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ORIGINAL ARTICLE

Fractional CO_2 laser treatment for women with stress predominant urinary incontinence: a randomized controlled trial

Teerayut Temtanakitpaisan[1] · Chompilas Chongsomchai[1] · Pranom Buppasiri[1]

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Abstract

Introduction and hypothesis To evaluate the efficacy of vaginal CO_2 laser in women with stress predominant urinary incontinence (SUI) compared with the sham treatment.

Methods A randomized controlled trial with sham treatment was conducted between January 2019 and April 2021. Women with predominant SUI were recruited and randomized into two groups: the CO_2 laser group (n = 29) and the sham group (n = 30). The International Consultation on Continence Questionnaire—Urinary Incontinence Short Form (ICIQ-UI SF) was used to evaluate the efficacy at 3 months postoperatively. All participants in both groups were advised to perform pelvic floor muscle training (PFMT) after the intervention.

Results A total of 59 women were studied. A total of 29 women were included in the CO_2 laser group and 30 women were included in the sham group. The baseline scores of the ICIQ-UI SF were similar in both groups. A significant improvement in urinary incontinence scores was found in both groups 3 months after treatment ($p < 0.001$). However, there were no statistically significant differences between the two groups at 3 months ($p = 0.8281$). There were no changes in bladder neck descent or levator hiatal area immediately after intervention or 3 months after completion of treatment in either group. Most participants who received the active intervention reported mild vaginal pain during the procedure that resolved spontaneously at the end of treatment.

Conclusions Fractional CO_2 laser treatment does not provide any benefit over the sham technique in alleviating SUI symptoms. The improvement in SUI symptoms in both groups might be related to PFMT.
This study was registered with the Thai Clinical Trial Register (TCTR20190131004).

Keywords CO_2 laser · Randomized controlled trial · Stress urinary incontinence

Introduction

The use of vaginal lasers is increasingly popular in urogynecology. It is a minimally invasive procedure that is considered a treatment for the relief of mild to moderate symptoms of pelvic floor disorders such as stress urinary incontinence (SUI), pelvic organ prolapse (POP) and genitourinary symptoms of menopause. However, there is no strong scientific evidence to confirm the potential benefit of vaginal lasers [1–3] compared to placebo.

Microablative fractional CO_2 lasers and non-ablative Er:YAG lasers are the two types of lasers that are commonly used in the vagina. The changes in the morphology of vaginal tissue due to its thermal effect lead to new collagen synthesis [4]. The pulsed laser photothermal effect stimulates collagen neogenesis and morphological changes in the upper dermis [5, 6] and adjacent pelvic floor tissue [7]. The collagen fibers in the vaginal epithelium are contracted when the temperature increases up to 63 ºC. This temperature also induces the processes of neocollagenesis, elastogenesis, neoangiogenesis, and increased fibroblast activity in the applied area [8]. Moreover, such a promising effect also promotes the density of capillaries and the thickness of the vaginal epithelium [9]. This is more theoretical than scientifically proven.

It is estimated that 25–45% of women experience urinary incontinence [10]. The most common type is stress urinary

✉ Teerayut Temtanakitpaisan
jacktemtanakitpaisan@hotmail.com; teerte@kku.ac.th

[1] Department of Obstetrics & Gynaecology, Faculty of Medicine, Khon Kaen University, 123 Mittraphap Highway, Muang Khon Kaen, Khon Kaen 40002, Thailand

incontinence, which is the involuntary loss of urine resulting in a sudden increase in abdominal pressure, for example, from physical exertion, sneezing, or coughing [11]. The loss of anatomical support causing pelvic floor weakness or bladder neck hypermobility and/or urethral sphincter deficiency are the causes of SUI in the majority of patients [12, 13]. The effect of SUI on quality of life depends on the severity of symptoms. There are many modalities to improve such symptoms. Pelvic floor muscle training, avoiding activities that increase intraabdominal pressure suddenly, can alleviate SUI symptoms. If the symptoms do not improve satisfactorily, surgery is often the next step. While surgery is often considered the most effective method to relieve the SUI symptoms, adverse events, while uncommon, are still reported. Vaginal CO_2 lasers are considered to be a minimally invasive therapy and are often considered a step to relieve symptoms before surgery [12, 13].

The data from Han et al. [14] established the association of collagen and SUI. Women with SUI had significantly lower expression levels of type I and type III collagen than women without SUI ($p < 0.01$); therefore, any interventions (i.e., vaginal laser application) that stimulate collagen production might improve SUI symptoms.

