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Fractional Co2 Laser Vs Topical Estrogen In The Treatment Of Vulvovaginal Atrophy In Perimenopausal Women

A dissertation Submitted to the Institute of Laser For Post Graduate Studies - University of Baghdad In Partial Fulfillment of the Requirement for the Degree of Higher Diploma in Laser in Medicine/ Gynaecology

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DEDICATED TO MY WONDERFUL FAMILY

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Abstract

Background: The genitourinary syndrome of menopause (GSM) can occur at any time in a woman's life cycle, although it is more common in the postmenopausal phase. Fractional carbon dioxide (CO_2) laser is effective for improving vaginal symptoms associated with GSM.

Aim of study: To compare the efficacy of Fractional Co2 Laser to topical estrogen in treatment of vulvovaginal atrophy among perimenopausal women.

Patients and Methods: The current study was a case series study conducted in private clinic in Baghdad city-Iraq in duration of four months throughout the period from 15th of September, 2021 till 15th of January, 2022 on convenient sample of 20 women with one or more symptoms of GSM. Assessment of outcomes was done by measuring the vaginal health index (VHI), Maturation value of Meisels and the 10-cm VAS for symptoms intensity. The patients were followed up for 12 weeks in a schedule of week 0, week 8 and week [12].

Results: The means of total VHI score at week 8 and week 12 were significantly lower among GSM women treated by Fractional Co2 Laser as compared to GSM women treated by topical estrogen ($p \leq 0.05$). The dysparunia intensity was significantly declined in GSM women treated by Fractional Co2 Laser after 12 weeks of treatment ($p=0.01$). Similarly, the urgency & urge incontinence intensity was significantly declined in GSM women treated by Fractional Co2 Laser after 12 weeks of treatment ($p=0.01$). The complications of laser therapy used in treatment of GSM were present in 4 (40%) women; 2 (20%) women with mild pain, one (10%) woman with mild swelling and one (10%) woman with mild numbness. The discomfort from laser therapy for GSM was mild in all treated women.

Conclusion: The fractional CO_2 laser therapy is effective method in management of genitourinary syndrome.

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List of Abbreviations

Abbreviation	Full Name
AMH	Antimullerian Hormone
AV malformation	Arteriovenous malformation
CO2 Laser	Carbon dioxide Laser
CW	Continuous wave laser
CS	Cesarean section
DHEA	dehydroepiandrosteron
E1	Oestrone
E2	0estradiol
E3	Oestriol
(Er):YAG	Erbium yag
FDA	Food and Drug Administration
FMB	Final menstrual period
FP	Fractional Photothermolysis
FSH	Follicular stimulating hormone
GSM	Genitourinary syndrome of menopause
GI bleeding	Gastrointestinal bleeding
HA	Hyaluronic acid
HCPs	Health care professionals
HRT	Hormonal replacement therapy

I cells	Intermediate cells
IEC	International Electro technical Commission
J	Joule
Laser	Light amplification by stimulated emission of radiation
MBS	Most bothersome symptoms
µm	micrometer
MPE	Maximum permissible exposure
MTZs	Microthermal Zones
ms	Millisecond
mm	Millimeter
mg	Milligram
MV	Maturation value of Measles
Nd:YAG	Neodymium: Yttrium- Aluminum-Garnet
NICE	National Institute For Health and Care Excellence
nm	Nanometer
NVD	Normal vaginal delivery
P cells	Para basal cells
Pg/ml	Pico gram per milliliter
S cells	Superficial cells
SERMs	Selective estrogen receptor modulators
SPSS	Software statistical Package for Social Science

Straw	Stages of reproductive aging workshop
UK	United Kingdom
USA	United States Of America
VAS	Visual analogue scale
VHI	Vaginal health index
VMI	Vaginal maturation index
VMS	Vasomotor symptoms
W	Watt

Chapter One

Introduction &BASIC CONCEPTS

Introduction

1.1. Background

As life expectancy continues to increase, women will spend more time in menopause. Genitourinary syndrome of menopause (GSM) is a constellation of symptoms that result from vulvovaginal atrophic changes that occur following the decline in circulating estrogen levels after menopause [1, 2]. It is also known as vulvovaginal atrophy (VVA) and atrophic vaginitis. These symptoms include vulvovaginal burning, decreased lubrication, dyspareunia and urinary symptoms, such as dysuria, frequency, or recurrent urinary tract infections. Fifty percent of women are affected by GSM, which can negatively impact their quality of life, yet only 7%of women request treatment of their symptoms [1, 3, 4, 5].

In recent years, fractional laser technology has been introduced and rapidly applied in various fields of medicine. It has become the most popular cosmetic (skin) and female reproductive function recovery technology. Laser technology has also been applied for the treatment of VVA. Previous studies have shown that fractional carbon dioxide (CO2) laser is effective and safe for improving vaginal symptoms associated with GSM [3, 6, 7] .

1.2. Perimenopauses

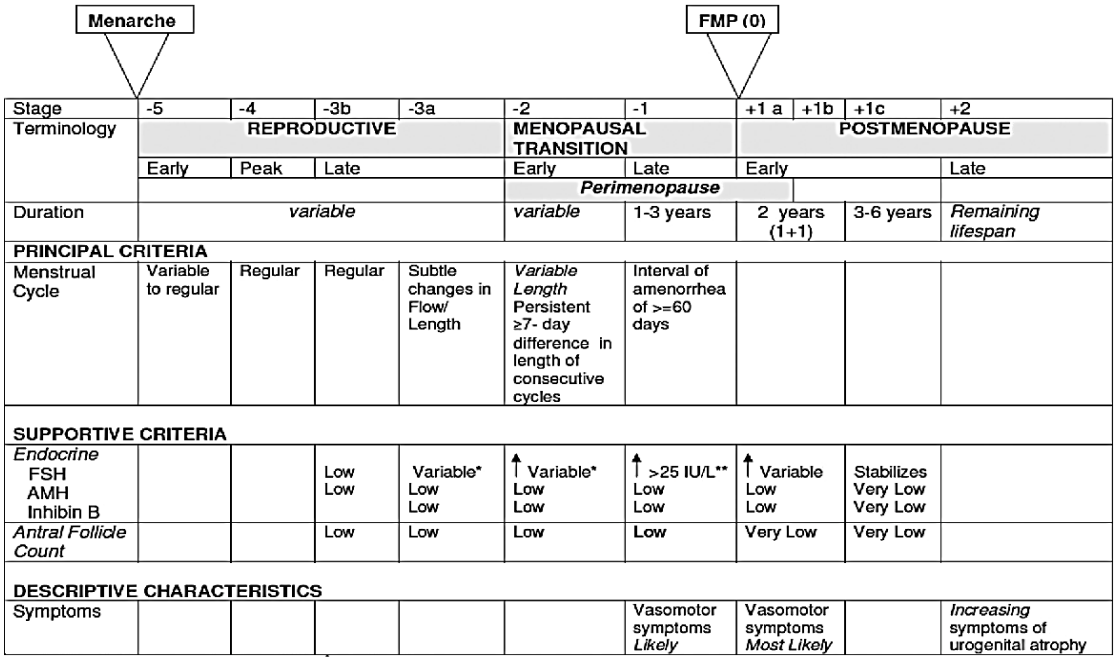
The perimenopause is an ill-defined time period that surrounds the final years of a woman's reproductive life. It begins with the first onset of menstrual irregularity and ends after 1 year of amenorrhea has occurred, thereby defining the final menstrual period (FMP). There are two stages to the perimenopause or menopausal transition: the early transition, where cycles are mostly regular, with

relatively few interruptions, and the late transition, where amenorrhea becomes more prolonged and lasts for at least 60 days, up to the FMP. Several worldwide cohorts have defined the natural history of the menopausal transition in sufficient detail such that these stages have been broken down and linked to specific hormonal events, which in turn are linked to symptoms. Perimenopause is a transitional time that ends in menopause. Menopause means that periods have ended. When no menstrual cycle for a full 12 months, this is officially reached menopause [8] .

The stages of reproductive aging have been well described in two workshops, with the acronym STRAW [9]. STRAW stages relevant to this topic include the late reproductive stages (−3b and −3a), the early and late menopausal transition stages (−2 and −1), and the early postmenopause (+1a and +1b). These stages are shown in Figure 1. It is important to note that the loss of ovarian reserve that accompanies the menopausal transition occurs before there is follicle failure, that is, an inability for granulosa cells to respond to a follicle-stimulating hormone (FSH) signal with estradiol production. Thus, the process is not simply a loss of estrogen accompanied by elevated FSH, at least not in its earlier stages[8,9].

Stages −3b and −3a encompass the late reproductive years when fertility may still be possible, but less likely than in earlier years. Ovarian reserve fluctuates over this time period, a reflection of a dwindling follicle pool that is variable over time. The cohort of ovarian follicles available for recruitment for the purpose of ovulation is ever diminishing. The hormones produced by small growing follicles in the ovary include antimullerian hormone (AMH) and inhibin B. These hormones have been used as peripheral serum markers of ovarian reserve, and AMH in

particular is very effective in predicting the probability of a poor outcome with fertility therapy when it is low [10].



Stage	-5	-4	-3b	-3a	-2	-1	+1 a	+1b	+1c	+2
Terminology	REPRODUCTIVE				MENOPAUSAL TRANSITION		POSTMENOPAUSE			
	Early	Peak	Late		Early	Late	Early			Late
					Perimenopause					
Duration	*variable*				*variable*	1-3 years	2 years (1+1)		3-6 years	*Remaining lifespan*
PRINCIPAL CRITERIA										
Menstrual Cycle	Variable to regular	Regular	Regular	Subtle changes in Flow/ Length	*Variable Length* Persistent ≥7- day difference in length of consecutive cycles	Interval of amenorrhea of >=60 days				
SUPPORTIVE CRITERIA										
Endocrine FSH AMH Inhibin B			Low Low	Variable* Low Low	↑ Variable* Low Low	↑ >25 IU/L** Low Low	↑ Variable Low Low		Stabilizes Very Low Very Low	
Antral Follicle Count			Low	Low	Low	Low	Very Low		Very Low	
DESCRIPTIVE CHARACTERISTICS										
Symptoms						Vasomotor symptoms *Likely*	Vasomotor symptoms *Most Likely*			*Increasing* symptoms of urogenital atrophy

*Blood draw on cycle days 2-5 ↑ = elevated
**Approximate expected level based on assays using current international pituitary standard

Fig 1.1 the stages of reproductive aging workshop + 10 staging system for reproductive aging in women . [8]

The body has been producing estrogen since puberty. Once your estrogen levels begin to decline, your body has to adjust to the changes in hormones.

The symptoms vary, but most people experience at least one of the following [8]:

- Irregular periods or skipping periods.
- Periods that are heavier or lighter than usual.
- Hot flashes (a sudden feeling of warmth that spreads across your body).
- Vaginal dryness and discomfort during sex.
- Urinary urgency (needing to urinate more frequently).
- Sleep problems (insomnia).

1.3. Genitourinary syndrome of menopause

1.3.1. Definition

The genitourinary syndrome of menopause (GSM) is a relatively new term, first introduced in 2014 by a consensus of the International Society for the Study of Women's Sexual Health and the North American Menopause Society. GSM, previously known as vulvovaginal atrophy, atrophic vaginitis, or urogenital atrophy, is a term that describes the spectrum of changes caused by the lack of estrogens during menopause [11] . GSM-like symptoms may also be present in 15% of premenopausal women due to the hypoestrogenic state [12]. Nonetheless, the vast majority of women suffering from GSM are of older age, with 50-70% of postmenopausal women being symptomatic at least to some degree [13]. To this day, GSM remains extremely underdiagnosed despite its high prevalence, mostly because of the reluctance among women to seek help due to embarrassment, or as a result of a tendency among many women to consider it as a normal feature of natural aging. However, in many cases, the reluctance of healthcare professionals to address these issues constitutes a major cause of the lack of awareness about this syndrome among affected women [14].

The terms *vulvovaginal atrophy* and *atrophic vaginitis* were widely used until recently, but they have been considered to be inadequate for referring to the constellation of symptoms and signs associated with the genitourinary system after menopause. The term *vulvovaginal atrophy* mentions the vulva and vagina only, and these words are not used comfortably in general social discussion and in the media. The

term *atrophic vaginitis* implies a state of inflammation or infection, which is not a primary component of menopausal changes. In addition, a limitation of the terms *vulvovaginal atrophy* and *atrophic vaginitis* is that they do not take into account the symptoms of the lower urinary tract, which are among the most important symptoms related to menopause [11].

1.3.2. Etiology

A hypoestrogenic state may be part of natural physiological menopause or induced (secondary to surgical, radiation, or chemotherapy treatments). Premenopausal women may develop a temporary hypoestrogenic state while lactating. Other conditions, such as exposure to medications, radiation therapy, chemotherapy, or hypothalamic dysfunction, may also result in a hypoestrogenic state. Medications that may induce a hypoestrogenic state include Selective estrogen receptor modulators, Selective estrogen receptor degrader, and antigonadotropins [15].

Decreased estrogen levels lead to changes in the vaginal environment, which causes a shift in the normal flora. Typically there is a decrease in Lactobacillus spp. resulting in overgrowth of skin and rectal pathogens [15].

1.3.3. Epidemiology

Genitourinary syndrome of menopause (GSM) can occur at any time in a woman's life cycle, although it is more common in the postmenopausal phase, a time of hypoestrogenism. Other causes of a hypoestrogenic state include lactation, various breast cancer treatments, and use of certain medications. In situations other than menopause, VVA may resolve spontaneously when estrogen levels are restored [16].

