

Evaluation of Fractional CO₂ Laser Treatment Efficacy and Comparison to Vaginal Conjugated Estrogen Cream in Postmenopausal Women with Vulvovaginal Atrophy: A Randomized Clinical Trial

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Abstract

Background: Vulvovaginal atrophy is common and bothersome among postmenopausal women. Hence in this study, the fractional CO₂ laser treatment efficacy was compared with vaginal conjugated estrogen cream in postmenopausal women with vulvovaginal atrophy was assessed.

Materials and Methods: In this randomized clinical trial, 130 consecutive postmenopausal women with vulvovaginal atrophy attending to urogynecologic clinic in Imam-Khomeini hospital in Ahvaz in 2015 were enrolled and were randomly assigned to receive either fractional CO₂ laser treatment or vaginal conjugated estrogen cream. The improvement of vulvovaginal atrophy symptoms, sexual satisfaction and function were compared across the groups after 12 weeks.

Results: There improvement of vulvovaginal atrophy symptoms, sexual satisfaction, and function were 86.2%, 87.7%, and 87.7%, respectively in laser group and 53.8%, 52.3%, and 52.3%, respectively in primarin group showing statistically significant differences (P=0.0001). There were no side effects.

Conclusion: Totally, according to obtained results, it may be concluded that efficacy of fractional CO₂ laser was higher than vaginal conjugated estrogen cream in postmenopausal women with vulvovaginal atrophy.

Keywords: Laser, Vaginal Conjugated Estrogen, Menopause, Vulvovaginal Atrophy

1. Introduction

Menopause is a natural stage in women's life accompanied with decreased estrogen secretion (Minkin, Maamari, & Reiter, 2013; Sparavigna, Tenconi, De Ponti, Bulgheroni, & Scarci, 2013). This reduction is accompanied with multiple alterations in vaginal mucus that may result in vaginal atrophy with symptoms such as dryness, redness, burning sensation, and post-coital bleeding (Mac Bride, Rhodes, & Shuster, 2010; Santoro & Komi, 2009). These symptoms would result in decreased quality of life, self-esteem, sexual satisfaction, etc. (Simon & Komi, 2007). The prevalence rate of vaginal atrophy in women older than sixty years is fifty percent leading to some health concerns in subjects (Suckling, Kennedy, Lethaby, & Roberts, 2006).

When the estrogen level is normal, the vaginal epithelium is wet and thick but estrogen deficiency would develop thin dry layer and for this matter estrogen products are essential to improve such symptoms. However, some studies have shown that hormone therapy in post-menopausal women is accompanied with increased risk of breast cancer, endometrial hyperplasia, thrombosis, and cardiac and cerebral ischemia (Prentice, 2014; Amanlou & Mostafavi, 2017; Salehi, Hadadi, & Tavallaei, 2019; Kilitci, Kaya, Acar, & Elmas, 2018). Hence use of non-estrogen modalities is grown currently. In recent years, need to safe long-acting therapeutic modalities with some effects on deeper vaginal mucosal layers is increased significantly. Hence use of regenerative tissue methods and anti-aging approaches for vaginal problems is entered to clinical trial phases leading to treatment of vaginal atrophy by fractional CO₂ laser (Tierney & Hanke, 2011). This method is accompanied by superficial and even deeper tissue alterations with small size leading to elastic and neo-collagen production resulting in improvement in pH and wetness that finally would lead to improvement in vaginal atrophy symptoms (Stefano,

Stavros, & Massimo, 2015; Mohammadi & Gupta, 2017). Majority of studies have shown good tolerability and safety of fractional CO₂ laser (Perino et al., 2015; Salvatore et al., 2014; Gaspar, Addamo, & Brandi, 2011; Salvatore et al., 2015; Tasnim & Farasat, 2018). Despite some studies about efficacy of fractional CO₂ laser there are few clinical trials in this era (Manonai, Theppisai, Suthutvoravut, Udomsubpayakul, & Chittacharoen, 2011; Eftekhari, Akhoondzadeh, Ghanbari, Iranshahr, & Haghollahi, 2009; <https://clinicaltrials.gov/ct2/show/NCT02419729>; Marx, Schade, Wilbourn, Blank, Moyer, & Nett, 2013; Leone Roberti Maggiore, Alessandri, Medica, Gabelli, Venturini, & Ferrero, 2012; Farzadnia, Hosseini, & Riahi, 2017; Hakiminya & Parnian, 2018; Haghghi & Asadi, 2019; Mirzaei, 2017). Hence in this study, the fractional CO₂ laser treatment efficacy was compared with vaginal conjugated estrogen cream in postmenopausal women with vulvovaginal atrophy was assessed.

2. Methods and Materials

In this randomized clinical trial, 130 consecutive postmenopausal women with vulvovaginal atrophy attending to outpatient urogynecologic clinic in Imam-Khomeini hospital in Ahvaz in 2015 were enrolled. Study was done under supervision by expert gynecologist in laser therapy. This study was approved by local ethical committee in Ahvaz University of Medical Sciences and also IRCT code was attained. The Helsinki declaration was respected across the study and all participants signed the informed consent form.

The understudy variables were age, literacy, body mass index (BMI), smoking, previous live births, sexual activity, and hormone replacement therapy history and duration. Inclusion criteria were aging from 45 to 65 years with amenorrhea for more than 24 months, clinical diagnosis of vaginal atrophy, and having coital activities. Also the exclusion criteria were estrogen therapy in past six months, current or previous cancer, changes in pap smear in last 12 months, renal or hepatic failure, previous steroid therapy, vaginal radiation history, vulvovaginitis, and substance use. Also the patients that were using vaginal or local lubricants were asked to uphold the use of these agents for 30 days. For all patients pap smear and vaginal swap was used to rule out the infections and local lesions.

