



Application of ultra pulse CO₂ lattice laser in the treatment of female urinary incontinence

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Background: This study aimed to explore the application of CO₂ lattice laser in the treatment of mild and moderate urinary incontinence in female patients.

Methods: We analyzed the clinical data of 33 female patients with mild to moderate urinary incontinence from a prospective cohort study, who were treated with FemiLift CO₂ lattice laser instrument (Alma Laser Ltd, Caesarea, Israel) at our hospital from January 2018 to December 2018. All the female patients were married and fertile, with a mean age of (43.15±6.49) years old (35–62 years old). There were 18 participants with mild urinary incontinence and 15 with moderate urinary incontinence. All participants received laser treatment 3 times, with an interval of 30 days. The International Consultation of Incontinence Questionnaire- Short Form (ICIQ-SF) survey was conducted before the treatment, 3 months after, and 6 months after the treatment. A 1-hour urine pad test was used to quantify the leakage of urine. Residual urine and urine routine examination were performed to exclude other combined diseases.

Results: After 3 times of treatment with FemiLift CO₂ laser, 13 cases were cured in 3 months, and 16 cases were cured in 6 months. 10 cases and 15 cases were significantly improved in 3 or 6 months, respectively. 2 patients had no significant changes, and no adverse reactions were recorded. The pad test showed that the symptom of all 33 patients were significantly improved, and the average scores of ICIQ-SF were significantly decreased ($P<0.05$) from 12.36 (Grade I) and 15.67 (Grade II) (5–21) before treatment to 3.73 (Grade I) and 5.49 (Grade II) (1–12) after 6 months of therapy.

Conclusions: The CO₂ lattice laser is safe and effective in the treatment of mild and moderate urinary incontinences in female patients, which can effectively improve the symptom of urinary leakage without obvious adverse reactions.

Keywords: Stress urinary incontinence (SUI); carbon dioxide; laser; treatment

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Introduction

Stress urinary incontinence (SUI) is a common disease in middle-aged and elderly women. In recent years, the incidence of SUI has been increasing alongside the

continuous growth of the aging population, and it has become a common health problem for women. The term SUI refers to the involuntary outflow of urine caused by a sudden increase in abdominal pressure, but it is not caused

Table 1 Baseline analysis

Variable	Grade I	Grade II	P value
Age (year)	36.13±5.39	45.86±7.58	>0.05

by detrusor systolic pressure or bladder wall tension pressure on urine. It is characterized by no enuresis in normal state, and automatic urine outflow when abdominal pressure suddenly increases (1). According to statistics, about 23–45% of women over the age of 20 globally have urinary incontinence, of which SUI accounts for about 50% (2). In Chinese women, SUI has been shown to occur mostly in women aged 45–55 years (3). Age, pregnancy, vaginal delivery, postmenopausal status, and obesity are the main risk factors of SUI (4). Gynecological operations such as uterine prolapse and hysterectomy double the risk of SUI (5).

Therefore, timely and effective diagnosis and treatment of SUI is very important. There are various treatments for SUI, including mid-urethral sling (MUS) and vaginal suspension (Burch colposuspension). These operations have certain surgical risks, such as bleeding, infection, bladder and urethral injury, dysuria, and pain. Laser therapy has become available as a novel treatment for SUI patients in recent years (6–8). Thus far, Erbium:YAG (Er:YAG) laser has been widely studied, but few studies have reported on the application of CO₂ laser in the treatment of SUI, which is worthy of further research to confirm the efficacy. In view of this, we analyzed the clinical data of 33 female patients with mild to moderate urinary incontinence, who were treated with FemiLift CO₂ lattice laser (Alma Medical Laser, Caesarea, Israel) at our hospital from January 2018 to December 2018. The results indicated that CO₂ lattice laser is safe and effective in the treatment of mild and moderate urinary incontinence in female patients.

We present the following article in accordance with the STROBE reporting checklist (available at <http://dx.doi.org/10.21037/tau-21-337>).