Numerous retrospective studies have evaluated the prevalence of symptoms of VVA. Although these studies differ in type of symptoms elicited, study design, and study population, they provide a range of estimates of VVA prevalence. They all used self-reported symptoms of vaginal dryness to determine the prevalence of VVA. In general, the prevalence ranged from about 4% in the early premenopausal groups to 47% in the late postmenopausal group [16].

The prevalence of VVA in some subgroups of women can be much higher. In a cohort of breast cancer survivors, vaginal dryness was present in 23.4% of the premenopausal patients and in 61.5% of the postmenopausal patients [16].

1.3.4. Pathophysiology

The female genitalia, the lower urinary tract, and the surrounding vasculature develop from the same embryologic tissue with similar estrogen receptors. Estrogen receptor alpha is primarily found in the uterus and pituitary gland. The estrogen receptor alpha is present during premenopause and postmenopause. Estrogen receptor beta is primarily found in the ovary. The estrogen receptor beta is present predominately in the premenopausal state, leading to the ovarian failure state experienced in menopause. Hypoestrogenic state results in the fusion of collagen fibers and fragmentation of elastin fibers in vulvovaginal tissue and decreased squamous cells, resulting in decreased mucosal elasticity and decreased rugae, and narrowing the vagina[17].

Premenopausal vaginal tissues mature in normal estrogen ranges of 30 to 40 pg/ml, which allows for adequate growth of vaginal epithelium with superficial squamous cells containing glycogen. Lactobacilli spp. utilize the glycogen from the cells and convert it into lactic acid, creating a

slightly acidic environment with a pH of 3.5 to 5.0. Free glycogen is also associated with lower pH and higher levels of lactobacillus. In menopause, vaginal tissue is exposed to estrogen less than 20pg/ml resulting in fewer superficial squamous epithelial cells with an increase in parabasal cells. The higher concentration of parabasal cells and reduced Lactobacillus spp. leads to a decrease in lactic acid conversion, producing a higher pH of 5.0 to 7.5 environment. The consequence of elevated vaginal pH is a shift in normal flora, *Lactobacilli* spp., and more susceptible to other pathogens such as Gardnerella, Prevoltella, Atopobium, and Streptococcus[18-20].

1.3.5. Histopathology

Atrophic pattern histologic findings demonstrate decreased superficial squamous cells, increased parabasal cells, decreased Lactobacilli. However, there are normal to low numbers of neutrophils. Increased neutrophils are noted in atrophic vaginitis when compared to the vaginal atrophy pattern [15].

The hypoestrogenic state results in loss of dermal collagen, elastin fibers, and blood vessels in the lamina propria. These changes result in decreased elasticity and vascularity. Decreased vascularity, in response to low estrogen levels, results in thin friable vaginal mucosa and decreased secretions [15].

1.3.6. Diagnosis

Clinical interviews and rating scales to score the most bothersome symptoms (MBS) (Table 1) are useful instruments to measure subjective symptoms and to identify risk factors for VVA/GSM. Objective diagnosis is confirmed by an accurate pelvic examination, including gentle inspection of the vulva, vestibule, vagina, and urethra in

order to recognize the signs of VVA/GSM (Table 1) which can be rated on validated scales [21]. The Vaginal Health Index Score is a clinical tool that, by evaluating 5 parameters (vaginal elasticity, vaginal secretions, pH, epithelial mucous membrane, vaginal hydration), allows to obtain a final score defining the degree of atrophy in the genitourinary tract by assigning a single score to each parameter. Total score ranges from 5 to 25, with lower scores corresponding to greater urogenital atrophy. Vulva Health Index evaluates labia, urethra, clitoris, introitus as well as elasticity and pain during intercourse; total score ranges from 0 to 24, with higher scores corresponding with greater vulvar atrophy. If the Vulva Health Index is over 8 or there is score of 3 (severe) in any category, vulvar atrophy is suggested [22]. In the most severe cases, tissues may be easily traumatized and irritated by touching or inserting the speculum [23]. Organ prolapse or hypertonicity of the pelvic floor with secondary vaginism may be also present, as well as vulvovaginal signs which require a differential diagnosis by performing colposcopy or carrying out bacteriological analyses [24]. In general, VVA/GSM is typically a clinical diagnosis and few laboratory tests may be used to support the evidence. Among them, the evaluation of vaginal pH and the vaginal maturation index (VMI) are the most used [11]. With the VMI it is possible to identify the relative proportion of parabasal, intermediate, and superficial vaginal epithelial cells. Hypoestrogenism and atrophy are suggested when there is a dominance of parabasal cells, calculated on specimens obtained directly from the lateral upper vaginal walls. Thus, the shift to a higher number of superficial cells is a primary end-point of any treatments prescribed to relieve symptoms of VVA. Even, vaginal pH alone is a simple outpatient procedure, influenced by infections and intimate products, which reflects the hormonal milieu and its effects on the vaginal epithelium. Indeed, it consistently correlated with parabasal

and superficial cells and the visual vaginal epithelial changes and symptoms of dryness and dyspareunia [25].

In both clinical and research settings, subjective assessment (the MBS approach) and objective assessments of VVA (measurement of vaginal maturation index and vaginal pH) should be combined according to a recent systematic literature search [26]. Even though a high rate of subjective symptoms is associated with a clinical diagnosis of VVA/GSM in over 90% of the cases, objective signs and subjective symptoms have a different prevalence distribution in the years after menopause and are not strictly associated [26]. However, self-reported and visible vaginal dryness do correlate and together with ph> 5, mucosal pallor, and rugae thinning seem to be the most important objective signs to make a diagnosis [26]. On the other hand, the presence of other vulvar and urinary signs are relevant to the severity of VVS/GSM and its impact on women's daily living [27].

Notwithstanding these findings, HCPs may pose very simple questions to facilitate an open conversation on urogenital health and to record the variety of vaginal, vulvar and urinary symptoms. Visual vaginal, vulvar and pelvic assessment by HCPs is a useful measure for diagnosing VVA/GSM and assessing response to treatment. Moreover, it may help HCPs to identify women at risk of vaginal dryness and dyspareunia, and allow them to proactively engage in conversations about sexual health [28].

Women with breast cancer and other gynecological malignancies are at very high risk of VVA and associated symptoms. Indeed, endocrine chemotherapy, surgery and/or radiation may induce profound changes at urogenital levels which have to be timely recognized in the oncologic care [29]. Moreover, we lack data on VVA/GSM in women with spontaneous premature ovarian insufficiency, even though it is likely that

the condition is more distressing due to the younger age of these patients[30]. Older women and those who abstain from sexual activity may suffer even more of VVA/GSM with vaginal and introital stenosis, fusion of the labia minora to the labia majora, and other urogenital conditions [31]. Preventive gynecology is significantly challenged by the presence of severe VVA/GSM. Indeed, it may be difficult to adequately assess both cytologic and colposcopic findings to prevent cervical cancer. On the other hand, an episode of postmenopausal bleeding, very common in women with VVA/GSM, may cause an urgent referral to exclude endometrial cancer and other malignancies. Finally, even if less common, an early diagnosis of cancer may be delayed by vaginal synechiae and hematocolpos due to vaginal occlusion [32].

Vulvovaginal atrophy symptoms were assessed using a 10 cm visual analogue scale (VAS) for each of the 5 VVA symptoms: vaginal dryness, itch, burning, dysuria and dyspareunia. The VAS scale uses 0–10 scale to rate symptoms from no symptoms (0) to worst possible symptoms (10) [33].

Table 1-1: Most common subjective and objective symptoms to diagnose vulvovaginal atrophy (VVA)/genitourinary syndrome of menopause (GSM) in daily practice [20].

Vaginal Dryness
Dyspareunia
Irritation/Burning/Itching
Dysuria
Bleeding with sexual activity

Elasticity
Vaginal folds
Fluid secretion
Epithelial thickness
Moisture
Color of the tissues

1.3.7. Management of GSM

The sequelae of GSM symptoms can have a detrimental effect on a woman's quality of life, and with an ageing population, this is likely to amplify. Contrary to vasomotor symptoms (VMS), which tend to become milder over time, symptoms of GSM are progressive and tend to deteriorate if left untreated and rarely resolve spontaneously. Consequently, they appear to have a greater impact on the sexual functioning and emotional wellbeing of affected women [34].

1.4. Palliative measures

1.4.1. Lifestyle changes and physical therapy

The expectation of the next generation surrounding healthcare is changing; women are seeking personalised solutions and expect healthcare to be holistic. When a woman presents with urogenital symptoms of the menopause, a detailed history should be taken to establish any potential contraindications to treatment and identify modifiable risk factors such as smoking, which is linked with an increase in oestrogen metabolism leading to vaginal atrophy [35]. A sexual history should be taken not only to establish if the woman suffers from vaginal dryness and dyspareunia—the most common and bothersome symptoms of GSM [36], but also to determine the presence of sexual dysfunction. Women should be educated regarding the benefits of physical therapy,

particularly in the presence of high-tone or non-relaxing pelvic floor muscle dysfunction that is triggered by painful sexual activity related to GSM [37]. Furthermore, women should be advised that it is safe and beneficial to continue with sexual activity and that there is a positive link between the lubricative response to sexual arousal and the maintenance of vaginal elasticity[38].

1.4.2. Lubricants

The first-line treatment for the symptoms of vaginal dryness and dyspareunia is the use of a non-hormonal vaginal lubricant during intercourse and the regular use of a long-acting vaginal moisturiser. They can be used alone or in combination with oestrogens [40].

1.4.3. Moisturisers

Vaginal moisturisers are an excellent option for women who experience ongoing discomfort due to vaginal dryness. Moisturisers are hydrophobic and have bio-adhesive properties. They are absorbed into the skin and adhere to the superficial cells of the vagina. They have the ability to retain moisture, which is then released locally, mimicking physiological vaginal secretions. Moisturiser can be used several times per week independent of sexual activity [41].

1.4.4. Hyaluronic acid

Hyaluronic acid (HA) has been widely used as an essential ingredient in topical hydrating and lubricating gels and has been injected for conditions such as dyspareunia. It is a naturally occurring polysaccharide and is one of the main components of the extracellular matrix present in the epithelium of many tissues, including the vagina. It has strong antioxidant properties that connect water to tissue and is considered a naturally occurring reservoir of body water that can increase

moisture levels within cells and improve atrophic symptoms [42]. Various prospective observational studies carried out on HA have shown that this compound is well tolerated without side effects among patients [43]. A recent systematic review comparing the efficacy of HA and oestrogen on atrophic vaginitis showed that all articles reported improvement with both treatments favouring oestrogen. However, studies were of poor quality, small sample size, and insufficient number to reach a conclusion [44].

1.5. Pharmacological treatment of GSM

1.5.1. Local oestrogens

Local vaginal oestrogen has been the treatment of choice for decades for the management of postmenopausal women with vulvovaginal symptoms of the menopause only. It allows for a lower dose of oestrogen than that used in systemic therapy for VMS [45]. A third of women on systemic hormonal replacement therapy (HRT) also have symptoms of GSM and require additional local oestrogens. Intravaginal oestrogen therapy is available in a variety of different oestrogen compounds, doses, and routes of administration, including oestriol (cream [Ovestin®] and pessary [Orthogynest®]), oestradiol (tablets [Vagifem®] and ring [Estring®]), and a conjugated preparation (cream [Premarin®]) [46]. The choice among different local oestrogen treatments depends on the severity of symptoms and the patient's preference [47].

The typical administration schedule, with the exception of the oestradiol ring, which is used continuously for 90 days, consists of an initial loading dose of daily applications followed by a maintenance regimen for as long as it is needed to manage symptoms, usually indefinitely. Ovestin® is applied daily for 3 weeks, then three times a week. Vagifem® is an

intravaginal tablet pessary that is administered daily for 2 weeks, followed by a twice-weekly maintenance schedule [47]. Systemic absorption has been shown to occur with Premarin vaginal cream and is not entirely safe in women who retain a uterus owing to the unopposed oestrogen hyperplastic effect on the endometrium. Premarin® has been withdrawn in the UK but is still available in other countries [47].

The rationale behind this administration regimen is that the absorption of oestrogens is highest during the first few days of treatment when the vaginal epithelium is most atrophic, has increased vascularity, and has a thinner superficial epithelial layer. Once the epithelium has matured, the absorption of local oestrogen decreases and therefore smaller doses of oestrogen are sufficient to prevent recurring atrophy while ensuring the systemic absorption from chronic use of oestrogen is minimized [48]. The safety and efficacy of these regimens were supported by two large randomised, double-blind, placebo-controlled trials from the same working group. The authors identified that the administration schedule of daily application of an oestradiol vaginal cream at 0.003% for 2 weeks then two or three times a week for women with the principle bothersome symptom of vaginal dryness or dyspareunia was effective and well tolerated [49, 50].

Systematic efficacy and safety reviews of vaginal oestrogen products for the treatment of moderate-to-severe GSM have reported them to be superior to placebo in achieving subjective improvement in vaginal dryness, dyspareunia, and urogenital symptoms. In addition, objective measures of improvement were found in gross vaginal epithelial appearance, maturation of vaginal epithelium, reduction in pH, and increased vaginal Lactobacillus [51]. The latest Cochrane review on local oestrogen for vaginal atrophy in postmenopausal women included 30

clinical studies with 6,235 postmenopausal women. It compared different vaginal oestrogen preparations with each other and placebo. The authors concluded that all compounds improved symptoms of VVA in comparison to placebo with minimal safety concerns. There were no significant differences in efficacy among the different preparations [52].

