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Impact of Microablative Fractional CO_2 Laser Applied in Menopausal Period on Vulvovaginal Atrophy and Dyspareunia: A Systematic Review and Meta-analysis Study

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ABSTRACT

Aim: This study aimed to synthesize current evidence on the clinical effectiveness of microablative fractional CO_2 laser ($MFCO_2$) therapy for the management of menopausal vulvovaginal atrophy and dyspareunia.

Methods: A meta-analysis was conducted to identify relevant studies published within the last ten years. Electronic database searches were performed between March and June 2024 using PubMed, EBSCOhost, Web of Science, Google Scholar, and the YÖK National Thesis Center. Following the screening process and eligibility evaluation according to established inclusion criteria, eight studies were ultimately retained for analysis. The methodological rigor of the selected studies was evaluated using design-specific critical appraisal instruments developed by the Joanna Briggs Institute (JBI). Quantitative data synthesis was performed using CMA Version 2 software, and findings were interpreted using both statistical meta-analytic techniques and descriptive synthesis.

Results: The pooled analysis demonstrated that $MFCO_2$ laser therapy produced a statistically significant improvement in vulvovaginal atrophy among menopausal women (SMD: 1.437, 95% CI: 0.646–2.228; $Z = 3.559$, $p < 0.001$; $I^2 = 94.93\%$). Similarly, treatment was associated with a significant reduction in dyspareunia severity (SMD: −1.820, 95% CI: −3.063 to −0.577; $Z = -2.871$, $p = 0.004$; $I^2 = 96.17\%$). These findings indicate that $MFCO_2$ laser therapy may contribute to meaningful symptom improvement in menopausal genitourinary disorders. However, considerable heterogeneity among included studies suggests variability in intervention protocols, patient characteristics, and outcome assessment methods.

Conclusion: Microablative fractional CO_2 laser therapy may serve as a beneficial non-hormonal intervention for improving menopausal genitourinary symptoms, especially dyspareunia among sexually active women. Nevertheless, large-scale clinical trials with uniform treatment protocols and longer follow-up are needed to confirm long-term therapeutic efficacy and safety.

Keywords: Dyspareunia, microablative fractional CO_2 laser, vulvovaginal atrophy, menopause.

Introduction

Vulvovaginal atrophy (VVA) is currently classified within the clinical spectrum of genitourinary syndrome of menopause (GSM) and represents one of the most common consequences of estrogen depletion following menopause. The condition is characterized by progressive

structural and functional changes in vulvovaginal tissues. It is commonly associated with vaginal dryness, vulvovaginal irritation or discomfort, pruritus, pain during sexual activity, and urinary symptoms [1,2]. These symptoms may gradually intensify over time and can substantially interfere with sexual health, interpersonal relationships, and psychosocial well-being. Epidemiological data indicate that symptoms associated with GSM affect nearly half of postmenopausal women and are closely linked to impaired sexual functioning and decreased overall quality of life [3,4].

A variety of therapeutic strategies have been developed to manage GSM, including both hormonal and non-hormonal interventions. Non-hormonal therapies, particularly vaginal moisturizers and lubricants, are commonly recommended as supportive measures for symptom relief; however, these products typically provide short-term improvement and do not directly address underlying tissue degeneration. In contrast, local vaginal estrogen therapy has been shown to restore epithelial integrity and improve symptom severity over longer treatment durations and is widely considered an effective therapeutic option [5,6]. Nevertheless, hormonal therapies may not be appropriate for all patients due to contraindications, safety concerns, or personal treatment preferences. Consequently, increasing attention has been directed toward alternative therapeutic modalities that aim to provide effective symptom control while minimizing systemic exposure. Among emerging treatment approaches, energy-based technologies, particularly laser therapies, have gained significant clinical interest due to their capacity to stimulate tissue remodeling and support restoration of normal vaginal physiology [7].