Methods

Clinical data

A total of 33 female patients with SUI who were treated at our hospital from January 2018 to December 2018 were selected as the research cohort for this prospective cohort study. All participants were married and fertile, with a mean age of (43.15±6.49) years old (35–62 years). There

were 22 participants with mild incontinence (Grade I) and 11 with moderate incontinence (Grade II), with no significant age between two groups (*Table 1*). All participants completed The International Consultation of Incontinence Questionnaire-Short Form (ICIQ-SF) survey before the treatment. A 1 hour urine pad test was used to quantify the leakage of urine, and other complications were excluded by residual urine examination and urine routine examination. Gynecological examination was conducted to exclude other types of incontinence, including bladder prolapse, uterine prolapse, rectocele, bladder vaginal fistula, and so on. All participants received laser treatment 3 times, with an interval of 30 days. The participants were followed up at 3- and 6 months after the treatment. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Ethics Review Committee of Changzhou Maternal and Child Health Care Hospital (201730). Informed consent was provided by all participants.

Inclusion and exclusion criteria

The inclusion criteria were as follows: (I) normal cytology, human papillomavirus (HPV) and leucorrhea test; (II) negative urine culture; (III) no injury or bleeding in the vaginal cavity, vaginal orifice, and vestibule.

The exclusion criteria were as follows: (I) injury or infection of the treatment area; (II) menstruation and bleeding of the vagina; (III) bladder prolapse, uterine prolapse, rectocele, bladder or vaginal fistula; (IV) pregnancy; (V) malignant tumor, patients who used corticosteroid or sex hormone drugs in the recent 6 months.

Instruments and methods

Instrument

The FemiLift CO₂ laser (Alma Laser Ltd, Caesarea, Israel) concentrated the laser through a holographic lens (30 W, 60–100 mj/ppxl, high energy mode, 0.5 Hz), thus providing micro-burning energy on a total area of 81 mm² (9×9 mm²).

Principle

The treatment utilized a special vaginal probe to shoot CO₂ laser, then to realize the ablation of the tissue surface in a small area and the heat deposition of deeper parts, thus leading to the effect of remodeling collagen and elastic fibers, increasing glycogen synthesis and surface exudation, and so on. Meanwhile, the micro burning effect of CO₂ laser

stimulated the interaction of heat shock proteins (HSPs), and activated fibroblasts to produce extracellular matrix components such as proteoglycan and glycosaminoglycan. Transforming growth factor- β (TGF- β) and epidermal growth factor and fibroblast growth factor (EGF and FGF) play an important role in promoting angiogenesis. In general, the whole process of photo eutrophication involves 3 stages: early heat loss, the proliferation of collagen and extracellular matrix in the medium term, and the final remodeling stage, including synchronous maturation of collagen and neoelastic fibers.

Treatment

At the bladder lithotomy position, the vulva and vagina were cleaned and disinfected (ensuring that the vulva vaginal area was clean and dry without any cream, lotion, or other substances that affect laser emission). The treatment sites were at the 11-12-1 position of 3 planes, including a plane from bladder neck to the middle and lower part of urethra, 1 cm above, and 1 cm below the above plane. Then CO₂ lattice laser was irradiated. The spot diameter was 9×9 mm²; intercourse was forbidden for 1 week after the operation, and sitting in a bath was avoided for 1 week.

Observation and judgment standard

Classification of incontinence

The following grades were used to classify level of incontinence: grade I: the involuntary leakage when coughing, sneezing or carrying heavy objects forcefully; grade II: leakage when walking fast, skipping rope, and exercising slightly; grade III: leakage with the change of body position; grade IV: leakage in a resting state or at night (9).

Questionnaire survey

The full-time nurses were responsible for the questionnaire survey, and the survey results of ICIQ-SF and the satisfaction of patience were recorded and analyzed.