The systemic absorption of oestrogens remains the primary concern surrounding the use of local oestrogens. While the local route of administration minimises the exposure, it is not entirely eliminated. Local oestrogen is associated with an acute rise in plasma oestradiol levels, with a peak at approximately 8 hours and a return to baseline at 12 hours, never rising again after that or when vaginal oestrogen is stopped and later restarted [52]. This sharp rise in plasma oestradiol level may be the cause of some systemic adverse effects reported, such as vaginal bleeding or breast tension. Oestradiol tablets and ring are associated with systemic absorption that is equal to or less than that produced by the postmenopausal adrenal gland [52].

1.5.2. Systemic hormonal replacement therapy

Systemic oestrogen therapy is the mainstay of treatment for VMS of the menopause and can have a beneficial effect in improving concurrent symptoms of GSM. However, systemic HRT for GSM alone is not FDA approved or NICE recommended but can be considered in the treatment of concurrent VMS and GSM symptoms. Oestrogen alone can be used for hysterectomised women but needs to be combined with progestogen therapy for women with an intact uterus. Although systemic HRT can be beneficial in improving symptoms of GSM, up to 25% of women will still experience symptoms of urogenital atrophy [53].

Prasterone (dehydroepiandrosterone)

There are three major naturally occurring oestrogens in women; oestrone (E1), oestradiol (E2), and oestriol (E3). In pre-menopausal women, the most abundant oestrogen is oestradiol, which is produced from the granulosa cells of the ovary; in addition, androgen production is significantly greater than that of oestrogens [54]. At menopause, the secretion of oestradiol by the ovaries stops and dehydroepiandrosterone (DHEA) becomes the exclusive precursor for all sex steroids made intracellularly in peripheral tissues independent of the ovary [55]. Sex steroid activity becomes exclusively dependent upon the ability of each tissue to transform DHEA into oestrogens and androgens for local and intracellular use [56].

Selective oestrogen receptor modulators (ospemifene)

The concerns issued regarding hormonal treatments and the potential stimulating effects of systemic oestrogens in breast and endometrial tissue have prompted the development of alternative treatments. Selective oestrogen receptor modulators (SERMs) are synthetic non-steroidal agents that have the potential to exert a variable agonistic, antagonistic, or neutral effect on oestrogen receptors in targeted tissues. Examples include ospemifene, lasofoxifene, raloxifene, bazedoxifene, and tamoxifen. Along with ospemifene, lasofoxifene has demonstrated a positive impact on vaginal tissue in postmenopausal women, and although several studies have found that lasofoxifene results in significant improvement in objective parameters of vaginal pH and VMI, the clinical development of this SERM is on hold [57].

1.6. Non-Pharmacological treatment of GSM

1.6.1. Laser

Light amplification by stimulated emission of radiation (laser) was first described over a century ago and has been used in various aspects of medicine since then. Following the formative study by Salvatore et al. [58], the use of vaginal laser has grown in popularity as an alternative non-hormonal treatment for GSM. In the UK to date, laser has been used in the private sector, where it is very expensive, or for research purposes. The two most commonly used laser technologies are non-ablative photothermal Erbium:YAG laser (Er:YAG laser) and CO2 laser [59] (Figures 1/2-3). Through thermomodulation, these laser technologies result in the restoration of the vaginal epithelium to a state similar to that of a pre-menopausal woman [60]. The controlled temperature rise causes collagen remodelling and synthesis, neovascularisation, vasodilatation, and elastin formation [61].

Figure 1-2: Er:YAG, Fotona Smooth SP[61].

Figure 1-3: CO_2 Laser (Mona Lisa Touch, DEXA[61]).

The safety profile surrounding energy-based devices is an area where robust research is lacking. In July 2018, the US Food and Drug Administration (FDA) issued a warning to healthcare professionals declaring that the safety and effectiveness of these devices for vaginal rejuvenation or cosmetic vaginal procedures are not proven. In addition, it stated that no energy-based device had been approved for these

procedures or the treatment of menopause-related vaginal symptoms, urinary incontinence, or sexual function. As a result of this, several international professional organizations have released consensus statements, with the majority reporting that the routine use of laser should not be recommended and that further research is needed. There are several complications reported, with the most common being procedure-related pain; other reported complications include numbness, burning, dyspareunia, bladder disturbance, worsening symptoms, scarring, and worsening of lichen sclerosis. Data are lacking to quantify these complications [62].

Systematic reviews of the literature have shown an overall improvement in the Vaginal Health Index (VHI) score and in subjective symptoms of GSM in the short term; however, studies were often non-randomised, lacked placebo/sham, and had a small sample size and follow-up duration[42]. This is an emerging area, and although early results appear promising, robust randomised controlled studies are required to determine the true safety and efficacy of this treatment modality [63].

1.6.2. Laser physics

Properties of laser light

Unlike other forms of light, laser light has special properties which make it significantly more effective and dangerous than conventional light of the same power. The laser light particles (photons) are usually:

- Monochromatic: consisting of a single wavelength
- Coherent: photons are in phase .
- Collimated: photons are almost in parallel (aligned), with little divergence from the point of origin

Components of a laser

A laser consists of 3 basic components:

1. A lasing medium or "gain medium": May be a solid (crystals, glasses), liquid (dyes or organic solvents), gas (helium, CO2) or semiconductors
2. An energy source or "pump": May be a high voltage discharge, a chemical reaction, diode, flash lamp or another laser
3. An optical resonator or "optical cavity": Consists of a cavity containing the lasing medium, with 2 parallel mirrors on either side. One mirror is highly reflective and the other mirror is partially reflective, allowing some of the light to leave the cavity to produce the laser's output beam – this is called the output coupler.

The laser is usually named according to the type of lasing medium. This also determines the type of pump required and the wavelength of the laser light which is produced [64].

1.6.3. Principle of operation at atomic level

One model in atomic physics describes an atom as a central nucleus of protons and neutrons, surrounded by a cloud of electrons which encircle the nucleus in different orbitals. When appropriate energy is supplied to the atom, electrons can jump from low-energy orbitals (ground state) near the nucleus to high-energy orbitals further away, leading to atomic excitation by the process of energy absorption.

Some of the electrons in the high-energy orbit spontaneously return to the ground state, releasing the difference in energy in the form of a photon, with a wavelength which depends exactly upon the difference in energy of the 2 states and has a random phase and direction. This process is

called spontaneous emission and forms the basis of light emitted by a neon sign, fluorescent light bulb and television tube.

This emitted photon can collide with one of the mirrors in the resonating cavity and reflect back into the lasing medium causing further collision with some of the already excited atoms. If an excited atom is struck, it can be stimulated to decay back to the ground state, releasing 2 photons identical in direction, phase, polarization and energy (wavelength). This process is termed stimulated emission.

A cascade effect of stimulated emission of photons occurs, resulting in further amplification (optical gain) and soon many of the atoms emit light along the same axis. For a laser to sustain function, the majority of the atoms must be maintained in the excited state, hence called “population inversion”. This is achieved by the continuous input from the energy pump (continuous wave laser) or by intermittent pumping resulting in a pulsed wave laser. A small number of photons are allowed to escape from the lasing medium though the partially reflective mirror of the output coupler. This is the usable laser light and may be in the visible spectrum or beyond (infrared or ultraviolet). It is directed to the target via a delivery system which consists of fibre-optic light guides for visible light or a series of mirrors for infrared [64].

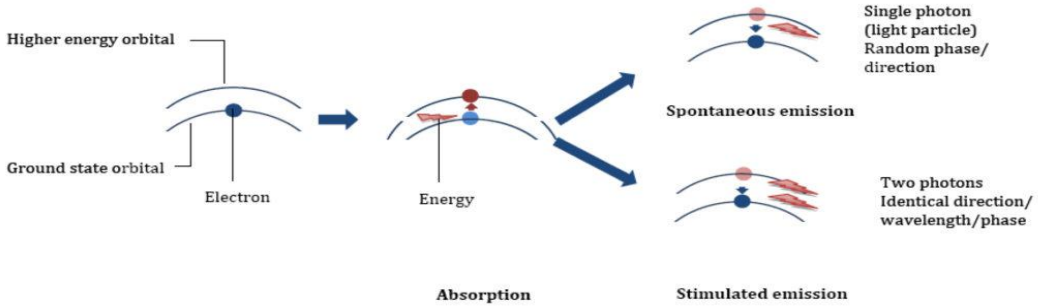


Figure 1-4: Absorption and emission[64].

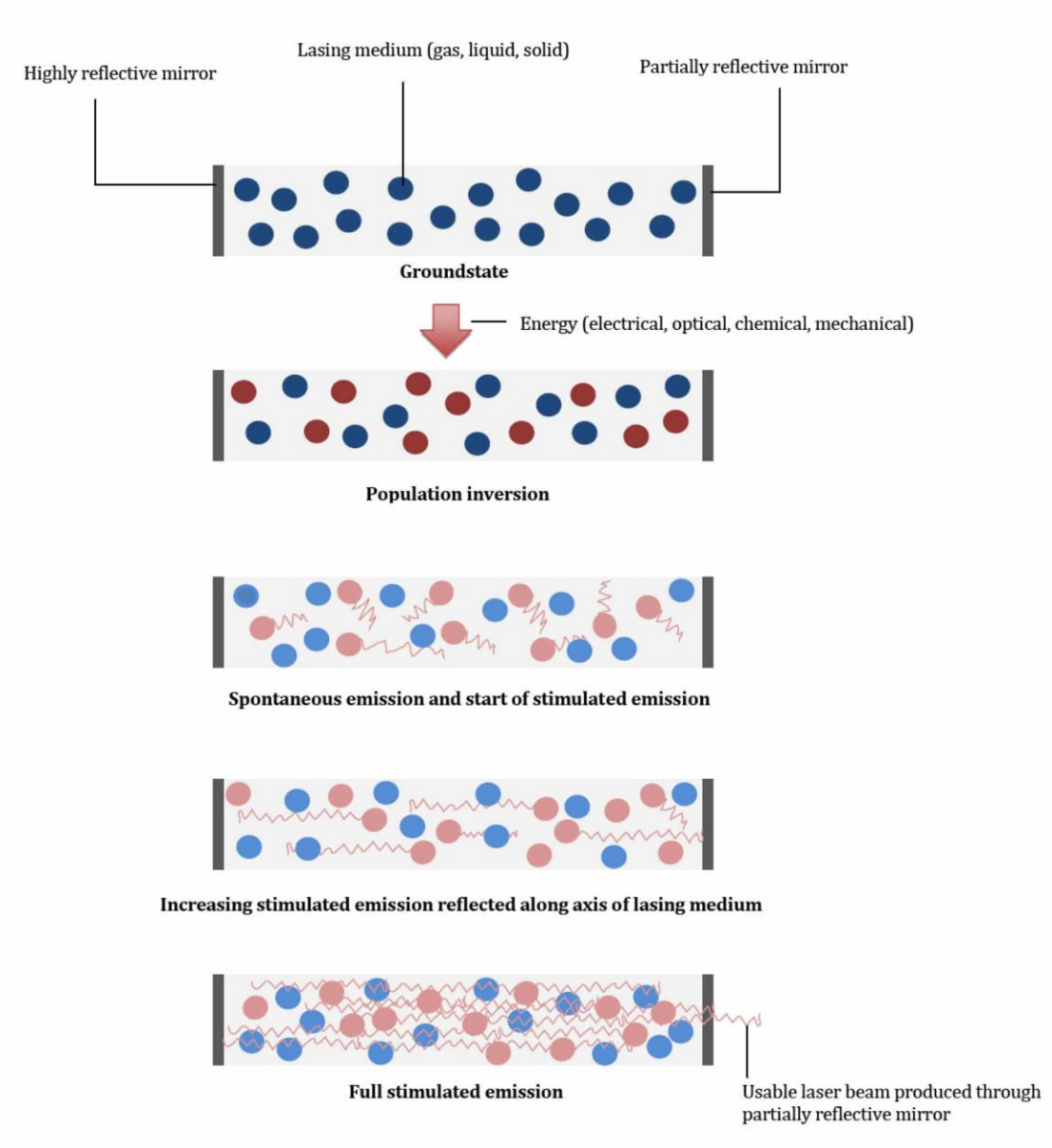


Figure 1-5: Production of the light beam[64].

1.6.4. Medical lasers

Medical lasers may be operated in continuous wave or pulsed wave modes. The output of continuous wave lasers is measured as power in watts, and for pulsed lasers the output is measured as energy in joules. Irradiance, or power density, refers to laser power per unit area (W/cm^2) Fluence, or energy density, is irradiance multiplied by exposure time (J/cm2) The interaction between the laser beam and the tissue is determined by the wavelength (figure 1-6), power density and exposure time. It is the monochromatic nature of laser light that is responsible for its selective effect on biological tissues. When the light comes into contact with the tissues, it can be transmitted, scattered, reflected or absorbed. This depends on the nature of the tissue and the wavelength of the light. The laser light has to be absorbed by the tissue in order to exert biological effects [64]. Examples of the main absorbing components in tissues are:

Water - absorbs infrared light

Haemoglobin - absorbs visible light, especially green

Melanin - absorbs visible and ultraviolet light

The wavelength also determines the depth of penetration. As the wavelength decreases towards the ultraviolet spectrum more scattering occurs which limits the depth of penetration within the tissues. Hence the Argon laser is used for retinal surgery and port-wine birthmarks. The Nd:YAG laser operates at the near infrared spectrum, which has a greater depth of penetration and is therefore used for the cutting and coagulation of tissues [64].

