the author. Any adverse effects or discomfort/painful were asked and recorded immediately after each treatment.

In the last visit (12 weeks after visit 1), all 50 participants still remained in the study. They were interviewed by the assisting nurse about any long term adverse effect and frequency of the SUI grade I. The first co-author did the Q-tip test, and evaluated the

BND by using transperineal ultrasound. All data were recorded and prepared for statistical analysis.

After each laser treatment, all women were not allowed to use any vaginal solutions/other substances for three days and should not have sexual intercourse for at least 48 hours.

Statistical analysis

IBM SPSS Statistics Software (23.0, SPSS Inc., Chicago, IL, USA) was use for data analysis. The difference between pre and post treatment ordinal data of the frequency of SUI grade I were analyzed by using Chi-squared or Fisher'sexact test. Paired t-test was used to assess the difference between pre and post-treatment continuous data of BND and the Q-tip test. A *p*-value <0.05 was considered statistically significant.

Results

From December 2015 to February 2016, 102 women were screened and 50 were recruited into the study. The mean age was 55.4 years; other general characteristics are shown in Table 1. Half of the women were in menopausal period.

Table 1. General characteristics of patients with Stamey grade 1 stress urinary incontinence

General characteristic	
Age (mean ± SD, years)	55.4±9.6
BMI (mean ± SD, kg/m^2)	24.7±2.9
Parity (median, range)	2 (0 to 6)
Menopause % (n)	50 (25)
Systemic HRT % (n)	4 (2)
Previous vaginal delivery % (n)	60 (30)

HRT = Hormone replacement therapy

Before treatment, no women had BND more than 25 mm. and the maximal pre-treatment BND was only 22.4 mm. The mean BND and Q-tip test were decreased significantly after 3-laser treatment (Table 2).

Before laser treatment, 30 (60%) of 50 women had urinary incontinence when coughing or straining less than 1 time per weeks, 14 (28%) women had grade I SUI at least 1 time per day and 6 (12%) had more than 2 times per day. The comparison of the frequency of SUI grade I between pre and post- laser treatment was shown in Table 3. Four weeks after the last third laser treatment, 15 (30%) women did not have any SUI.

Only mild discomfort and minimal abrasion were seen in two women after the first laser treatment and in one woman after the third treatment. There was no serious short term adverse effect or long term complication after each laser treatments. The visual analog scale score for evaluation of the patients' discomfort /pain during and after all treatments was 0 to 3, meaning of only mild symptom.

Discussion

This prospective, single-armed clinical trial study enrolled 50 women with Stamey grade I SUI and found that the fractional CO_2 treatments using a 90° vaginal probe targeted at the area under bladder neck may help improve anatomical function of the bladder neck support. As in this study, the average BND before treatment significantly decreased when compared with

Table 2. Comparison between pre-treatment and post-treatment parameters of SUI

SUI parameters	Pre-treatment	Post-treatment	*p*-value
Bladder neck descent (mm ± SD) (range)	12.03±7.3 (2.0 to 22.4)	8.6±3.7 (2.0 to 17.0)	0.002
Q-tip test (degree ± SD)	32.7±5.8	30.0±2.1	0.003

Table 3. Comparison between pre- and post-treatment frequency of SUI grade I

SUI grade I	Pre-treatment (%, n)	Post-treatment (%, n)	*p*-value
None	0	30 (15)	
<1 time/week	60 (30)	56 (28)	<0.001
At least 1 time/day	28 (14)	4 (2)	
≥2 times/day	12 (6)	10 (5)	

BND after treatment. While the cutoff value of BND for diagnosis of SUI is 25 mm[18], the maximum BND value in this study group was only 22.4 mm. This may probably due to the women in this study had only mild SUI and they would havea little defect ofthe support so we could not see the significant high mobility of the bladder neck in thisstudy group. However, after receiving 3 laser treatments, the BND decreased significantly.

The Q-tip test, the angle with straining of more than 30 degree is considered abnormal[19]. The average straining angle was 32.4 degree before treatment and after treatment the average angle was 30.0 degree with a statistical significant difference. Both BND and Q-tip test as the objective assessments of the laser treatment seem to support the hypothesis.

For the subjective assessment, the frequency of the SUI grade I before and after laser treatment, fifteen (30%) women had no SUI after treatment. There was a significantly decreasing in the frequency of SUI grade I when compare between pre and post treatment groups. However, only one from six women who had mild SUI more than 2 times per day reported decreasing of frequency after treatment.

About the treatment technique, all women were satisfied with the procedure and no serious short termed or long termed adverse effect was found. The pain scores were very low in the range of 0 to 3. And no patients dropped out from the study.

