Vulvo-vaginal rejuvenation: fact or fiction?

Fractional carbon dioxide laser for Genitourinary Syndrome of Menopause

Short running head: **Vulvo-vaginal laser**

Authors: **Victoria Harris[1,2], Phillipa Dickson[2], Adrian Lim[1,2,3], Gayle Fischer[1,2]**

1. Department of Dermatology, Royal North Shore Hospital, Reserve road, AUS. 2. University of Sydney, AUS.
3. uRepublic Cosmetic Skin & Laser Clinic, AUS.

Abstract

Introduction: Genitourinary syndrome of menopause (GSM) is new terminology, initiated in 2014, which describes vaginal and/or vulval dryness, burning, dyspareunia, dysuria, urgency and increased frequency resulting from low circulating oestrogen in women. There is a growing interest in microablative fractional carbon dioxide (CO_2) laser of vulval and vaginal mucosa for GSM despite the lack of evidence on efficacy.

Method: A prospective case series of six women attending a vulval clinic treated for GSM using CO_2 laser treatment was performed. We report on the short-term safety, tolerability and outcomes after three laser treatments over a period of three months. Clinical outcomes were measures by two independent clinicians grading vulval mucosa for colour, vulval architectural changes moisture with clinical photography. Patient recorded outcome measures included Vulval Disease Quality of Life Index (VQLI), Dermatology Life Quality Index and Female Sexual Distress Scale (FSDS).

Results: Four out of six women reported some improvement in their symptoms with overall statistically significant improvements in quality of life and sexual functioning scores. However, only two out of six women reported compelte resolution of GSM symptoms.

Discussion: The majority of women in this small case series found microablative laser improved some of their symptoms of GSM and was well tolerated. Whilst these reports are favourable there is a need for larger, blinded studies need to be performed to assess the long term efficacy of microablative laser for GSM.

Learning Points

- Genitourinary syndrome of menopause (GSM) is new terminology, which describes vaginal/vulval dryness, burning, dyspareunia, dysuria, urgency and increased frequency resulting from low circulating oestrogen in women.
- Burden of suffering in women with GSM has lead to a growing interest in microablative fractional carbon dioxide ($CO_{2)}$ laser of vulval and vaginal mucosa
- The medical and non-medical use of CO_2 laser has emerged despite lack of data on its efficacy and safety.

Key Words:

- Vulval dermatology
- Genitourinary Sydrome of Menopause
- Ablative laser

INTRODUCTION

The epithelia of the vulva, vagina and bladder are oestrogen responsive tissues (1). Genitourinary syndrome of menopause (GSM) refers to a constellation of symptoms involving the genital and lower urinary tract which occurs as a result of low circulating oestrogen in women. The symptoms include vaginal and/or vulval dryness, burning, dyspareunia, dysuria, urgency, increased frequency and recurrent urinary tract infection (2).

Signs include pallor, lack of rugae, dryness of the vestibule so that the labia minora stick together, petehciae, redness and erosion of the fourchette after intercourse.

Local vaginal oestrogen therapy after breast cancer is a reasonable therapeutic option for the control of urogenital symptoms (3). However, women are reluctant to use oestrogen replacement therapy (4). The anxiety and confusion about the perceived risks of oestrogen therapy is an unnecessary barrier to the effective treatment of most women (5).

There is an understandable reluctance to use hormonal therapy for women who have reached menopause resulting from chemotherapy for oestrogen dependent cancers as there is always a potential risk of tumour recurrence. The reluctancey of women to use hormonal therapies for GSM has created a considerable burden of suffering for women. This lack of statisfaction with treatments that do not involve hormonal therapy has seen the rise in popularlity of alternative therapies with less rigorous evidence. One such treatment is ablative fractional laser. Ablative fractional laser has been enthusiastically adopted by many practitioners despite a lack of quality data on its safety as well as short and long term efficacy. There is a need for more quality research on the evidence of the safety and efficiacy of ablative fractional laser before it can be safely adopted into treatment regimen for GSM.