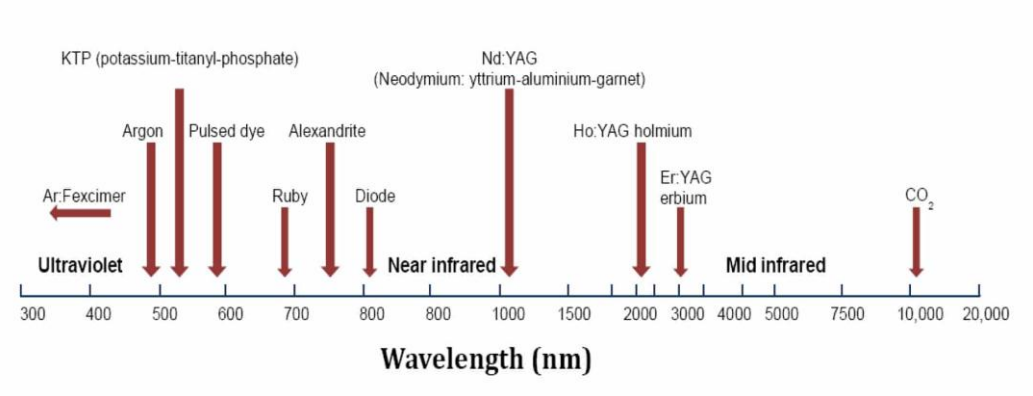


Figure 1-6: Wave lengths of medical laser[64].

1.6.5. Examples of lasers in medical practice

CO2 laser: Used for cutting and coagulation of soft tissue, which consists primarily of water, e.g. laryngeal surgery. It creates a photo-thermal effect, rapidly heating the tissues. Depending on the exposure time, tissue vaporisation (ablation), coagulation, or both may occur. Pulsing the laser exposure can minimize thermal conduction that may cause collateral tissue damage [64].

Holmium:YAG laser: Used for tissue ablation or lithotripsy via a photo-mechanical effect. An extremely intense, but very brief, pulse of laser causes an explosive expansion of the tissue or water within the renal calculi, causing photoacoustic disruption.

Excimer (Argon:Florine) laser: Used for corneal reshaping. The laser breaks down the covalent bonds in the protein molecules (photodissociation), resulting in non-thermal ablation [64].

Table 1-2: Examples of medical lasers[64].

LASER MEDIUM	TYPE	PUMP SOURCE	COLOUR/ WAVELENGTH	APPLICATIONS
CO2	Gas	Electrical discharge	Far infrared 10 600 nm	Cutting, coagulation, laser scalpel, skin resurfacing
Ho:YAG Holmium	Solid	Laser diode	Mid infrared 2070 nm	Tissue ablation, lithotripsy, endoscopic sinus surgery
Nd:YAG	Solid	Flash lamp, other laser	Near infrared 1064 nm	Cutting and coagulation, GI bleeding, black tattoo removal
Diode	Solid (Semiconductor)	Electric current	Red- infrared 630 - 900 nm	Laser pointer, hair removal, bar code scanners
Argon	Gas	Electrical discharge	Blue-green 500nm	Retinal surgery, AV malformations, thick port wine birthmarks
Eximer (Ar:F)	Gas	Electrical discharge	Ultraviolet 193 nm	Corneal vision correction
Ruby	Solid	Flash lamp	Red 694 nm	Hair removal, tattoo removal, holography
Pulsed dye	Liquid	Flash lamp, other laser	Yellow 390 - 640 nm	Birthmark removal, vascular skin lesions

1.6.6. Hazards and safety

The properties of laser light make it significantly more effective and dangerous than conventional light of the same source, i.e. a 30W surgical CO2 laser compared with a 60 W incandescent light bulb. A laser delivers much greater irradiance than a conventional light source of the same power, as the light is coherent (resulting in constructive interference at the target) and collimated (negligible loss of power with distance from the source). Both direct and reflected laser beams are therefore potentially dangerous. The principle dangers are injury to the eye, burns and ignition. Laser light from the ultraviolet to the far infrared wavelengths can cause burns to the skin [64].

If a parallel laser output beam is focused on a smaller spot using a lens, it greatly increases the power density at the focal point. The lens of the eye may refocus stray visible or near infrared laser light onto the retina, causing painless retinal burns which can result in a permanent blind spot in the field of vision due to damage to the photoreceptors. Staring directly

into a laser beam should be avoided. Safety goggles must be appropriate for the specific laser in use, giving protection at the appropriate wavelength [64].

1.6.7. Classification

The classification of lasers is based on the Maximum Permissible Exposure (MPE) levels and effects on the eyes and skin. MPE is a calculation of the highest power density (W/cm2) or energy density (J/cm2) allowed for a laser that is considered to be safe and unlikely to cause damage. MPE is measured at the skin or the cornea of the eye, for a given wavelength or exposure time. The International Electrotechnical Commission (IEC) standard 60825-1 (2007) include methods of calculating MPE levels and defines seven classes of lasers. Class 1, 1M, 2, 2M, 3R, 3B and 4 with Class 1 the safest and class 4 the highest and most dangerous class of laser. Medical lasers are in category 4 [64].

1.7. CO_2 Laser

Carbon dioxide (CO2) lasers have been in use since the 1960s. CO2 lasers were initially used primarily for cutting and destruction of tissue, using a continuous wave mode, which ablates tissue to a depth of 400-500 μm. This technique was used for diverse applications, such as for the treatment of cervical intraepithelial neoplasia and laser surgical blepharoplasty [65]. In the 1990s, CO2 laser technology was advanced to create high-energy pulsed CO2 lasers, which ablate tissue at a more superficial depth, between 20 to 100 μm, while minimizing thermal injury to deeper tissue [66].

These high-energy pulsed CO2 lasers are effective for less aggressive treatments, including cutaneous laser resurfacing. Fractional CO2 laser

treatment was subsequently developed in 2004. Fractional treatment involves splitting the laser beam into a large number of microbeams. This creates columns of ablation in the skin surrounded by normal undamaged skin and can provide an improved side effect profile as compared with non-fractional treatment [66].

1.7.1. Anatomy and physiology

Laser resurfacing is a process whereby energy generated at a specified wavelength is used to ablate the most superficial layers of skin. This process may be total, whereby all portions of the treatment area are ablated; or fractional, where smaller regions are ablated and adjacent areas are left untreated, typically in a pattern of closely spaced ablated and non-ablated areas. CO2 lasers emit energy with a peak wavelength of 10,600 nm, which is preferentially absorbed by intracellular water [67].

Absorption of this wavelength by the epidermis ablates the most superficial layers, promoting subsequent re-epithelialization from residual skin appendages and adnexal structures in the dermis. The thermal injury that occurs below the zone of ablation induces heat mediated contraction of collagen and subsequent collagen remodeling in the dermis [67].

A contraction in collagen length causes tightening of the skin. Compared with other lasers, such as the erbium-YAG laser, CO2 lasers generate heat and cause greater coagulation of small blood vessels in the dermis, leading to less bleeding when a large area is ablated in its entirety. This heat has an additional effect of stimulating the deep dermal layers to more rapidly promote re-epithelialization as well as producing a near-sterile ablated surface [67].

1.7.2. Indications

Carbon dioxide lasers can be employed for many cutaneous conditions and indications. These include treatment and prevention of photoaging and reduction in the appearance of scarring. They may also be used for prophylaxis and treatment of precancerous lesions and keratinocyte skin cancers (squamous cell carcinoma and basal cell carcinoma), as well as cutaneous vascular lesions such as hamartomas. CO2 laser resurfacing has the most optimal results in patients with Fitzpatrick type I-II skin [67].

Cosmetic indications include the treatment of photoaging and rhytids. Photoaged skin is characterized by increased laxity, irregular color and texture, and the presence of static rhytids. In comparison to other currently available modalities for photoaging, such as microdermabrasion and chemical peels, the use of CO2 lasers allows for more precise control over the area, depth, and extent of thermal damage. A number of blinded studies have shown significant improvement in photoaging of the cosmetic units of the forehead, glabella, as well as the periorbital region, and most notably, the perioral region. This results in collagen remodeling that occurs after laser treatment [67].

Treatment of scarring from acne, trauma, or surgical procedures can be done effectively with carbon dioxide laser resurfacing. Carbon dioxide lasers provide an approach with more precise control over treatment depth and area as compared to microdermabrasion, which is among the most commonly used modality for acne scar treatment. Carbon dioxide lasers can reduce the appearance of acne scarring by inducing thermal damage below the area of scarring and subsequently stimulating collagen production. They also reduce the appearance of the shoulder of the scar.

For the treatment of surgical scars, CO2 lasers have been noted to produce less bleeding and crusting as compared to dermabrasion [68].

For the treatment of pre-malignant lesions and actinic damage, CO2 lasers may not be as effective as other methods such as chemical peels or dermabrasion. When compared with topical 5-fluorouracil and trichloroacetic acid chemical peel for prophylaxis of keratinocyte malignancies, CO2 lasers have been shown to be as effective in reducing the number of pre-malignant actinic keratoses and also the number of keratinocyte skin cancers that developed. However, trichloroacetic acid was found to have the lowest cancer incidence rate and highest patient satisfaction when compared with the other modalities [69].

CO2 lasers can be employed for the treatment of keratocystic skin cancers. CO2 lasers may have an advantage as a treatment modality for patients who are on anticoagulation medication (as carbon dioxide lasers will induce coagulation and reduce bleeding), and also in cases where patients have multiple malignant lesions that are not readily amenable to surgical excision. A disadvantage to their use is the lack of histological confirmation of malignant lesion removal. In one study, Nouri et al. treated a large number of basal cell carcinomas with CO2 lasers and at follow up visits assessed for residual malignant tissue by Mohs micrographic surgery. Histology confirmed a lack of malignant tissue in these treated areas [70].

1.7.3. Contraindications

Contraindications to therapy with CO2 laser resurfacing include the presence of active acne lesions, as there is a risk of infection or abnormal colonization following the procedure. Adnexal damage from autoimmune disease, burns, or irradiation could interfere with re-

epithelialization, and patients with these in their medical history may not be candidates for treatment with CO2 lasers. Furthermore, a history of diseases associated with kobnerization phenomenon, including vitiligo and psoriasis, are also contraindications for this therapy [70].

1.٧.4. Technique

Appropriate pain control should be selected. Typically, general anesthesia or dissociative anesthesia is used for full facial carbon dioxide laser resurfacing. For smaller areas or fractional resurfacing, a series of topical anesthetic applications followed by a local anesthetic block or infiltration may be sufficient for patient comfort. Occlusive inserts, eyewear, or laser goggles may be chosen for patient ocular safety depending upon the area being treated, and extreme caution should be exercised with the possibility of light becoming reflected onto the cornea. Antibacterial and antiviral medications (for herpetic reactivation prevention) can be prophylactically administered or prescribed [71].

The general standard of practice is to initiate antiviral therapy for all patients 2 days prior to the CO2 laser procedure. Most patients have been exposed to the herpes simplex virus, and this significantly reduces the risk of infectious complications. Antibiotics such as cefadroxil, dicloxacillin, doxycycline, or ciprofloxacin are often prescribed postoperatively. It has been shown that patients treated with antifungals such as fluconazole have faster healing times, and an antifungal is often given on the day of laser surgery [72].

To achieve successful ablation of the skin without causing excessive thermal damage, a fluence of 5 J/cm2 is administered with a pulse duration of less than 1 millisecond. A short pulse duration allows the skin to have sufficient thermal relaxation time. Individual pulse duration and

depth should be personalized based on the patient's concerns and skin type, as per the individual machine manufacturer guidelines [73].

Re-epithelialization typically occurs in 6 to 7 days after treatment. Following the procedure, crusting and serous exudate may develop over denuded skin in the treated area. Post-operative care includes the use of bio-occlusive films, petroleum-based ointments, or hydrogels for the first 48 hours to decrease the formation of substantial crusting over the treated area, which can facilitate appropriate healing. Swelling, pain, and erythema can persist for 1 to 2 weeks following treatment, with inflammation typically resolving over the course of the following 6 weeks. In some cases, this inflammation can last up to 6 months post-treatment. A regimen combining hydroquinone and glycolic acid can be used to reduce the occurrence of hyperpigmentation [74].

1.7.٥. Complications

The typical post-operative course involves the development of erythema, peeling, and skin fragility, which can last up to 3 months after the treatment.

Short-term complications of treatment include the formation of milia and acneiform eruptions in the treated area. Herpes simplex virus reactivation may also occur, for which prophylactic valacyclovir should be given in patients with a known medical history of herpes simplex virus infection.

Any procedure carries the risk of infection. Bacterial and fungal are less commonly seen after CO2 laser resurfacing and are often seen in the setting of prolonged use of occlusive dressings, which should usually be removed 48 hours after the procedure.

Changes in pigmentation, both hyperpigmentation, and hyperpigmentation, are also common. The likelihood of occurrence of

these changes is increased with Fitzpatrick skin types III-IV as compared with types I-II. Pigmentation changes can be, at times, self-limited. Bleaching preparation and chemical peels may be used to reduce the appearance of this side effect. Hypopigmentation is more common with the use of CO2 lasers than for other laser types [75].