This study could support our hypothesis that the fractional CO_2 laser could help improve the anatomical function of the bladder neck support by using the objective assessments as BND and Q-tip test. The statistical changes of these outcomes after treatment could imply the efficacy of fractional CO_2 laser on the SUI grade I. However, the limitation of this study was the small sample size and half of the women in this study were in postmenopausal period that could be a confounding factor. A trophic vagina is an important risk factor of stress incontinence and there are some studies shown that fractional CO_2 laser could be used as an alternative treatment for this symptom[14,20]. Even though these anatomical changes had statistical significant difference between pre and post BND and Q-tip test, these changes were very small and might not have clinical significance for the patients. Since this study included the women with stress incontinence grade I and there was no comparing intervention, the statistical significant improve in the frequency of the symptom that shown in the study might be from the placebo effect. Due to the limitations of the study including the small sample size, high number of menopausal women and placebo effect, we could not clearly conclude that the fractional CO_2 laser has a good efficacy and can be used for the treatment of stress incontinence. Whether this laser treatment seems to be worldwide acceptable and satisfied by the women as all 50 Thai women in this study and it seems to be safe without serious complication, the physician should not introduce this procedure to their patient with stress incontinence as an alternative treatment. The further well-controlled large clinical comparing trial with long term observation need to be conducted to confirm the its efficacy and cost-effectiveness.

Conclusion

This first study of fractional CO_2 treatment in Thai women with grade I stress urinary incontinence. They were all accepted and satisfied with the procedure. It is safe without any serious short termed adverse effect but it lacks for long term observation. This study could not clearly confirm the efficacy of the fractional CO_2 laser for treatment of SUI grade I because of some limitations of the study. The physician should not advice this treatment technique to their patient with stress incontinence.

What is already know on this topic?

In dermatological field, fractional CO_2 laser can increase the thickness of the epithelial cell layers as shown in many macro-and microscopic studies.

What this study adds?

In gynecologic field, fractional CO_2 laser can help improve the vulvovaginal atrophic symptoms in menopausal women and seems to increase the vaginal epithelial cell layer in a small histological study. About the stress urinary incontinence, there are some studies reported the significant improvement of the mild symptom of SUI in western women.

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Potential conflicts of interest

None.

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ประสิทธิผลของการใช้คาร์บอนไดออกไซด์เลเซอร์ในภาวะไอจามปัสสาวะเล็ดระยะ 1

ภัคจิรา เอี่ยวเจริญ, อรวรรณ เล็กสกุลไชย, ชำนาญ แท่นประเสริฐกุล

วัตถุประสงค์: เพื่อศึกษาประสิทธิผลประสิทธิผลของการใช้คาร์บอนไดออกไซด์เลเซอร์ในภาวะไอจามปัสสาวะเล็ดระดับ 1

วัสดุและวิธีการ: การศึกษาทดลองแบบไปข้างหน้าทำในช่วงระหว่างเดือนธันวาคม พ.ศ. 2558 ถึง เดือนกุมภาพันธ์ พ.ศ. 2559 ที่ รพ. ธรรมศาสตร์เฉลิมพระเกียรติ โดยอาสาสมัครที่มีภาวะไอจามปัสสาวะเล็ดระยะแรกจะทำการรักษา โดยใช้เลเซอร์ทางช่องคลอด 3 ครั้ง และเปรียบเทียบการรักษาก่อนและหลังในงานวิจัยนี้มีการทำ Bladder neck descent (BND) and Q-tip test เพื่อเปรียบเทียบกันก่อนและหลังการรักษาด้วยเช่นกัน ภายใต้สมมติฐานของงานวิจัยนี้คือการใช้ fractional CO_2 laser สามารถทำให้เกิดการเปลี่ยนแปลงทางกายภาพของผนังช่องคลอดใต้คอกระเพาะปัสสาวะและช่วยเพิ่มความแข็งแรงของส่วนค้ำยันของคอกระเพาะปัสสาวะ

ผลการศึกษา: อาสาสมัคร 50 คนที่มีภาวะไอจามปัสสาวะเล็ดระยะแรกมีอายุเฉลี่ย 55.4 ปี และพบว่าปัญหาภาวะไอจามปัสสาวะเล็ดระยะแรก และอาการปัสสาวะตอนกลางคืนลดลงอย่างมีนัยสำคัญ เมื่อเปรียบเทียบก่อนและหลังรักษาค่าเฉลี่ยของคอกระเพาะปัสสาวะ (bladder neck descent) ก่อนการรักษาเท่ากับ 12.03±7.3 มิลลิเมตร เมื่อเปรียบเทียบกับค่าเฉลี่ยหลังการรักษา 8.6±3.7 มิลลิเมตร ซึ่งลดลงอย่างมีนัยสำคัญค่า Q-tip test ลดลงอย่างมีนัยสำคัญ อาสาสมัครทุกคนไม่มีภาวะแทรกซ้อนที่รุนแรง

สรุป: การรักษาโดยใช้ Fractional CO_2 laser ดูเหมือนสามารถทำให้ลักษณะทางกายภาพของคอกระเพาะปัสสาวะดีขึ้น ซึ่งอาจช่วยปรับปรุงส่วนที่ช่วยพยุงคอกระเพาะปัสสาวะ ลดอาการไอจามปัสสาวะเล็ดที่ไม่รุนแรงอย่างไรก็ตาม ควรจะมีการศึกษาที่มีการควบคุมที่ดี เพื่อลดปัจจัยรบกวนและอคติที่อาจเกิดขึ้นระหว่างการวิจัย