1-hour urine pad test

The clean urine pad was weighed and recorded before inspection, and the participant was instructed to empty the bladder as much as possible and use the clean urine pad. After drinking 500 mL of water within 15 minutes, the patient walked for 30 minutes, including going up and down the stairs. The following exercises were performed within 30 minutes: (I) sitting position to standing position

for 10 times; (II) cough exercise for 10 times; (III) running in place for 1 min; (IV) bend to pick up small objects on the ground for 5 times; (V) wash hands with water for 1 min. Then, the urine pad was removed, inspected, and recorded. The difference between the weight of the pad before and after inspection was calculated as the leakage (1 g = 1 mL urine). Finally the patient drained their bladder, and the amount was recorded. According to the classification of urine leakage, slight incontinence: 1 hour leakage ≤ 1 mL; moderate incontinence: 1 hour leakage >1 mL and <10 mL; severe incontinence: 1 hour leakage >10 mL and <50 mL; extremely severe incontinence: 1 hour leakage >50 mL. Results: (I) weight gain of the urinary pad >1 g was considered positive, (II) the weight of the pad >2 g, attention should be paid to whether there were weighing errors, sweating, and vaginal secretion; (III) weight gain of the urinary pad <1 g, indicating that a basic drying or experimental error was found (10). Efficacy of the treatment was judged by: the number of leakages, decrease of urine leakage, whether subjective consciousness was improved, and whether the grade of stress incontinence was degraded or not. In the assessment of postoperative complications, the participants were followed up regarding residual urine volume and flow rate at 3- and 6 months after the operation to further clarify whether there was urethral stricture or not. Participants were asked if they were experiencing any vaginal bleeding, altered frequency of urine, urgency, pain, itching vagina, sexual pain, and other accompanying symptoms

Statistical analysis

Statistical analysis was carried out using the software SPSS 18.0 (IBM Corp., Chicago, IL, USA). The measurement data were expressed as mean \pm standard deviation ($\bar{x} \pm s$), compared with *t*-test, and a P value <0.05 was considered statistically significant

Results

Therapeutic efficacy

As shown in *Table 2*, a total of 33 patients were recruited, and after 3 rounds of FemiLift CO₂ laser treatment, 13 cases and 16 cases were cured at 3 months and 6 months after operation, respectively. A total of 10 cases and 15 cases were significantly improved at 3 months and 6 months after operation, respectively, and 2 cases had no significant change. *Table 3* indicated that the mean score of ICIQ-SF

decreased from 12.36 (Grade I) and 15.67 (Grade II) [5–21] before treatment to 3.73 (Grade I) and 5.49 (Grade II) [1–12] at 6 months after treatment, and the difference was statistically significant ($P < 0.05$). *Table 4* showed the effects of different factors on ICIQ-SF score after 6 months of operation based on our current data, the results indicated that the grade of urine leakage was significantly affected the ICIQ-SF score, and the disease duration, and preoperative urine pad test was near the critical value, while the rest of the factors had no effects on the score.

Discussion

Women with SUI may leak urine during coughing, laughing, vigorous exercise, and so on. Severe SUI can involve urine leakage when standing or walking, which can seriously affect daily work and life, and reduce the quality of life. It has been shown that women with urinary incontinence have lower collagen content in the pubic cervical fascia (11), and that women with SUI have lower collagen content in the anterior vaginal wall (12). *Figure 1* shows a vagina after the first CO₂ lattice laser treatment, in which prominent vaginal wall enlargement can be observed and dotted marks made by the laser beam can be observed.

Table 2 Grading of female patients with SUI before and after CO₂ lattice laser treatment

Time	Grade (n)		
	No leakage	Grade I	Grade II
Before operation	0	18	15
3 months after operation	13	10	2
6 months after operation	16	15	2

SUI, stress urinary incontinence.

Table 3 Comparison of urine pad test and ICIQ-SF score of female patients with SUI before and after CO₂ lattice laser treatment (n=33, $\bar{x} \pm s$)

Variable	Before treatment	3 months after operation	6 months after operation
Urine pad test (g)			
Grade I group	8.19±2.42	1.02±0.54	0.80±0.41
Grade II group	9.09±5.38	2.41±2.29	2.01±1.98
ICIQ-SF score			
Grade I group	12.36	5.78	3.73
Grade II group	15.67	9.82	5.49

ICIQ-SF, International Consultation of Incontinence Questionnaire-Short Form; SUI, stress urinary incontinence.

The photograph in *Figure 2* was taken after the second treatment, and the enlargement of the vaginal wall has improved significantly. The vaginal images in *Figures 3* and *4* were taken 3- and 6 months after treatment, and it can be clearly seen that the vaginal wall swelling had basically disappeared; interview with the patient also revealed that the symptoms of urinary incontinence had completely disappeared.