1.7.6 Safety with the CO_2 Laser

Safety with lasers is paramount for the well-being of the patient and all in the operating room. This is particularly so for the CO_2 laser given its range of use in deliberate destructive indications. As the eye is the most vulnerable target for optical energy, eye protection is mandatory for all in the treatment room. However clear glass or plastic will stop the CO_2 beam completely: this is why normal quartz fibers cannot be used as a beam transmission system for the CO_2. Ordinary prescription lenses can be used, but dedicated glasses or goggles incorporating lateral shields are always recommended. The 10,600 nm beam is also a "safe" wavelength for the eye, or at least the retina, because all of the energy will be absorbed in the water in the cornea at the front of the eye. This makes the CO_2 laser marginally safer than the visible and nearinfrared lasers, because the latter will pass straight through the cornea, be focused by the lens, and severely damage the macula/fovea complex in the retina [75].

Protecting the patient is also a priority, and for the CO_2 laser this means draping the skin around the target area with damp drapes or gauze, and keeping these materials damp throughout the procedure because the CO_2 energy is absorbed in water. If a beam of CO_2 energy strikes dry gauze or cotton, the potential for starting a fire is very high. When using the CO_2 laser to excise tissue held under traction, a backstop of some kind should be employed, either a dampened wooded tongue depressor or a

damp cotton bud depending on the site. Finally, as already discussed, the laser plume created by the CO_2 laser can contain potentially harmful substances such as viable viral particles, [7] so the use of a dedicated smoke evacuator is extremely important. The use of masks alone will not suffice [76].

1.8. Fractional CO_2 laser

Carbon dioxide (CO_2) laser is an ablative laser device that produces energy in the far-infrared region at a wavelength of 10,600 nm. Resurfacing with CO_2 laser is highly effective in treating scars and ageing skin. However, a really long down-time and high incidence of adverse effects has limited its use in routine dermatology practice. Some long-term adverse effects can also occur including permanent hypopigmentation, hyperpigmentation and permanent scarring [77].

Fractional photothermolysis (FP) circumvents many of the above-mentioned disadvantages of laser resurfacing. With FP, only a fraction of the whole skin is treated in a pixelated pattern while the intervening skin remains intact. Treatment with FP leads to formation of longitudinal microthermal zones (MTZs) in the skin which are separated by healthy, untreated skin with an intact epidermis. This allows the treating physicians to go for much deeper treatment than with traditional laser resurfacing. Additionally, the adverse effects encountered with FP are transient and less severe than with full skin resurfacing. Fractional CO_2 laser resurfacing has been successfully used in the treatment of atrophic acne scars and for skin rejuvenation. There are also some reports of its usefulness in hypertrophic as well as burn scars [77].

1.8.1. Fractional CO_2 Laser in GSM

Laser treatment is a novel non-hormonal treatment approach for GSM. The concept behind laser procedures to treat vulvovaginal conditions is to use a wavelength having high water absorption, such as the carbon dioxide (CO_2) laser (10,600 nm), to ablate and coagulate vaginal and vulvar tissues. The Er:YAG laser also stimulates non-ablative photothermal effects by thermal diffusion to the vaginal walls. A wound response is initiated due to the heating and results in tissue remodeling with neoformation of collagen and elastic fibers in atrophic skin. The muscle tone of the vagina is then restored by tightening the supportive structures of the vulvovaginal complex. CO_2 laser treatment has previously demonstrated significant improvement in GSM symptoms in postmenopausal women. Fractional CO_2 laser application has also been shown to restore the vaginal mucosa structure in postmenopausal, non-estrogenized women[6, 78].

In the published trials to date, only postmenopausal women have been studied, primarily with short-term follow-up of 12 weeks after treatment[6,67]. As symptoms of VVA can occur at any time in a woman's life cycle, this study investigated the effects of fractional CO_2 laser in perimenopausal women treated by resurfacing and coagulation of the vaginal canal tissues and mucosal tissues of the introitus. Clinical outcome was evaluated at 12 weeks and longer term at 6 months after the final treatment [79]

Aim of The study

To compare the efficacy of Fractional Co2 Laser to topical estrogen in treatment of vulvovaginal atrophy among perimenopausal women.

Chapter Two

Patients & Methods

Patients & Methods

2.1 . Introduction

The current study was a case series study conducted in private clinic in Baghdad city-Iraq in duration of four months throughout the period from 15th of September, 2021 till 15th of January, 2022. Patients with Genitourinary syndrome (GSM) presented to private clinic were the study population after taking an agreement of hospital authorities in addition to oral informed consent of patients enrolled in the study and management of complications.

The selected sample was a convenient sample of 20 women with one or more symptoms of genitourinary syndrome of menopause (GSM) was selected from private clinic after eligibility to inclusion and exclusion criteria.

2.2. The inclusion criteria

The inclusion criteria were patient with at least one or two symptoms of vulvovaginal atrophy (VVA) at perimenopause.

2.3. The exclusion criteria.

- Pregnancy
- Undiagnosed vaginal bleeding,
- Active genital or urinary tract infection,
- Patient using hormonal replacement therapy and vaginal lubricant,
- Drugs induced menopause,
- Prolapse stage 2 and more based on examination based on pelvic organ prolapse
- Those suffering from hormonal imbalance or any serious disease or Chronic condition that could interfere with study compliance,
- Smokers.

- History of any form of cancer, previous vaginal reconstructive surgery, Lost to follow up and patients refused to participate in the study .

2.4 . Methods

The data was collected from women with GSM directly by the researcher and filled in a prepared questionnaire. The questionnaire was designed by the researcher and supervisor depending on previous literatures. The questionnaire included the following information:

1. General characteristics of women with GSM: Age, parity, mode of delivery, number of cesarean sections, history of vaginal reconstructive surgery including episiotomy, menopause and years since menopause.
2. Chief complaints of women with GSM.
3. Vaginal health index scores of women with GSM.
4. 10_cm VAS scales of symptoms intensity for women with GSM.
5. Maturation value of Meisels of women with GSM.
6. Laser procedure complications of women with GSM.
7. Laser procedure discomfort of women with GSM.

The enrolled women in the study were diagnosed and outcomes validated by the researcher through subjective and objective assessment of GSM. The patients were followed up for 12 weeks in a schedule of week 0, week 8 and week 12.

The subjective assessment including the bothersome symptoms of VVA like dryness, dyparunia, burning, vaginal discharge, urgency & urge incontinence and dysurea.

Participants reported intensity of VVA symptoms using a 10-cm VAS. The scale's left extremity indicates the complete absence of symptoms (0)

and the right extremity indicates the worst possible symptom (10). Participants rated VVA symptoms (dyspareunia, dryness, or burning, vaginal discharge and bleeding and urgency and urge incontinence) from 0 to 10.

- 0 indicate no symptoms
- 1,2,3 indicate mild symptoms
- 4,5,6 indicate moderate symptoms
- 7,8,9 indicate sever symptoms
- 10 indicate extreme or very severe symptoms.

The objective assessment was also done by the researcher through pelvic examination including gentle inspection of vulva, vagina, vestibule and urethra in order to recognize the signs of VVA which can be rated on validated scale which was vaginal health index (VHI).

The VHI analyzes the following five components on a scale of 1 to 5: elasticity, fluid volume, pH, epithelial integrity, and moisture. A minimal total score of 5 points indicates severe VVA, and a maximal total score of 25 points indicates no clinical signs of VVA.

Each parameter is graded from 1-5 where one indicates worst condition and five indicate best condition (Table 1).

The objective assessment was done also by Ph measurement (Litmus paper was placed in the vagina and kept for one minute and the color was compared to standard color.

Additionally, the objective assessment included Maturation value of Meisels of women. They were assessed at weeks 0, 8, and12 and consisted of the analysis of vaginal smear samples. Vaginal smear samples were collected in a single scraping of the middle third of the

lateral vaginal wall with an Ayre spatula; 100 cells were analyzed per specimen by the pathology examination. Parabasal (P), intermediary (I), and superficial (S) cell counts were performed and multiplied by 0.0, 0.5, and 1.0, respectively. The sum of all three values comprises the maturation value.

(MV) of Measles, and an increased percentage of P cells and I cells suggests a decrease in estrogen levels.

- MV values ranging from 0 to 49 indicate low estrogen effect.
- MV values ranging from 50 to 64 indicate moderate estrogen effect.
- MV values ranging from 64 to 100 good estrogen effect.

Table 2-1: Vaginal Health Index[79].

Score	**Overall elasticity**	**Fluid secretion characteristics**	**Vaginal PH range**	**Epithelial mucosa**	**Moisture**
1	None	None	≥6.1	Petechiae noted before onset	None, mucosa inflamed
2	Poor	Scant thin yellow	5.6-6	Bleeds with light contact	None, mucosa not inflamed
3	Fair	Superficial thin white	5.1-5.5	Bleeds with scrapping	Minimal
4	Good	Moderate thin white	4.7-5	Not friable, thin mucosa	Moderate
5	Excellent	Normal (white flocculent)	≤4.6	Not friable, normal mucosa	Normal

The fractional CO_2 laser therapy was implemented by the researcher under supervision of supervisor. Laser machine used (Figure 2-1) in this study was co_2 laser Therapy system manufactured in China Model (Femi Med) and Company name (Laser Tell). The laser parameters used in this study were Fractional CO2 laser, wavelength 10600 nm, power 40 watt, duration 1ms, point number 40, distance 1.0 mm, scan mode normal, scan times 3 and scan Rows 8.

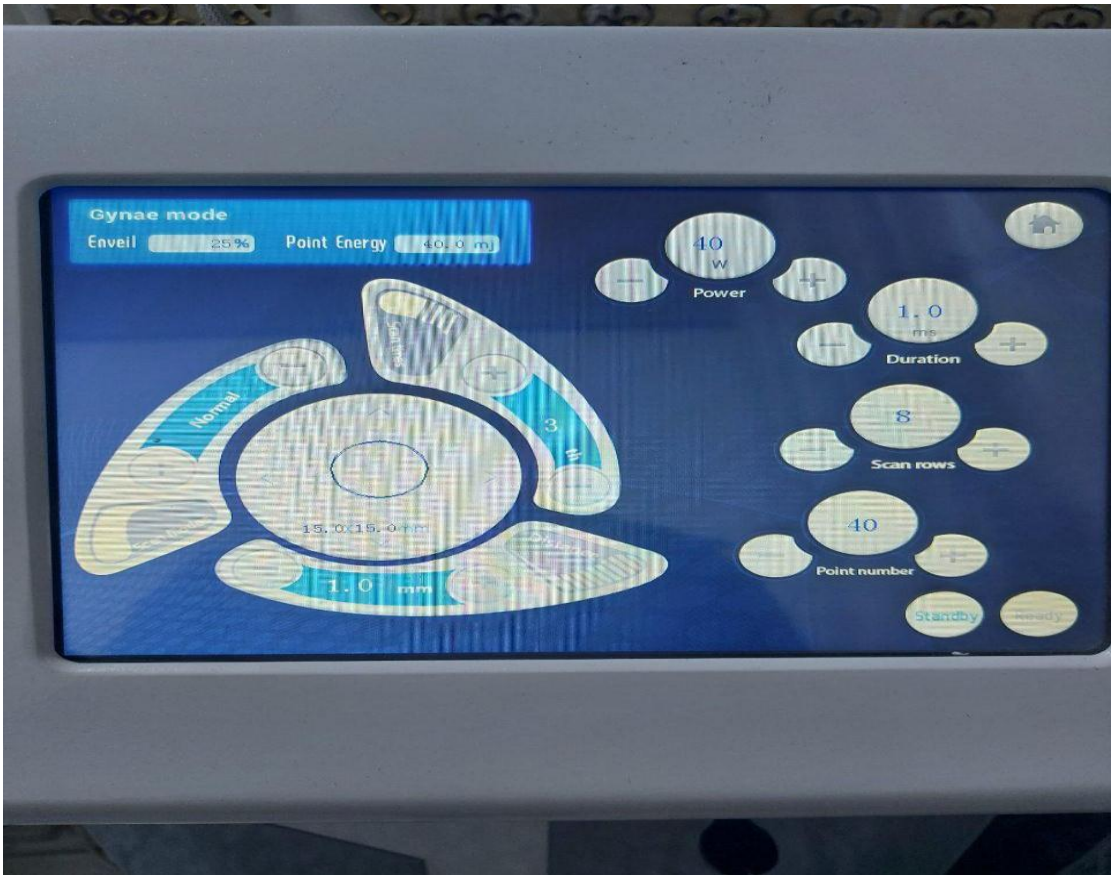


Figure 2-1: Fractional CO_2 laser machine setting.

2.5. The procedure

included the following:

1. Preparation of the patients: two days after menstruation for the patients who still menstruated.
2. Few minutes before starting, asked patient to empty bladder.
3. Insert topical anaesthesia Amla cream 5% (2.5 % lidocaine and 2.5 % prilocaine) at the introits then ask the patient to wait 10 minutes to anaesthetized area.
4. Proper eye protection for patient, physician and anyone else in the room is essential when using this laser.
5. A specially designed laser speculum (The speculum cage)) was introduced into the patient's vagina to serve as a guide for the laser beam delivery system. When the laser speculum is properly positioned into the patient's vagina, the laser beam delivery system) is introduced into the laser speculum A simple step-bystep withdrawal of the laser hand piece outwards from the laser speculum. The hand piece was positioned with contact to the vaginal wall and pulses were applied at each 1 cm marking and then retracted, the hand piece was reinserted two times. producing a non-ablative precisely controlled, thermal-only effect on the vaginal wall that causes immediate tissue shrinkage and initiates collagen remodeling and new collagen synthesis in the vaginal mucosa. The safety and tolerability of the procedure was assessed by observation and documentation of potential adverse effects during and after the procedure. The operative time taken about 20 minutes to complete.