METHODS

Six women with signs and symptoms of GSM were consecutively recruited from a public genital dermatology clinic. All were post-menopausal and one had previously used systemic and topical oestrogen replacement. Treatment was carried out in the outpatient department at a public tertiary Hospital at no cost to the patinets. Five women underwent a total of three fractional microablative CO_2 laser treatments each spaced every four weeks. Prior to every laser session the women applied one finger-tip unit of AnGel (Amethocaine gel 4%) to vulval area thirty minutes prior to treatment. The patients were treated with CO_2 laser (GynoLaser,

Ilooda). For the vaginal wall, a laser probe was inserted in the vaginal canal to approximately 11cm and laser delivered through the end of a cylinder. The vaginal vestibule was also treated. Identical laser protocols were used for all three sessions [*Vaginal*: dot power 120mJ, stacking 2Th, dot spacing 0.8mm. *Vulval/ external* area: dot power 12mJ, stacking 1Th, and 8mm square spot treatment area].

At baseline and on completion of laser treatment the women completed three validated questionnaires: [Dermatology Life Quality Index (DLQI) and Vulval Disease Life Quality Index (VQLI)] and Female Sexual Dysfunction Scale (FSDS). The third to sixth women recruited were asked to rate the discomfort of the internal and external laser out of 10 (0 being no pain). Clinical photographs were taken for each woman at every laser session and severity of signs was recorded by two independent observers.

The data were analysed with IBM SPSS Statistics Version 22. The pre and post-treatment scores from the surveys were analysed using Wilcoxon's Signed Rank Test. A *p*-value of <0.05 was considered significant. The project was assessed by the Northern Sydney Local Health District

RESULTS

The median age of the women was 52 years (range 39 to 61 years). Overall, the laser was well tolerated by all the women. One woman described a discomfort that lasted for 24 hours post all three laser treatments. Another woman described increased discharge immediately following the first treatment that resolved within 48 hours and was not reported on subsequent laser treatments. A third woman had some streaking of blood noted on vaginal laser probe immediately following second laser treatment. She was subsequently found to have dense liver metastases from a recurrence of breast cancer and only completed two out of three laser sessions (Table 1). The average discomfort of the internal laser across the

treatments was less than the discomfort of the external laser in three of the four cases. (Table 2)

Four out of six women reported some improvement in their symptoms with overall improvements in VQLI, FSDS and DLQI scores. The median pre-treatment VQLI score for the cohort was 16/45 and median post treatment VQLI score was 6/45, which was found to be statistically significant (z=-2.023; p=0.043). The median pre-treatment FSDS score was 29 and post treatment 18. This improvement in quality of life and sexual functioning scores was statisitically significant (z=-2.023; p=0.043) (Table 3). Pre and post clinical photograph of **Case 4,** who self-reported complete resolution of sysmptoms, shows visible improvement in mucousal colour and lubrication (**Image 1 + 2**).

DISCUSSION

Topical and systemic oestrogen has traditionally been the treatment of choice for GSM. However there are situations where it is not tolerated or contra-indicated. This includes allergy, irritancy, secondary candidiasis and the relative contra-indication of previous carcinoma of the breast. Although low dose topical oestrogen is now sanctioned in breast carcinoma survivors, these patients are frequently fearful of its use. These patients are keen to be offered alternative treatments.

The symptoms of GSM can be debilitating particularly in young sexually active women and include vaginal dryness, burning and dyspareunia. Additionally the atrophy of the vaginal vestibule around the urethral opening frequently results in urinary issues including frequency, urgency and recurrent urinary tract infection.

During the last 2 years there has been increasing interest in and use of fractional carbon dioxide laser in the treatment of GSM in Australia despite very limited evidence in support of

safety and long-term efficacy. There is also no evidence comparing it head to head with topical oestrogen. Despite lack of quality evidence, vulvo-vaginal laser treatment is now being offered widely by gynaecologists and laser clinics at considerable cost to patients.