Carbon dioxide (CO_2) laser technology, among the earliest gas-based laser systems developed for medical applications, has been widely used across various clinical fields, including gynecology [8,9]. Early clinical investigations into fractional vaginal CO_2 laser therapy were reported by Gaspar et al. in 2011, demonstrating improvements in both clinical symptomatology and histological characteristics of vaginal atrophy [10]. Subsequent observational studies have further supported these findings. For example, Salvatore and colleagues evaluated symptom outcomes following three monthly sessions of $MFCO_2$ laser therapy over 12-weeks period in a cohort of 49 women. Their findings demonstrated improvement in vaginal dryness (86.0%), vaginal burning (90.0%), vaginal itching (80.0%), and dyspareunia (74.0%) [11]. In addition, improvement in dyspareunia was reported among all sexually active women included in the study [12].

Despite increasing scientific and clinical interest in laser-based treatments, much of the existing literature consists of small-scale, short-term pilot studies, which limit the strength of the available evidence [13]. Currently, three main non-surgical energy-based therapeutic modalities are utilized in the management of menopausal vulvovaginal symptoms: fractional $MFCO_2$ laser therapy, erbium laser applications, and temperature-controlled radiofrequency treatments. Available research suggests that vaginal laser therapies, including both erbium and CO_2 laser techniques, may offer clinically meaningful improvements in symptom severity and vaginal tissue health [14].

Fractional CO_2 laser therapy is believed to promote regeneration of vaginal tissues through several biological mechanisms. These mechanisms include stimulation of collagen synthesis, increased glycogen production, thickening of the epithelial layer, and enhanced of local vascularization, all of which contribute to the restoration of vaginal mucosal integrity toward a premenopausal-like condition [15]. Although clinical improvements following laser therapy have been reported, the duration of therapeutic benefits remains uncertain, with current evidence suggesting symptom improvement may persist for approximately 12 months in many patients [14]. In addition to histological improvements, fractional CO_2 laser treatment has been associated with reductions in both patient-reported symptom severity and objective clinical findings, further supporting its therapeutic potential [16].

While recent investigations have indicated potential therapeutic benefits of laser interventions in GSM, the overall coherence and robustness of the available findings remain limited. Variations in study design, patient characteristics, intervention protocols, outcome measurement tools, and follow-up durations contribute to heterogeneity among published findings. Furthermore, while individual clinical studies have reported encouraging outcomes, comprehensive quantitative synthesis focusing specifically on the effectiveness of $MFCO_2$ laser therapy in the treatment of VVA and dyspareunia remains limited. Therefore, the present meta-analysis was conducted to evaluate the effectiveness of $MFCO_2$ laser therapy administered during the menopausal period in alleviating VVA and dyspareunia symptoms. In addition, this study aimed to synthesize available scientific evidence to support clinical decision-making processes and to identify areas requiring further high-quality research.

The hypotheses of the study

Primary Hypothesis: $MFCO_2$ laser therapy applied during the menopausal period significantly improves vulvovaginal atrophy in postmenopausal women.

Secondary Hypothesis: $MFCO_2$ laser therapy significantly reduces dyspareunia severity in menopausal women.

Additional Hypothesis: $MFCO_2$ laser therapy represents a safe and effective non-hormonal therapeutic alternative for the management of GSM.

Methods

This study was designed as a systematic review and meta-analysis and followed the PRISMA reporting standards (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) [17]. To enhance methodological rigor and reduce the risk of bias, the processes of literature searching, study selection, and data extraction were carried out independently by four investigators (A.Ç., H.Ö., Y.Ç.B.). Each stage of the review was conducted separately by the assigned reviewers to ensure consistency and objectivity.

Following independent evaluations, the reviewers compared their decisions, and any disagreements were resolved through discussion until consensus was achieved. In addition, the number of screening steps performed for each record and the reviewers responsible for each phase were systematically documented to ensure transparency throughout the review process. The methodological quality of the studies included in the meta-analysis was also evaluated independently by the same research team, thereby strengthening the reliability and validity of the synthesized findings.

Study Selection and Eligibility Requirements

The studies were screened according to the PICOS framework:

P: Patient: Postmenopausal women with symptom/s

I: Intervention: Microablative fractional CO_2 laser ($MFCO_2$ laser) therapy

C: Comparison: No treatment, placebo, sham treatment, or other non-laser-based therapeutic approaches (e.g., hormonal or non-hormonal treatments), depending on the design of the included studies

O: Outcomes: Vulvovaginal atrophy, dyspareunia

S: Study design: Studies designed using experimental or quasi-experimental methodologies and published in either Turkish or English were considered eligible.