In this study, CO₂ lattice laser was used to stimulate tissue remodeling by burning superficial cells and activating deep cells. This process involved a small family of proteins, HSPs. Once activated, HSPs can cause changes in cell metabolism and selectively induce the expression of cell surface receptors in treated tissues. The key cytokine TGF- β plays an important role in collagen and extracellular matrix production during inflammation and fibrosis. It can stimulate the metabolism and nutritional recovery of vaginal mucosa, thus improving elasticity and moisture. Local normal tissue cells and blood vessels can quickly promote the local tissue thickness and elasticity (13). The pathological mechanism of SUI is that the loss of urethral supporting structures causes the urethra and bladder neck to descend to different degrees and the closure of bladder neck and urethra to decrease (14). The CO₂ lattice laser can cause collagen and elastic fibers to proliferate and reorganize locally, which both increases the stability and reduces the mobility of the urethra. To enhance the local connection of the vaginal wall and urethral wall, the elasticity of the anterior vaginal wall was increased, and local thickening also improved the stability of the urethra, which achieved good urinary control (15).

In this study, we used the Spearman method to study the correlation of etiology, age, grade of urine leakage, disease duration, obesity index, preoperative pad test, and so on. The results showed that the grade of leakage ($r = -0.348$,

Table 4 Effect of different factors on ICIQ-SF score after 6 months of operation

Factor	Value	Score
Etiology	r	0.157
	P	0.156
Age	r	-0.145
	P	0.191
Obesity index	r	-0.095
	P	0.398
Disease duration	r	0.058
	P	0.667
Grade of urine leakage	r	-0.348
	P	0.007
Preoperative urine pad test	r	-0.321
	P	0.061

ICIQ-SF, International Consultation of Incontinence Questionnaire-Short Form.



Figure 1 Changes of vagina after the first time of laser therapy.

$P < 0.05$) showed a certain correlation with the ICIQ-SF score after treatment; that is, patients with grade II leakage or moderate or severe leakage before treatment had lower comprehensive scores after treatment. Domestic and foreign guidelines also recommend weight loss and continuous pelvic floor exercises to improve mild urinary incontinence. Cumulative studies have shown that patients with mild to moderate SUI experience more benefit after treatment, those with normal BMI benefit more than obese patients,



Figure 2 Changes of vagina after the second therapy (one month) of CO₂ laser.



Figure 3 Changes of vagina after three months' of treatment with CO₂ laser.

and young patients benefit more than older patients. In addition, CO₂ lattice laser is a precise and minimally invasive tool, which can improve the clinical symptoms and quality of life for women with SUI. It can provide a new and convenient treatment to improve urinary incontinence symptoms. The CO₂ lattice laser has many strengths, including being safe, easy to operate, easy to start, painless (no need for local anesthesia), minimally invasive, and time-saving. In recent years, extensive studies and investigations

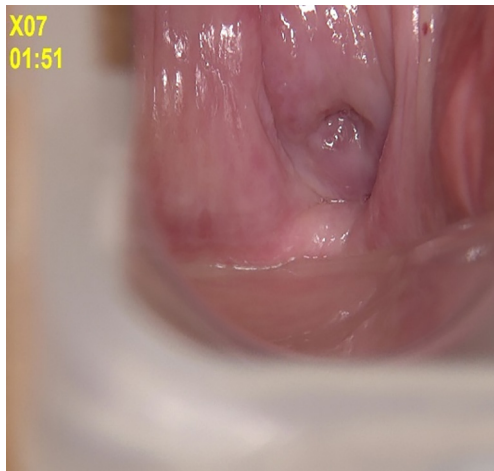


Figure 4 The changes of vagina after finished with six months' of treatment.

of laser therapy have been made by researchers in China and internationally. The shortage of this study was that, the sample size is relatively small, and more patients should be recruited to verify the current conclusions.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are

appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Ethics Review Committee of Changzhou Maternal and Child Health Care Hospital (201730). All enrolled patients voluntarily participated in this study and signed an informed consent form before colposcopic biopsy or treatment.

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