2.6. Postoperative Instructions

After laser session all the patients were given instructions that including

1. Commitment to follow up appointments in the exact date.
2. No post-op therapy was needed.
3. Patients were only requested to restrain from sexual activities for a period of 7 days after each of the treatment sessions.

2.7. Vaginal estrogen group:

Premarin (conjugated estrogen) vaginal cream was used three times a week for three consecutive months for patient with vulvovaginal atrophy 0.625 mg.

2.8. Statistical analysis

All women's data entered using computerized statistical software; Statistical Package for Social Sciences (SPSS) version 22 was used. Descriptive statistics presented as (mean ± standard deviation) and frequencies as percentages. Multiple contingency tables conducted and appropriate statistical tests performed, Fishers exact test was used for categorical variables. Independent sample t-test was used to compare between two means. In all statistical analysis, level of significance (p value) set at ≤ 0.05.

Chapter Three

Results, discussion

Results and discussions

3.1 Introduction

This chapter presents the results, the discussion to explain these results, conclusion and suggestion about this study.

3.2 Results

This study included 20 women with one or more symptoms of genitourinary syndrome of menopause (GSM); 10 women treated by topical estrogen and 10 women treated by Fractional Co2 Laser. No significant differences were observed between GSM women treated by topical estrogen and GSM women treated by Fractional Co2 Laser regarding age (p=0.3), mode of delivery (p=0.17), number of cesarean sections (p=0.1), history of vaginal reconstructive surgery including episiotomy (p=0.3), menopause (p=0.6) and years since menopause (p=0.6). The mean parity history was significantly higher among GSM women treated by Fractional Co2 Laser as compared to GSM women treated by topical estrogen (p=0.04). (***Figure 3- 1and Table 3-1***)

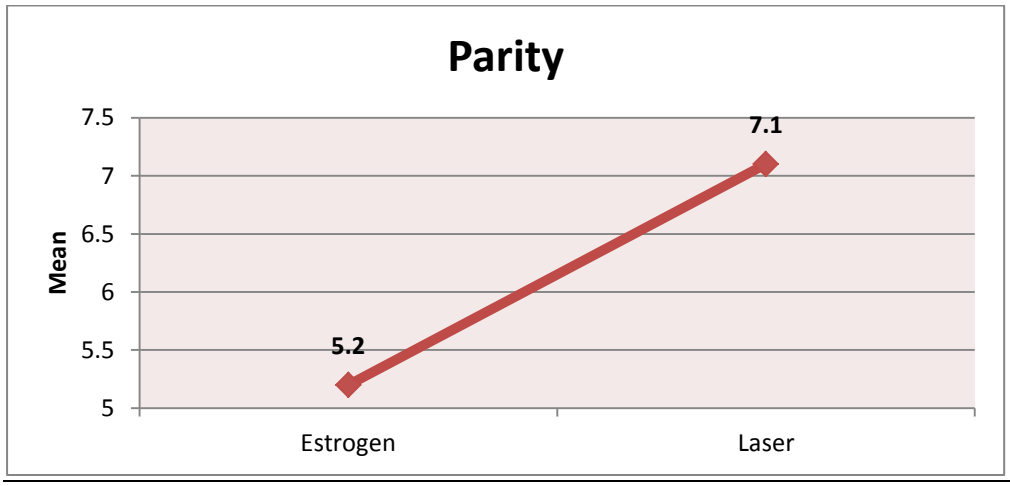


Figure 3-1: Parity distribution according to study groups.

Table 3-1: Distribution of women's general characteristics according to study groups.

Variable	Study groups				P
	Estrogen		Laser		
	No.	%	No.	%	
Age					0.3*[NS]
<60 years	6	60.0	8	80.0	
≥60 years	4	40.0	2	20.0	
Parity					**0.04****[S]
Mean±SD	5.2±1.9		7.1±1.9		
Mode of delivery					0.17*[NS]
Normal vaginal	5	50.0	7	70.0	
Cesarean section	3	30.0	0	-	
NVD & CS	2	20.0	3	30.0	
Number of cesarean sections					0.1**[NS]
Mean±SD	2.6±0.9		1.6±0.5		
History of vaginal reconstructive surgery including					0.3*[NS]
Yes	2	20.0	4	40.0	
No	8	80.0	6	60.0	
Menopause					0.6*[NS]
Yes	5	50.0	4	40.0	
No	5	50.0	6	60.0	
Years since menopause					0.6**[NS]
Mean±SD	9.6±5.9		11.7±8.4		

**Fishers exact test, **Independent sample t-test, S=Significant, NS=Not significant.*

No significant differences were observed between GSM women treated by topical estrogen and GSM women treated by Fractional Co2 Laser regarding chief complaints (p=0.3). (***Table 3-2***)

Table 3-2: Distribution of women's chief complaints according to study groups.

Variable	**Study groups**				**P**
	Estrogen		**Laser**		
	No.	**%**	**No.**	**%**	
Chief complaints					0.64*^{NS}
Dryness	4	40.0	1	10.0	
Urge incontinence	1	10.0	1	10.0	
Burning & dysurea	1	10.0	0	-	
Dyspareunia	1	10.0	3	30.0	
Urgency & urge	1	10.0	1	10.0	
Stress incontinence	1	10.0	2	20.0	
Burning	1	10.0	1	10.0	
Urgency	0	-	1	10.0	

**Fishers exact test, NS=Not significant*.

No significant differences were observed between GSM women treated by topical estrogen and GSM women treated by Fractional Co2 Laser regarding most VHI scores at different weeks ($p>0.05$), except for fluid secretion at week 12 ($p=0.01$), vaginal PH at week 12 ($p=0.03$) and moisture at week 8 ($p=0.02$), as mean VHI score were significantly lower among GSM women treated by Fractional Co2 Laser. The means of total VHI score at week 8 and week 12 were significantly lower among GSM women treated by Fractional Co2 Laser as compared to GSM women treated by topical estrogen ($p\leq0.05$). (***Table 3-3 and Figures 3/2-4***)

Table 3-3: Distribution of women's vaginal health index scores according to study groups.

VHI indices	**Study groups**		**P**
	Estrogen Mean±SD	**Laser Mean±SD**	
Elasticity at week 0	3.1±0.73	2.8±0.91	0.4*^{NS}
Elasticity at week 8	3.6±0.6	3.2±0.6	0.19*^{NS}
Elasticity at week 12	3.9±0.87	3.6±0.84	0.4*^{NS}
Fluid secretion Characteristics at week 0	2.6±0.51	2.6±0.51	1.0*^{NS}
Fluid secretion Characteristics at week 8	3.1±0.31	3±0.47	0.58*^{NS}
Fluid secretion Characteristics at week 12	4.2±0.78	3.3±0.67	**0.01***^{S}
Vaginal PH at week 0	2.6±0.84	2.6±0.69	1.0*^{NS}
Vaginal PH at week 8	3.6±0.51	3.2±0.63	0.31*^{NS}
Vaginal PH at week 12	4.3±0.67	3.6±0.69	**0.03***^{S}
Epithelial integrity at week 0	2.4±0.51	2.7±0.67	0.27*^{NS}
Epithelial integrity at week 8	3.1±0.56	3±0.81	0.75*^{NS}
Epithelial integrity at week 12	3.9±0.56	3.5±0.7	0.18*^{NS}
Moisture at week 0	1.9±0.73	1.8±0.63	0.74*^{NS}
Moisture at week 8	3.9±0.99	2.9±0.73	**0.02***^{S}
Moisture at week 12	4.3±0.67	3.8±0.91	0.18*^{NS}
Total VHI score at week 0	12.6±1.7	12.5±2.3	0.9*^{NS}
Total VHI score at week 8	17.2±1.3	15.3±2.3	**0.03***^{S}
Total VHI score at week 12	20.8±2	17.8±2.4	**0.009***^{S}

** Independent sample t-test, S=Significant, NS=Not significant.*

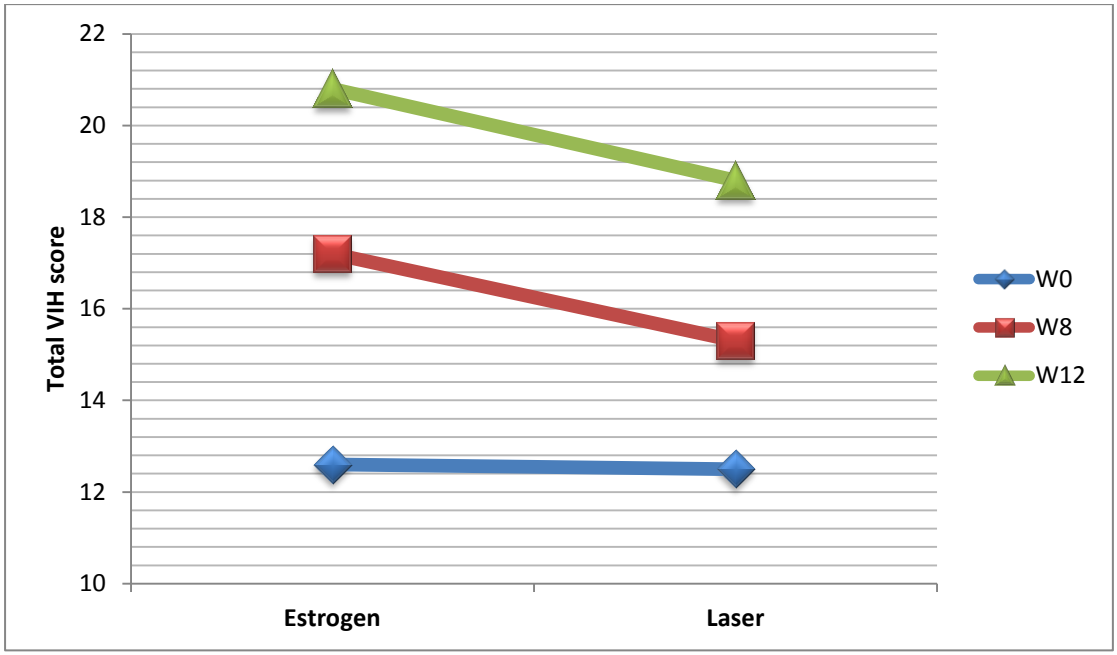


Figure 3-2: Total VHI score distribution according to study groups.

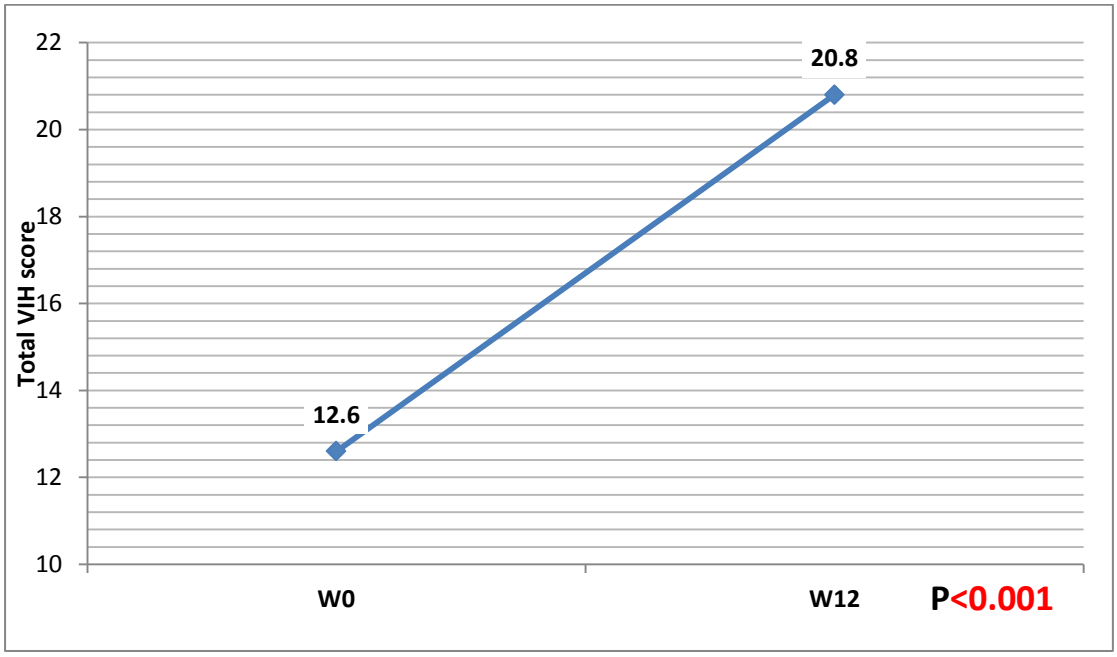


Figure 3-3: Total VHI score of women pre and post topical estrogen.