Subjects were randomly assigned to receive either fractional CO₂ laser treatment or vaginal conjugated estrogen cream. In laser group the fractional CO₂ was made by MX-7000 (Angela) smart pulse CO₂ by vaginal probe after analgesic or aesthetic use with energy per dot of 70mj; fluency of 356/7j/mm; dot of 121, depth level of 2, and dot size of 100µm. If required dot power of 20 or 30 watts was used for introitus because of high sensitivity of this region (Perino et al., 2015). The laser was used for three sessions with 4-week intervals (weeks 0, 4, and 8) (Salvatore et al., 2015). For reduction of vaginal irritation the sexual intercourse was inhibited for a week after laser therapy. All adverse effects were recorded. In conjugated estrogen group (Primarin) it was used 1-gram (0.625mg) for two weeks daily and then 1 gram twice a week till eighth week that was prescribed by 1-gram same applicators (Manonai, Theppisai, Suthutvoravut, Udomsubpayakul, & Chittacharoen, 2011; Eftekhari, Akhoondzadeh, Ghanbari, Iranshahr, & Haghollahi, 2009).

The improvement of vulvovaginal atrophy symptoms, sexual satisfaction and function were compared across the groups at first day (before treatment initiation) and after 12 weeks (Salvatore et al., 2015). The treatment response (improvement in vulvovaginal atrophy symptoms including itching, vaginal burning, dryness, dyspareunia, and overall satisfaction with sexual life) (Salvatore et al., 2014; Leone Roberti Maggiore, Alessandri, Medica, Gabelli, Venturini, & Ferrero, 2012) was assessed by Female Sexual Function Index (FSFI) and visual analog scale (VAS). The FSFI was used as validated version (Mohammadi, Heydari, & Faghizade, 2008). The patients' satisfaction was assessed by likert scale of five categories ranging from very satisfied to very dissatisfied.

After data collection was completed the data analysis was done by SPSS version 24.0. The utilized statistical tests were chi-square, fisher, and independent-sample-T tests. The significance level was considered less than 0.05 in all comparisons.

3. Results

The mean age was 53.47±8.89 years and 52.92±8.44 years in laser and primarin group, respectively ($P > 0.05$). Duration of marriage was 27.77±7.44 and 28.43±1.32 years, in laser and primarin group, respectively ($P > 0.05$). The mean menopausal age was 51.12±2.77 years and 51.33±2.81 years, in laser and primarin group, respectively ($P > 0.05$). The mean BMI was 22.74±3.77kg/m² and 23.69±3.71kg/m², in laser and primarin group, respectively ($P > 0.05$). The smoking history was positive in three cases and four patients in laser and primarin groups, respectively ($P > 0.05$). As shown in Table 1, gestational history was alike across the groups.

There improvement of vulvovaginal atrophy symptoms, sexual satisfaction, and function were 86.2%, 87.7%, and 87.7%, respectively in laser group and 53.8%, 52.3%, and 52.3%, respectively in primarin group showing statistically significant differences ($P=0.0001$). There were no side effects.

Table 1. Gestational history in two groups

Group	Laser	Primarin	P Value
Gravid	2.35±1.41	2.44±1.44	> 0.05
Parity	2.32±1.93	2.10±1.87	> 0.05
Living child	2.02±1.23	2.29±1.42	> 0.05
Abortion	0.88±0.46	0.76±0.44	> 0.05

Table 2. Symptoms, satisfaction and function status in two groups

Group	Laser	Primarin	P Value
Symptom improvement	86.2%	53.8%	0.0001
Sexual satisfaction	87.7%	52.3%	0.0001
Sexual function	87.7%	52.3%	0.0001

4. Discussion

Majority of studies have shown good safety of CO₂ fractional laser (Perino et al., 2015; Salvatore et al., 2014; Gaspar, Addamo, & Brandi, 2011; Salvatore et al., 2015). CO₂ laser has been extensively used for treatment of vaginal atrophy symptoms. There was higher efficacy in all aspects in laser versus primarin group. Also there were no adverse effects. Perino et al. (Perino et al., 2015) in a study among 48 patients reported increased vaginal health index after three treatment stages. This study showed that 91.7% of patients were satisfied and there were no adverse effects as well as our study.

Salvatore et al. in a pilot study in 2014 showed that fractional CO₂ laser is effective in vaginal atrophy treatment that is accompanied with improved mental status and quality of life. The satisfaction rate was 84 percent that is similar to our results. Gaspar et al. (Gaspar, Addamo, & Brandi, 2011) in a study in 2011 assessed efficacy of CO₂ laser beside PRP in treatment of vaginal atrophy and found that these combination therapy was better than PRP alone. However, the good efficacy for CO₂ laser was established in our study. The study by Salvatore et al. (Salvatore et al., 2015) among 77 cases revealed that patients' sexual satisfaction was significantly improved after 12 weeks. Also similarly the symptoms of vaginal atrophy were improved.

Totally, according to obtained results, it may be concluded that efficacy of fractional CO₂ laser was higher than vaginal conjugated estrogen cream in postmenopausal women with vulvovaginal atrophy. However further studies with larger sample size are required to attain more definite and comparable results and with generalization potential.

Conflict of interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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