Letters to the editor, case reports, case presentations, and studies of a systematic or narrative review nature were excluded from the scope of this research.

Literature Identification Strategy

Between March and June 2024, a search was conducted using the keywords "carbon dioxide laser", "CO2 Laser", "vulvovaginal atrophy", "vaginal atrophy", "genitourinary syndrome of menopause", and "GSM" in PubMed, Web of Science, EBSCOhost, YOK National Thesis Center, and Google Scholar. The studies were then transferred to Mendeley. In order to review the current literature, studies from the past 10 years were included in the search.

Study Screening and Selection

The initial search resulted in 5359 records. After duplicates and irrelevant studies were removed, 5249 records were screened for selection based on abstract and title. As a result of this screening, 64 studies were selected for full-text review. Subsequently, the 64 articles were reviewed according to inclusion and exclusion criteria for the application of $MFCO_2$ laser in menopausal VVA and dyspareunia, with 8 studies reporting the effects included in the analysis. The flow of study identification and inclusion is shown in Figure 1.

Data Retrieval and Extraction

A structured data extraction template developed by the research team was used to collect study data. This template facilitated the documentation of study characteristics such as author name, publication year, research design, study location, assessment tools employed, and sample size (Table 1). The extraction process was performed independently by two investigators using an identical standardized form. Any disagreements were resolved through discussion until agreement was reached. This systematic methodology enhanced both the transparency and reproducibility of the study.

Ethical Principles

This study employed a meta-analytic approach by synthesizing findings from previously published research.

Quality Evaluation of Included Studies

The methodological quality of the studies incorporated into this systematic review and meta-analysis was examined using study design–specific critical appraisal tools developed by the JBI [18]. The selection of appraisal instruments was based on the methodological structure of each study. Randomized controlled trials were evaluated using a 13-item checklist, whereas quasi-experimental studies were assessed using a 9-item checklist [19]. The checklists provide four response options: “Yes,” “No,” “Unclear,” and “Not Applicable.” Two independent researchers conducted the quality assessment process, and disagreements were resolved through discussion until consensus was obtained. The outcomes of the quality assessment are presented in Table 1 as Quality Scores.

Synthesis of the Collected Data

Statistical calculations were performed using the Comprehensive Meta-Analysis program (CMA, Version 2). Statistical heterogeneity across the included studies was