This pilot study using a fractional carbon dioxide laser specifically designed to deliver ablative laser to the vaginal wall and vaginal vestibule aimed to assess this instrument prior to futher investigation by a controlled trial.

Fractional CO_2 laser delivers electromagnetic radiation at 10 600nm wavelength that targets water resulting in columns of tissue ablation. The controlled tissue ablation and associated residual thermal energy trigger the wound repair cascade and subsequent tissue remodelling. This leads to clinical and histological skin rejuvenation that is characterised by increased elasticity and decreased laxity (6). Histological changes in vaginal mucosa post fractional CO_2 resurfacing include fibroblast activation, increased cellular glycogen and reversal of post-menopausal atrophy (7). Improvement in the elasticity and laxity of the vaginal vault post-laser may also account for the symptomatic improvements in urinary incontinence.

Fractional CO_2 laser has been reported to be efficacious in vulval dermatological conditions such as severe lichen sclerosus (8). Non-ablative laser modalities have also been reported to be efficacious in the treatment of GSM, including the vaginal erbium laser (9).

There have been limited reports on the efficacy of CO_2 laser for the treatment of GSM. *Salvatore* reported histological vaginal biopsies of five women who had undergone CO_2 laser had demonstrated remodelling of the connective tissue without damage to adjacent vaginal wall (10). This study had a very small sample size, did not evaluate symptoms and the authors had financial affilitations with the laser being analysed.

Recently, there has been an observational study over one year involving 30 women who had undergone CO_2 laser for GSM which demonstrated ongoing improvement in symptoms with little adverse events (11). This study however was sponsored by the laser manufacturer. An independent retrospective study of GSM symptoms in 26 women with a history of breast cancer also found there was a significant improvement after fractional microablative laser (12). The data from all these studies are sparse and have poor research methodology, small sample size, or are mostly not independent.

The limitations of this pilot study include its size. Despite this it indicates that the CO_2 laser has potential as adjunctive treatment in some women, at least in the short term. The treatment was well tolerated by all patients, there were no significant adverse events and no "down-time" was required. The time to carry out a treatment was five to ten minutes and patients were able to go home afterwards. Though analysis of the surveys demonstrated significant improvements, only two of six patients reporting complete resolution of symptoms. Better controlled data with larger sample sizes is required so that patients and clinicians can make an informed decision regarding this new treatment modality.

Although the laser was invasive, it was well tolerated and there were no serious adverse events reported. This may be an additional treatment option for women suffering from GSM. Further high grade evidence is required before this treatment evolves to standard of care for patients who are not able to be treated with oestrogen.

References

1. Hodgins M, Spike R, Mackie R et al. An immunohistochemical study of androgen, oestrogen and progesterone receptors in the vulva and vagina. *BJOG* 1998; 105: 216-222

2. Portman DJ, Gass ML. Vulvovaginal atrophy terminology consensus conference panel. Genitourinary syndrome of menopause: new terminology for vulvovaginal atrophy from the International Society for the Study of Women's Sexual Health and the North American Menopause Society. *Menopause*. 2014; 21: 1063-8.

3. The Royal Australian and New Zealand College of Obstetricians and Gynaeocologists (2014). Management of the menopause after breast cancer. College Statements and Guidelines.

4. Kingsberg SA, Wysocki S, Magnus L, Krychman ML. Vulvar and vaginal atrophy in postmenopausal women: findings from the REVIVE (REal Women's VIews of Treatment Options for Menopausal Vaginal ChangEs) survey. *J Sex Med*. 2013; 10:1790–9.

5. Manson J, Kaunitz A. Menopause Management — Getting Clinical Care Back on Track. *N Engl J Med* 2016; 374(9): 803-806.

6. Tierney EP, Kouba DJ, Hanke CW. Review of fractional photothermolysis: treatment indications and efficacy. *Dermatol Surg*. 2009. 35(10):1445–1461.