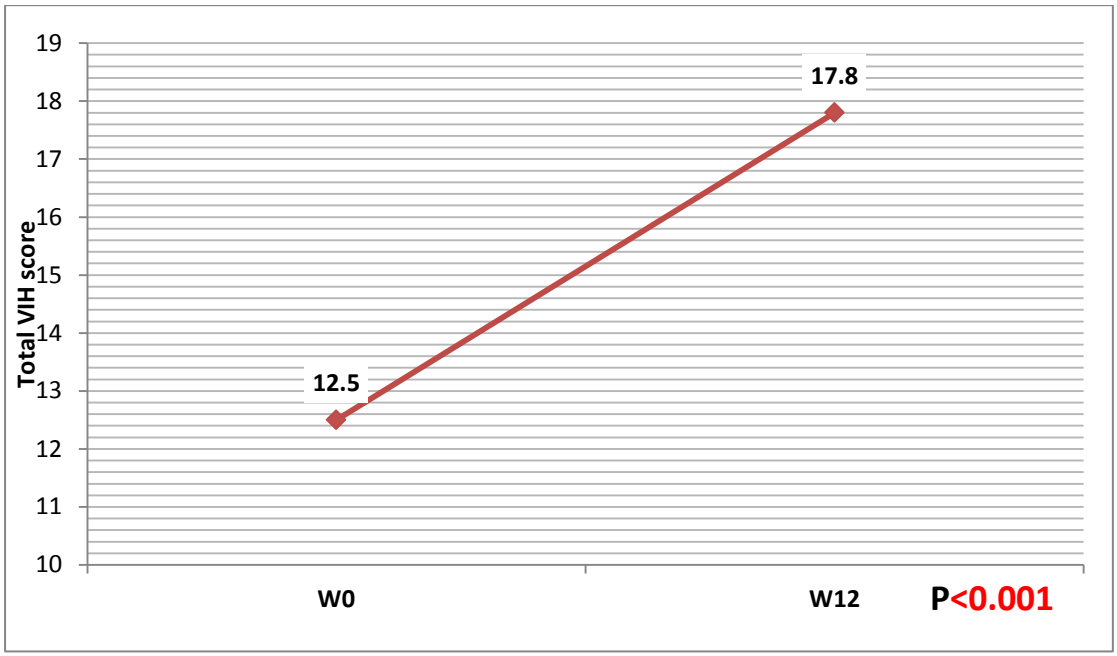


Figure 3-4: Total VHI score of women pre and post Laser.

There were no significant differences between GSM women treated by topical estrogen and GSM women treated by Fractional Co2 Laser regarding dysparunia intensity at weeks 0 & 8, dryness intensity at different weeks, burning intensity at different weeks, vaginal discharge & bleeding intensity at different weeks, urgency & urge incontinence intensity at weeks 0 & 8 and dysurea intensity at different weeks. The dysparunia intensity was significantly declined in GSM women treated by Fractional Co2 Laser after 12 weeks of treatment (p=0.01). Similarly, the urgency & urge incontinence intensity was significantly declined in GSM women treated by Fractional Co2 Laser after 12 weeks of treatment (p=0.01). (***Table 3-4A-C and figures 3/5, 6***)

Table 3-4A: Distribution of women's intensity of symptoms according to study groups.

Variable	Study groups				P
	Estrogen		Laser		
	No.	%	No.	%	
Dysparunia at week 0					0.7*[NS]
No	1	10.0	3	30.0	
Mild	2	20.0	2	20.0	
Moderate	7	70.0	2	20.0	
Severe	0	-	3	30.0	
Dysparunia at week 8					0.28*[NS]
No	1	10.0	3	30.0	
Mild	7	70.0	3	30.0	
Moderate	2	20.0	3	30.0	
Severe	0	-	1	10.0	
Dysparunia at week 12					**0.01***[S]
No	1	10.0	7	70.0	
Mild	9	90.0	3	30.0	
Dryness at week 0					0.6*[NS]
Moderate	7	70.0	8	80.0	
Severe	3	30.0	2	20.0	
Dryness at week 8					0.47*[NS]
Mild	6	60.0	4	40.0	
Moderate	4	40.0	5	50.0	
Dryness at week 12					0.17*[NS]
No	0	-	1	10.0	
Mild	10	100.0	7	70.0	
Moderate	0	-	2	20.0	

**Fishers exact test, S=Significant, NS=Not significant*.

Table 3-4B: Distribution of women's intensity of symptoms according to study groups.

Variable	Study groups				P
	Estrogen		Laser		
	No.	%	No.	%	
Burning at week 0					0.67*[NS]
No	1	10.0	3	30.0	
Mild	4	40.0	4	40.0	
Moderate	3	30.0	2	20.0	
Severe	2	20.0	1	10.0	
Burning at week 8					0.51*[NS]
No	1	10.0	3	30.0	
Mild	7	70.0	5	50.0	
Moderate	2	20.0	2	20.0	
Burning at week 12					0.87*[NS]
No	2	20.0	3	30.0	
Mild	7	70.0	6	60.0	
Moderate	1	10.0	1	10.0	
Vaginal discharge at week 0					-
No	10	100.0	10	100.0	
Vaginal discharge at week 8					-
No	10	100.0	10	100.0	
Vaginal discharge at week 12					-
No	10	100.0	10	100.0	
Urgency & urge incontinence at week 0					0.9*[NS]
No	4	40.0	5	50.0	
Mild	2	20.0	1	10.0	
Moderate	2	20.0	2	20.0	
Severe	2	20.0	2	20.0	
Urgency & urge incontinence at week 8					0.8*[NS]
No	4	40.0	5	50.0	
Mild	3	30.0	2	20.0	
Moderate	3	30.0	3	30.0	

**Fishers exact test, NS=Not significant*.

Table 3-4C: Distribution of women's intensity of symptoms according to study groups.

Variable	Study groups				P
	Estrogen		Laser		
	No.	%	No.	%	
Urgency & urge incontinence at week 12					**0.01***S
No	4	40.0	10	100.0	
Mild	6	60.0	0	-	
Dysurea at week 0					0.93*NS
No	4	40.0	5	50.0	
Mild	1	10.0	1	10.0	
Moderate	3	30.0	3	30.0	
Severe	2	20.0	1	10.0	
Dysurea at week 8					0.28*NS
No	6	60.0	5	50.0	
Mild	2	20.0	4	40.0	
Moderate	2	20.0	0	-	
Severe	0	-	1	10.0	
Dysurea at week 12					0.89*NS
No	6	60.0	5	50.0	
Mild	3	30.0	4	40.0	
Moderate	1	10.0	1	10.0	

**Fishers exact test, S=Significant, NS=Not significant*.

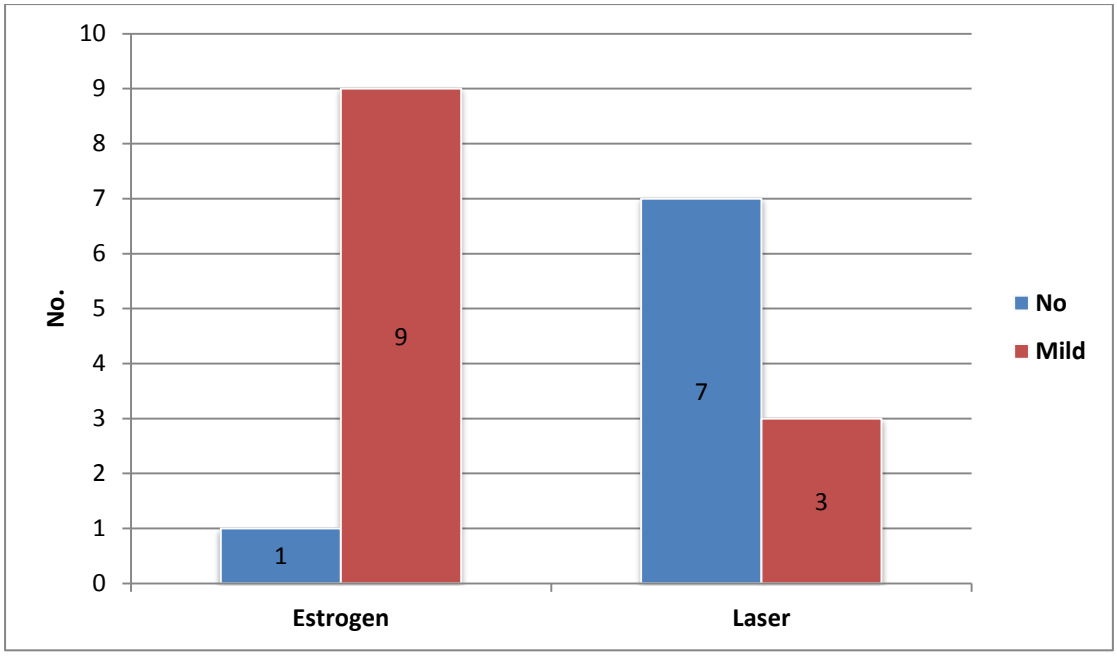


Figure 3-5: Dysparunia intensity after 12 weeks treatment by estrogen and laser therapy.

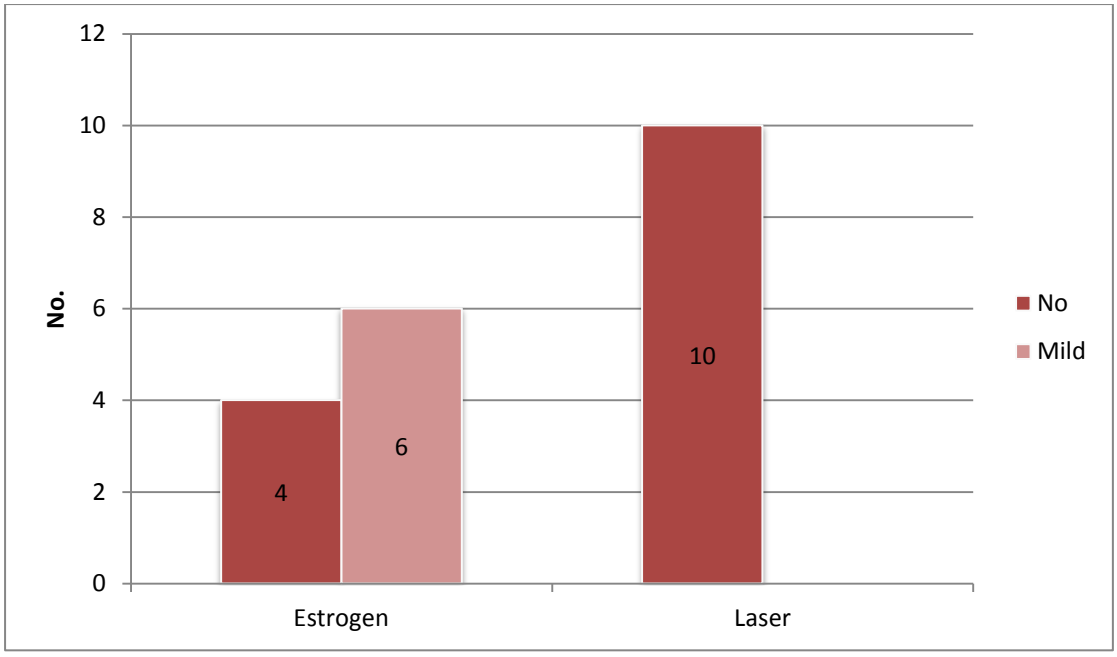


Figure 3-6: Urgency & urge incontinence after 12 weeks treatment by estrogen and laser therapy.

There were no significant differences between GSM women treated by topical estrogen and GSM women treated by Fractional Co2 Laser regarding percentage of para basal cells at different weeks and maturation value at different weeks. (***Table 3-5***)

Table 3-5: Distribution of women's maturation value of Meisels according to study groups.

Meisels indices	**Study groups**		**P**
	Estrogen Mean±SD	**Laser Mean±SD**	
Percentage of para basal cells at week 0	45±11.5	45±8.1	1.0*^{NS}
Percentage of para basal cells at week 8	34±9.6	35±5.2	0.77*^{NS}
Percentage of para basal cells at week 12	29.5±4.3	28±3.4	0.4*^{NS}
Maturation value at week 0	40±11.7	40±9.5	1.0*^{NS}
Maturation value at week 8	53.2±10.8	52.2±2.7	0.78*^{NS}
Maturation value at week 12	57.7±4.7	59.7±3.6	0.3*^{NS}

** Independent sample t-test, S=Significant, NS=Not significant*.

The complications of laser therapy used in treatment of GSM were present in 4 (40%) women; 2 (20%) women with mild pain, one (10%) woman with mild swelling and one (10%) woman with mild numbness. The discomfort from laser therapy for GSM was mild in all treated women. (***Table 3-6 and Figure 3-7***)

Table 3-6: Laser procedure complications and discomfort of GSM patients.