The aim of our study was to compare the efficacy of vaginal CO_2 lasers to sham therapy in women with SUI immediately following therapy and at 3 months posttreatment.

Materials and Methods

A randomized controlled trial with the sham technique was conducted in the female pelvic medicine and reconstructive surgery unit, Department of Obstetrics and Gynaecology, Faculty of Medicine, Srinagarind Hospital, Khon Kaen University, Thailand, from January 2019 to April 2021. This study was approved by the Khon Kaen University Ethics Committee for Human Research (HE611135).

Women with SUI and mixed urinary incontinence, stress predominant, were recruited for this study. Patients with pelvic organ prolapse stage II or more, those with a history of recurrent UTI, previous anti-incontinence surgery, body mass index (BMI) > 30 kg/m^2, use of hormonal treatments in postmenopausal women, current use of drug treatment for urinary incontinence, pain in the vagina with or without sexual intercourse, pregnancy, current active vaginal infections, abnormal uterine bleeding with unknown causes, and a history of vaginal laser treatment were excluded. This trial was performed and reported following the CONSORT statement and was registered with the Thai Clinical Trial Register (TCTR20190131004).

The participants who met the inclusion criteria were randomly allocated using computer generated randomization into two groups. All randomization sequences were kept in sequentially numbered opaque seal envelopes. The participants and assessor were blinded.

The intervention group was treated with transvaginal fractional microablative CO_2 lasers (MonaLisa TouchTM®; Deka, Florence, Italy). Applicators of 360° and 90° were used. The rotational and withdrawal technique was performed after insertion of the 360° applicator using the entire length of the vagina. The CO_2 energy was administered according to the product instructions. The 90° applicator was subsequently applied to the suburethral area of the anterior vaginal wall with a power setting of 40 W, 1000 µs of pulse duration, and 1000 µm spacing. The administration of CO_2 was applied four times, 28–35 days apart on an outpatient basis. All participants were advised to avoid sexual intercourse for a week following treatment. Women in the sham group were treated in the same manner as the intervention group but with no energy administered. There was noise from the machine without power. The same urogynecologist performed both interventions. All participants in both groups were advised to perform pelvic floor muscle training regularly after the intervention and were provided handouts.

The validated Thai version of the International Consultation on Incontinence Questionnaire—Urinary Incontinence Short Form (ICIQ-UI SF) questionnaire [15] was used to evaluate symptoms. All women were studied using 4D transperineal pelvic floor ultrasonography before and immediately after four courses of CO_2 energy administration and at 3 months after treatment.

The sample size was calculated using a 90% power and 0.05% level of significance to detect a difference in the ICIQ-UI SF score of 3 points, which was considered to be clinically significant. A 20% dropout rate was also considered [16].

Statistical analyses were performed using Stata 10 (Stata Corporation, College Station, Texas). Baseline characteristics are presented as descriptive information. Student's t test was used to compare continuous variables. The chi-square or Fisher's exact test was employed to compare categorical variables. Differences between the comparison groups were evaluated as the mean difference (MD) or relative risk (RR) with a 95% confidence interval (CI). Statistical analysis was conducted using mixed analysis of variance. A p *value* < 0.05 was considered to be statistically significant. All analyses were carried out based on the intention-to-treat analysis.

Results

A total of 64 participants were assessed for eligibility. Four participants did not meet the inclusion criteria, and one refused to participate in the study. Therefore,

59 participants were randomized into two groups; 29 women in the CO_2 laser group and 30 in the sham group, as shown in the CONSORT flow diagram (Fig. 1). During the follow-up time, three participants withdrew from the study for personal reasons. Twenty-eight patients in the CO_2 group and 28 patients in the sham group were studied using an intention-to-treat basis.

Patient characteristics are shown in Table 1. The percentages of SUI and MUI were not different between the two groups. The baseline scores of the ICIQ-UI SF were similar in both groups. There was no statistical significance in bladder neck descent or levator hiatal area between the two groups.

The urinary incontinence symptom scores improved significantly in both groups ($p < 0.001$ and $p < 0.001$, respectively). However, there were no statistically significant differences between the two groups immediately after four laser treatments ($p = 0.9129$) or 3 months after the last application of CO_2 energy ($p = 0.8281$) (Table 2).