7. Zerbinati N, Serati M, Origoni M et al. Microscopic and ultrastructural modifications of postmenopausal atrophic vaginal mucosa after fractional carbon dioxide laser treatment. *Lasers Med Sci.* 2015; 30:429–436.

8. Lee A, Lim A, Fischer G. Small case series: Fractional carbon dioxide in recalcitrant vulval lichen sclerosus. *Aust J Dermatol*. 2016; 57: 39-43.

9. Gambacciani, Levancini M. Short –term effect of vaginal erbium laser on the genitourinary syndrome of menopause. *Minerva Ginecol.* 2015; 67:97-102.

10. Salvatore S, Maggiore U, Athanasiou S et al. Histological study on the effects of microablative fractional CO laser on atrophic vaginal tissue: an ex vivo study. *Menopause.* 2015; 22(8): 845-849.

11. Sokol E, Karram M. Use of a novel fractional CO laser for treatment of genitourinary syndrome of menopause: 1-year outcomes. Menopause. 2017; 24(7): 1-5.

12. Pagano T, De Rosa P, Vallone R et al. Fractional microablative CO laser for vulvovaginal atrophy in women treated with chemotherapy and/or hormonal therapy for breast cancer: a retropsepctive study. *Menopause*. 2016; 23(10): 1108-1113.

Figure Legends:

Image 1 – Pre-treatment clinical photograph of subject 4 showing atrophy, pallor and dryness of vulval mucosa.

Image 2 – Post laser treatment of subject 4 showing improvement of colour (pink) of vulval mucosa.

1. Background characteristics of patients with CO for Genitourinary Syndrome Menopause

Characteristic	**Case 1**	**Case 2**	**Case 3**	**Case 4**	**Case 5**	**Case 6**
Age	53	51	39	61	49	57

Ethnicity	Caucasian	Caucasian	Caucasian	Caucasian	Caucasian	Caucasian
Menopause	Yes	Yes	Yes	Yes	Yes	Yes
History of oestrogen replacement therapy	Contra-Indicated (oestrogen positive breast ca)	Contra-Indicated (exacerbation CVVC)	Contra-Indicated (oestrogen positive breast ca)	Contra-Indicated (oestrogen positive breast ca)	Contra-Indicated (oestrogen positive breast ca)	Vagifem pessaries, previous HRT. Requested alternate Rx
Other vulval conditions	Recurrent Urinary tract infections	Chronic vulvo-vaginal candidiasis	nil	nil	nil	Lichen sclerosus
No Laser Treatments	3	3	3	3	2	3
Symptoms	Itch, dryness	Dyspareunia, dryness, itch	Dyspareunia, dryness, itch, incontinence	Dyspareunia, dryness, itch, incontinence	Dyspareunia, dryness, itch, incontinence	Itch, incontinence
Symptom resolution	Partial	No change	Partial	Complete	Complete	No change

2. <u>Tolerability of laser treatment</u>

Case	**Average pain (internal) /10**	**Average pain (external) /10**
3	1	3
4	1	2
5	3	2
6	3	7

3. <u>Results of questionnaires completed by patients at baseline and completion of treatment</u>

Case	Age-Years	VQLI pre	VQLI post	DLQI pre	DLQI post	FSDS pre	FSDS post	No.s sessions	Adverse events
1	53	12	6	1	2	28	24	3/3	Minor vulval discomfort 24hrs post treatment
2	51	6	5	2	2	22	13	3/3	Discharge 48hrs post treatment
3	39	15	10	7	2	47	19	3/3	nil
4	61	26	2	10	0	22	6	3/3	nil
5	49	24	11	10	1	43	18	2/3	Bleeding thrombocytopenia

Key: Vulval Disease Quality of Life Index (VQLI), Dermatology Life Quality Index (DLQI), Female Sexual Dysfunction Scale (FSDS), Adverse Events (AE)