Variable	**No.**	**%**
Complications		
Yes	4	40.0
No	6	60.0
Total	10	100.0
Pain		
No	8	80.0
Mild	2	20.0
Total	10	100.0
Swelling		
No	9	90.0
Mild	1	10.0
Total	10	100.0
Numbness		
No	9	90.0
Mild	1	10.0
Total	10	100.0
Discomfort by VAS		
Mild	10	100.0
Moderate	0	-
Severe	0	-
Total	10	100.0

**Fishers exact test, NS=Not significant*.

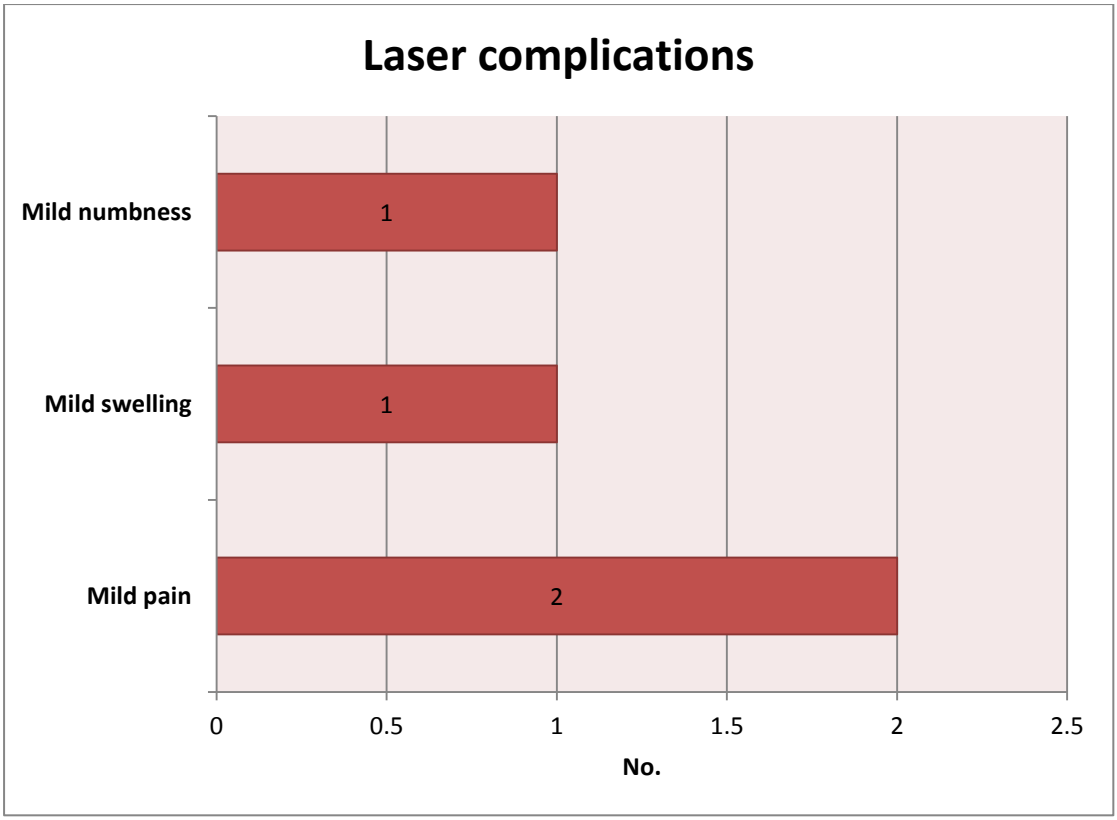


Figure 3-7: Laser therapy complications.

3.3 . Discussion

The genitourinary syndrome of menopause (GSM) is a collection of symptoms and signs affecting women genital tract related to estrogen deficiency [80]. With advancement of medical technology, the fractional laser technique evolved rapidly in different medical specialties and commonly for aesthetic medicine and women vulvovaginal atrophy [81].

The present study showed that mean parity history was significantly higher among GSM women treated by Fractional Co_2 Laser as compared to GSM women treated by topical estrogen ($p=0.04$). Sun et al [82] study in China revealed a significant relationship between each of nulliparity and multi-parity with severe symptoms and signs of genitourinary syndrome among postmenopausal women. However, a study conducted in Thailand by Ruanphoo and Bunyavejchevin [83] to compare the efficacy of micro-ablative fractional CO_2 laser in treatment of vulvovaginal atrophy in women found no significant effect of parity history on efficiency of treatment methods. It was found that physiologic changes in a woman's life, such as childbirth, weight fluctuations, and hormonal changes due to aging and menopause, may alter the laxity of the vaginal canal, damage the pelvic floor, and devitalize the mucosal tone of the vaginal wall [84]. Despite that, our study revealed no significant differences between GSM women treated by topical estrogen and GSM women treated by Fractional Co_2 Laser regarding age, mode of delivery, number of cesarean sections, history of vaginal reconstructive surgery, menopause and chief complaints. These findings are in agreement with results of many literatures such as Li et al [85] prospective multicenter cohort study in China and Schachar et al [86] study in USA which all reported no significant differences in general &

menopausal characteristics and chief complaints of women with GSM treated by fractional Co_2 laser and women with GSM treated by topical estrogen.

In present study, the means of total vaginal health index score at week 8 and week 12 were significantly lower among GSM women treated by Fractional Co_2 Laser as compared to GSM women treated by topical estrogen ($p \leq 0.05$). These findings are similar to results of Dutra et al [87] randomized clinical trial study in Brazil including 25 postmenopausal women with GSM divided into (12 treated by topical estrogen and 13 treated by fractional Co_2 laser) which found that GSM women treated by topical estrogen had higher maturation index and higher vaginal health index at end of treatment period as compared to GSM women treated by fractional CO_2 laser, however, they revealed an equalized vaginal epithelium index and sexual function between both groups [87]. Inconsistent to our study findings, Politano et al [88] clinical trial study in Brazil on 72 women with GSM reported a significantly higher mean vaginal health index score among women treated by fractional Co_2 laser as compared to women treated by topical estrogen. In other study carried out in China by Li et al [85], no significant differences in vaginal health index score between GSM women treated by fractional CO_2 laser as compared to women treated by topical estrogen. These inconsistencies might be attributed differences in menopausal status, inclusion criteria and methodologies between different studies. Although these differences, our study showed a significantly increase in vaginal health index score from week 0 to week 12 in both study groups.

The current study showed a highly significant increase in vaginal health index score for GSM women treated by fractional CO_2 laser therapy after 12 weeks ($p<0.001$). This finding is consistent with results of Sokol et al [5]

clinical trail study in USA on 30 women with GSM treated by fractional CO_2 laser for 18 weeks which found a highly significant increase in vaginal health index score at end of treatment. Our study also found a highly significant increase in vaginal health index score for GSM women treated by topical estrogen therapy after 12 weeks ($p<0.001$). This finding coincides with results of Lethaby et al [52] systematic review study in New Zealand which reported a significant increase in vaginal health index score for GSM women treated by topical estrogen at end of treatment. Although these findings, many authors reported that treating women with symptoms and signs of GSM with vaginal lubricants and moisturizers are temporarily and relieving symptoms only, while the topical estrogen therapy are contraindicated or harmful in numerous women with hormonal disorders and malignancies. They revealed that fractional CO_2 laser is a novel non-invasive, long-term solution in management of genitourinary syndrome [33, 63, 89].

In current study, there were no significant differences between GSM women treated by topical estrogen and GSM women treated by Fractional Co2 Laser regarding woman's GSM intensity of symptoms. These findings are inconsistent with results of Adabi et al [90] prospective study in Iran on 140 women with genitourinary syndrome which revealed that fractional CO_2 laser is effective in treating vaginal atrophy, sexual and urinary symptoms of genitourinary syndrome. However, our study, showed that dysparunia intensity was significantly declined in GSM women treated by Fractional Co2 Laser after 12 weeks of treatment ($p=0.01$). This finding is similar to results of many literatures like Behnia-Willison et al [91] study in USA and Tovar-Huamani et al [92] study in Peru which all reported higher efficacy of Fractional Co2 Laser in improving sexual function and improving dyspaunia after 12 weeks of

treatment. Our study also revealed that urgency & urge incontinence intensity was significantly declined in GSM women treated by Fractional Co2 Laser after 12 weeks of treatment (p=0.01). This finding is parallel to results of Perino et al [93] study in Italy which reported higher efficacy of by Fractional Co2 Laser therapy in improving overactive bladder symptoms of GSM in postmenopausal women.

This study showed no significant differences between GSM women treated by topical estrogen and GSM women treated by Fractional Co2 Laser regarding woman's maturation value of Meisels (p>0.05). This finding is similar to results of Cruz et al [3] Randomized, double-blind, placebo-controlled clinical trial study in Brazil which showed a higher efficacy of Fractional Co2 Laser alone or with topical estrogen in genitourinary syndrome, however, the maturation value (MV) of Meisels was not significantly different.

Present study showed that complications of Fractional Co2 Laser used in treatment of GSM were present in 4 (40%) women; 2 (20%) women with mild pain, one (10%) woman with mild swelling and one (10%) woman with mild numbness. These findings are close to results of Ghanbari et al[94] clinical trial study in Iran on 47 women with genitourinary syndrome which found that Fractional Co2 Laser is effective and safe method in treating GSM. Our study showed that the discomfort from fractional CO_2 laser therapy for GSM was mild in all treated women. This mild discomfort of fractional CO_2 laser therapy for GSM treatment was documented also by Arroyo study in Spain [95].

3.4. Conclusions & Recommendations

Conclusions

- The fractional CO_2 laser therapy is effective method in management of genitourinary syndrome.
- The vaginal health index of women with genitourinary syndrome is improved after 12 weeks treatment by fractional CO_2 laser therapy.
- The vaginal health index of women with genitourinary syndrome is also improved after 12 weeks treatment by topical estrogen therapy.
- The sexual function of women with genitourinary syndrome is improved after 12 weeks treatment by fractional CO_2 laser therapy.
- The urinary symptoms of women with genitourinary syndrome are improved after 12 weeks treatment by fractional CO_2 laser therapy.
- The complications of fractional CO_2 laser therapy are few with minimal discomfort.

Recommendations

- ❖ Encouraging physicians to adopt the option of fractional CO_2 laser therapy in management of women with genitourinary syndrome.
- ❖ Application of fractional CO_2 laser with topical estrogen is accompanied with higher efficacy in women with no contraindication to estrogen therapy.
- ❖ Supporting more national large sized researches in evaluating fractional CO_2 laser therapy.

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وزارة التعليم العالي والبحث العلمـــي

جامعـــــــــــة بغـــــــــــداد

معهـــد الليـــــزر للدراســـات العليا

ليزر ثنائي اوكسيد الكاربون التجزيئي مقابل الاستروجيـــــــن الموضعي لعلاج اعراض ضمور المهبل للنساء في فترة ماحول سن اليـــأس

دراسة مقدمة إلى معهِد الليزر للدراسات العليا/ جامعة بغداد كجزء من متطلبات نيل الدرجة الدبلوم العالي في تطبيقات الليزر في الطب/ النسائيه والتوليد

من قبـــل

يســـرى وحيـــد عبـــد الحســـــن

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دبلوم عالي نسائية وتوليد – جامعة الكوفة

بأشراف

الدكتـــورة منـــال ابراهيـــم مـــزعل

زميلة المجلس العربي لأختصاص النسائية والتوليد

زميلة المجلس العراقي لأختصاص للنسائية والتوليد

دبلوم عالي ليزر

١٤٤٣هـ

الخلاصـــــــة

نبذة: يمكن أن تحدث المتلازمة التناسلية البولية لانقطاع الطمث في أي وقت في دورة حياة المرأة ، على الرغم من أنها أكثر شيوعًا في مرحلة ما بعد انقطاع الطمث. ليزر ثاني أكسيد الكربون فعال وآمن لتحسين الأعراض المهبلية المرتبطة بـالمتلازمة التناسلية البولية لانقطاع الطمث.

هدف الدراسة: لمقارنة فعالية ليزر ثاني أكسيد الكربون الجزئي بالإستروجين الموضعي في علاج ضمور الفرج المهبلي بين النساء في فترة ما حول سن اليأس.

المرضى وطرق البحث: الدراسة الحالية عبارة عن دراسة حالة متسلسلة أجريت في عيادة التجميل الخاصة في بغداد - العراق لمدة أربعة أشهر طوال الفترة من ١٥ سبتمبر ٢٠٢١ حتى ١٥ يناير ٢٠٢٢ على عينة ملائمة من ٢٠ امرأة مع واحدة أو أكثر من أعراض المتلازمة التناسلية البولية لانقطاع الطمث. تم تقييم النتائج عن طريق قياس مؤشر الصحة المهبلية وقيمة النضوج و مؤشر١٠ سم ومؤشرشدة الأعراض. تمت متابعة المرضى لمدة ١٢ أسبوعًا في جدول الأسبوع ٠ والأسبوع ٨ والأسبوع ١٢.

النتائج: كانت متوسطات مجموع نقاط مؤشر الصحة المهبلية في الأسبوع ٨ والأسبوع ١٢ أقل بشكل ملحوظ بين نساء المتلازمة التناسلية البولية لانقطاع الطمث اللواتي عولجن بواسطة ليزر ثاني أكسيد الكربون الجزئي مقارنة بنساء المتلازمة التناسلية البولية لانقطاع الطمث اللواتي عولجن بالإستروجين الموضعي ($p\leq0.05$). انخفضت شدة خلل التنسج بشكل ملحوظ في النساء اللواتي عولجن بواسطة ليزر ثاني أكسيد الكربون الجزئي بعد ١٢ أسبوعًا من العلاج ($p=0.01$).

وبالمثل ، انخفضت شدة الإلحاح وسلس البول الإلحاحي بشكل كبير في النساء اللاتي عولجن بواسطة ليزر ثاني أكسيد الكربون الجزئي بعد ١٢ أسبوعًا ($p = 0.01$). كانت مضاعفات العلاج بالليزر المستخدم في علاج المتلازمة التناسلية البولية لانقطاع الطمث موجودة في ٤ (٤٠٪) نساء. امرأتان (٢٠٪) مصابات بألم خفيف ، وامرأة (١٠٪) تعاني من تورم خفيف وامرأة (١٠٪) تعاني من خدر خفيف. كان الانزعاج الناجم عن العلاج بالليزر لـ GSM خفيفًا في جميع النساء المعالجات.

الخلاصة: العلاج بليزر ثاني أكسيد الكربون الجزئي طريقة فعالة في علاج المتلازمة التناسلية البولية لانقطاع الطمث.