There were no changes in bladder neck descent immediately after intervention ($p = 0.5414$) or 3 months after completion of treatment ($p = 0.4803$) in either group, and the area of the levator hiatus at rest as well as the levator hiatal area on the maximal Valsava did not change significantly in the CO_2 laser or the sham group immediately after treatment or 3 months after completion of treatment. However, the

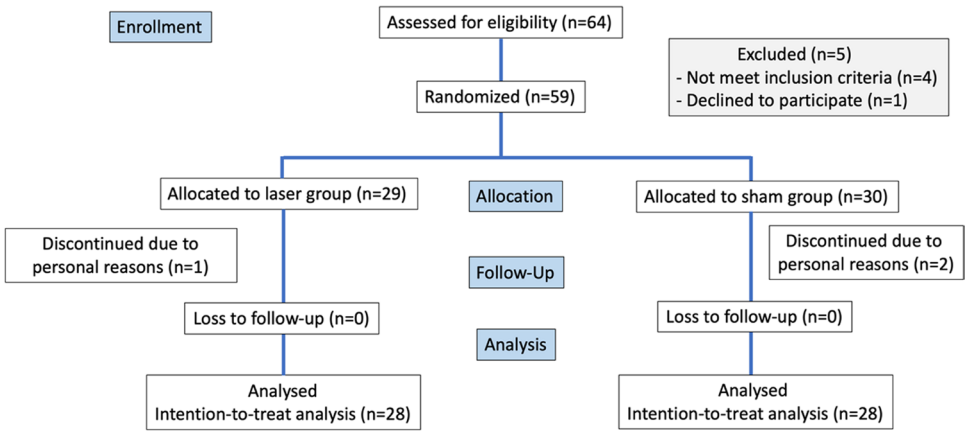

Fig. 1 CONSORT flow diagram

Table 1 Baseline characteristics N = 56

	CO_2 laser n = 28	Sham n = 28	*p*-value
Age, mean (SD)	49.7 (10.9)	52.8 (11.8)	0.316
Menopausal status, n (%)	14 (50.0)	14 (50.0)	0.060
Parity			
-Nulliparous, n (%)	2(7.1)	1(3.6)	> 0.999
-Parous, n (%)	26 (92.9)	27 (96.4)	
BMI, mean (SD)	23.19 (3.15)	23.16 (2.48)	0.9739
Diagnosis			
-SUI, n (%)	19 (67.9)	22 (78.6)	0.3653
-MUI, n (%)	9 (32.1)	6 (21.4)	0.3653
ICIQ-UI SF score pre-treatment, median (IQR)	10 (7, 14.5)	9 (7, 12.25)	0.4152
Pelvic floor ultrasonography			
Bladder neck at rest (mm), median (IQR)	25.95 (23.6,28.08)	27.95 (25.6,28.95)	0.1424
Bladder neck on maximal Valsalva (mm), mean (SD)	9.99 (8.56)	8.66 (9.52)	0.5852
Bladder neck descent (mm), mean (SD)	15.57 (9.52)	18.04 (11.06)	0.3746
LHA at rest (cm^3) mean (SD)	20.33 (5.37)	21.26 (3.39)	0.444
LHA on maximal Valsalva (cm^3), mean (SD)	24.6 (7.48)	28.15 (6.18)	0.058
The differences of LHA (cm^3), mean (SD)	4.27 (5.25)	6.89 (5.12)	0.063

BMI, body mass index, *SUI*, stress urinary incontinence, *MUI*, mixed urinary incontinence, *ICIQ-UI SF*, International Consultation on Incontinence Questionnaire-Urinary Incontinence Short Form, *LHA*, levator hiatal area

Table 2 The changes after treatment and 3 months later among two groups (N = 56)

	CO_2 laser n = 28	Sham n = 28	*p*-value
The changes of ICIQ-UI SF score			
after treatment, mean (SD)	-3.86 (3.94)	-3.57 (3.33)	0.9129
3 months follow up, mean (SD)	-3.54 (3.97)	-3.32 (3.36)	0.8281
Pelvic floor ultrasonography			
Bladder neck descent			
after treatment, mean (SD)	18.3 (8.93)	19.02 (9.13)	0.7668
3 months follow up, mean (SD)	19.43 (9.31)	19.89 (7.81)	0.8436
The changes of bladder neck descent			
after treatment, mean (SD)	2.73 (9.72)	0.98 (11.51)	0.5414
3 months follow up, mean (SD)	3.86 (12.51)	1.84 (8.27)	0.4803
LHA at rest			
after treatment, mean (SD)	20.2 (4.62)	22.09 (4.26)	0.118
3 months follow up, mean (SD)	19.82 (3.89)	21.56 (3.94)	0.103
LHA on maximal Valsalva			
after treatment, mean (SD)	24.95 (6.63)	28.48 (5.99)	0.041*
3 months follow-up, mean (SD)	24.81 (6.05)	26.54 (6.27)	0.296
The changes of LHA			
after treatment, mean (SD)	4.75 (3.26)	6.39 (4.18)	0.108
3 months follow up, mean (SD)	4.98 (4.01)	4.98 (3.7)	0.999