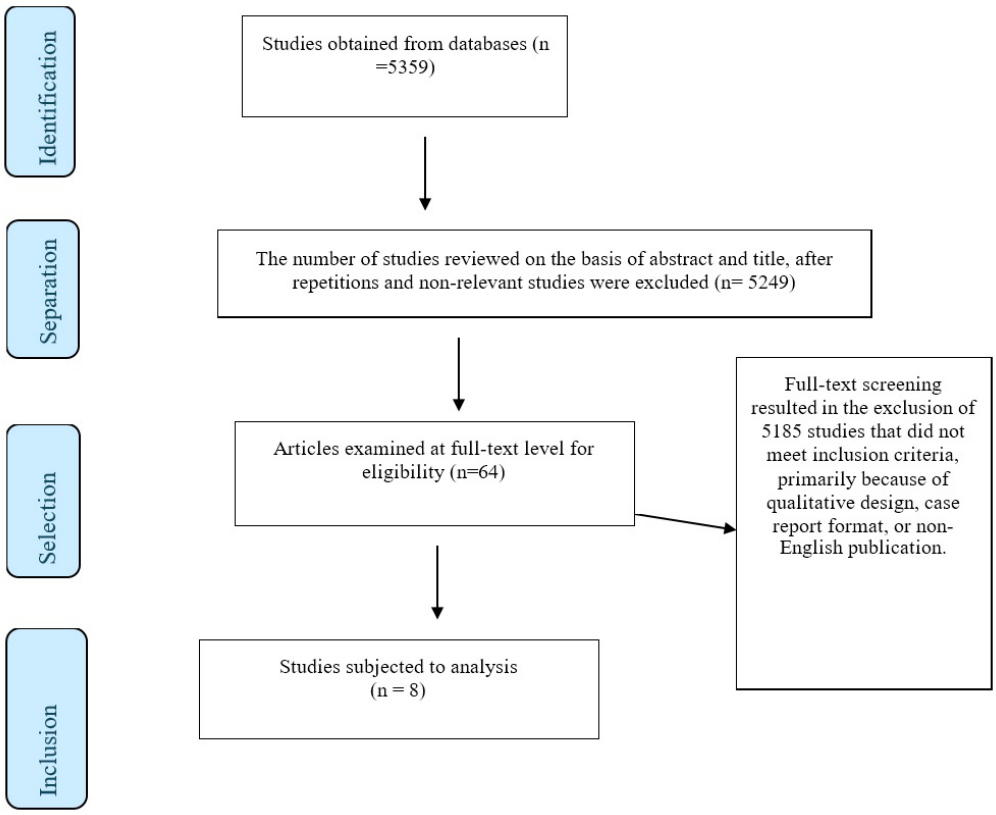

Figure 1 – Selection of studies according to PRISMA flow diagram

Table 1 Characteristics and results of the included studies

Author/Year	Study design	Sample size	Scale	Outcomes	Patient population	Quality Score
Eder SE. et al., 2018	Quasi-experimental	28 participants	Vaginal Health Index (VHI)	CO_2 laser therapy may represent an effective treatment alternative for postmenopausal women, as symptom improvement has been reported even after a single treatment session.	Postmenopausal women, dryness, itching, burning, dysuria or dyspareunia).	Yes:7/9 No:2/9 Uncertain:0/9 Not applicable:0/9
Pitsouni E. et al., 2016	Quasi-experimental	53 participants	Vaginal Health Index Score (VHI)	The findings of this study indicate that intravaginal CO_2 laser therapy may be a beneficial treatment option for postmenopausal women presenting with clinical manifestations of genitourinary syndrome of menopause (GSM), contributing to improvements in both vaginal tissue physiology and symptom severity. Furthermore, women in both comparison groups demonstrated enhanced sexual function and reduced levels of sexual distress.	Postmeno-pausal women with symptom/s (dyspareunia, genital dryness, burning, itching, dysuria, urinary frequency, urgency)	Yes:7/9 No:2/9 Uncertain:0/9 Not applicable:0/9
Ruanphoo P. et al., 2020	Randomized Control	Experimental group:44 Control group:44	Vaginal Health Index (VHI) Visual Analog Scale (VAS)	The findings of this study indicate that microablative fractional CO_2 laser therapy is associated with improvements in vaginal atrophy. This approach may represent a promising alternative treatment option for postmenopausal women experiencing this condition.	Postmeno-pausal women, dyspareunia, dryness, itching, burning, dysuria	Yes: 10/13 No:2/13 Uncertain:0/13 Not applicable: 1/13
Salvatore et al., 2015	Quasi-experimental	77 participants	Visual Analog Scale (VAS)	Fractional microablative CO_2 laser therapy has been associated with significant improvements in sexual function and overall sexual satisfaction among postmenopausal women experiencing symptoms of vulvovaginal atrophy (VVA).	Postmeno-pausal women, dyspareunia, dryness, itching, burning, dysuria	Yes:7/9 No:2/9 Uncertain:0/9 Not applicable:0/9
Salvatore S. et al., 2021	Randomized Control	Experimental group:28 Control group:30	Visual Analog Scale (VAS)	The findings of this study indicate that CO_2 laser therapy provides significant and sustained improvement in GSM-related symptoms. Moreover, compared with sham interventions, CO_2 laser treatment may serve as an effective alternative therapeutic option in the management of genitourinary syndrome of menopause.	Postmenopausal women diagnosed with GSM and bothersome dryness and dyspareunia	Yes: 10/13 No:2/13 Uncertain:0/13 Not applicable: 1/13
Siliquini GP. et al., 2017	Quasi-experimental	87 participants	Vaginal Health Index (VHI)	The results of this study indicate that CO_2 laser therapy is associated with significant and sustained symptom improvement.	Postmeno-pausal women, dyspareunia, dryness, itching, burning, dysuria	Yes:7/9 No:2/9 Uncertain:0/9 Not applicable:0/9
Sophie Page A. et al., 2022	Randomized Control	Experimental group grubu:28 Control group:29	Vaginal Health Index Visual Analog Scale (VAS)	Among women with GSM, treatment outcomes evaluated 12 weeks after laser therapy were found to be comparable to those observed following sham interventions.	Postmenopausal women GSM genitourinary syndrome of menopause	Yes: 10/13 No:2/13 Uncertain: 0/13 Not applicable: 1/13
Tenerowicz AR. et al., 2022	Quasi-experimental	205 participants	Vaginal Health Index (VHI)	Ablative CO_2 laser therapy may contribute to the reduction of vulvovaginal atrophy symptoms, including vaginal laxity, dryness, dyspareunia, and burning sensation, and may also lessen the severity of stress and urge urinary incontinence.	Perimenopausal dryness, dyspareunia, burning, vaginal laxity, urinary incontinence	Yes:7/9 No:2/9 Uncertain:0/9 Not applicable:0/9