ICIQ-UI SF, International Consultation on Incontinence Questionnaire-Urinary Incontinence Short Form, *LHA*, levator hiatal area

area of levator hiatus on maximal Valsalva was significantly reduced in the CO_2 laser group immediately after treatment ($p = 0.041$), as shown in Table 2.

The majority of women treated with CO_2 energy reported that minimal vaginal pain during the procedure resolved spontaneously after finishing the procedure. No one reported vaginal infection or dyspareunia after the procedures.

Discussion

Many prospective observational studies [17–20] have evaluated the effectiveness of CO_2 lasers for treating SUI and many have found that SUI symptoms were improved significantly after CO_2 application (in both subjective and objective outcomes). One study [21] included patients with both SUI and MUI symptoms and reported significant improvement in symptoms after three sessions of fractional microablative CO_2 laser treatment. However, there is little data comparing laser therapy to placebo or sham therapy to establish its contribution to symptom improvement. Therefore, the current randomized sham controlled trial was conducted to evaluate the effectiveness of a CO_2 laser for SUI treatment. This study found that there were significantly improved urinary incontinence symptoms from ICIQ-UI SF scores in both treatment and sham groups, but there were no significant differences in ICIQ-UI SF scores between the groups immediately or 3 months after treatment. This means that the reduction in symptom scores might be due to the recommended pelvic floor muscle exercises or placebo effect.

The data of another prospective randomized trial published in 2022 [22] revealed that both CO_2 lasers and Er:YAG improved SUI symptoms significantly over the sham procedure. These results contradict the findings in the present study. That study and the present study had a similar number of participants, so it is difficult to reconcile the differences. However, the most significant difference between the two studies is that the present study participants were recommended to undergo pelvic floor muscle training. For the present study the authors felt that due to the ethical concerns of not providing any therapy for the sham group, the protocol should include a recommendation for pelvic floor muscle training and a handout on this therapy was provided to both groups. Participants in the present study did not undergo any specific training sessions for pelvic floor exercises. Therefore, the improvement in UI symptom scores in both groups might be due to the additional pelvic floor muscle training recommended in this setting or it might simply be a placebo effect.

In the context of pelvic floor ultrasonography, the thermal effect from the CO_2 application did not show any significant changes to the bladder neck descent when compared to the sham technique. The area of the levator hiatus on maximal Valsalva was significantly reduced in the CO_2 laser group immediately after treatment. It might be the effect of thermal energy that causes collagen tightening around the vaginal hiatus, but the effect did not last long. The differences were no longer detected at the 3-months follow-up exam.

There were few reported adverse events after CO_2 application, with only minimal pain during the procedure that resolved spontaneously, which is similar to other studies [22]. Moreover, there was no report of serious adverse events from vaginal laser [23–26]. This suggests that CO_2 vaginal application is safe with no serious adverse events in the short term. There are no data on long-term adverse events from laser use.

This study set out to explore a randomized placebo/sham controlled trial to investigate the efficacy of CO_2 lasers for treating stress-predominant urinary incontinence. This study did not demonstrate the benefit of CO_2 lasers over the sham technique in terms of SUI treatment. This study enrolled patients with both SUI and MUI, stress predominant, and the sample size, while appropriate, was small. Therefore, RCTs with larger sample sizes should be conducted.

Conclusions

Fractional CO_2 laser treatment did not provide a benefit over the sham technique in alleviating SUI symptoms. The improvement in SUI symptoms might be due to pelvic floor muscle training that was recommended during the study period. There were no changes in bladder neck descent or levator hiatal area immediately after intervention or 3 months after completion of treatment in either group.

Authors' contribution Teerayut Temtanakitpaisan: Protocol development, Data collection or management, Data analysis and Manuscript writing.

Chompilas Chongsomchai: Protocol development and Manuscript editing.

Pranom Buppasiri: Protocol development and Manuscript editing.

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Data Availability The data will be available on request.

Declarations

Conflicts of interest None.

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