examined using Cochran's Chi-square (Q) test and Higgins' I^2 statistic. The I^2 statistic was interpreted to quantify the proportion of total variation attributable to between-study heterogeneity rather than chance. An I^2 value above 50% was interpreted as indicating moderate to substantial heterogeneity, whereas lower values suggested acceptable consistency across studies. In addition, the statistical significance of heterogeneity was evaluated using the Q test, with a p-value threshold of 0.10, as recommended for heterogeneity testing due to the limited statistical power of this test in meta-analyses with small sample sizes.

Model selection was determined according to heterogeneity levels. A fixed-effects model was applied when heterogeneity was considered low ($I^2 \leq 50\%$ and $p > 0.10$), assuming that the included studies estimated a common underlying effect size. In contrast, when substantial heterogeneity was detected ($I^2 > 50\%$), a random-effects model was employed to account for potential variability in true effect sizes across studies [20]. Furthermore, Tau-square (τ^2) statistics were calculated to estimate the variance in true effect sizes among studies and to support the interpretation of between-study variability.

To allow comparison of outcomes measured using different assessment tools, standardized mean differences (SMD) were calculated along with their corresponding 95% confidence intervals (CI). The magnitude and direction of treatment effects were visually presented using forest plots, which illustrated individual study effect sizes and pooled estimates. The overall pooled effect size was obtained by calculating the weighted average of individual study effect sizes. The statistical significance of pooled results was determined by transforming the D statistic into a Z score and evaluating the associated p-value.

Publication bias was evaluated using both graphical and statistical approaches. Funnel plots were visually inspected to

assess potential asymmetry, which may suggest the presence of publication bias or small-study effects. Egger's regression test was additionally performed to provide a quantitative assessment of funnel plot asymmetry. All statistical analyses were performed using two-sided tests, and statistical significance was defined as a p-value less than 0.05 [21].

Results

The final analysis involved three randomized controlled experimental studies and five quasi-experimental studies. Overall, the studies included 100 participants in intervention groups, 103 participants in control groups, and 450 participants evaluated in single-group studies (Table 1).

Across all studies included in this systematic review and meta-analysis, more than half of the items in the quality appraisal checklists were satisfied (Table 1). This result indicates that the evidence synthesized in the present review is derived from studies demonstrating an acceptable level of methodological quality.

Meta-Analysis of $MFCO_2$ laser Effects on Vulvovaginal Atrophy

Two techniques were employed to examine potential publication bias, including graphical evaluation through funnel plot analysis and statistical testing using Egger's regression method [22].

Publication bias within the included studies was evaluated using Egger's regression test. The analysis yielded an intercept (B0) value of 4.21023 with a 95% confidence interval ranging from −6.60736 to 15.02783 (t = 1.08060, df = 4). The two-tailed p-value was calculated as 0.34068, indicating no statistically significant evidence of publication bias among the included studies.

Figure 3 presents the pooled findings of eight studies examining the effects of $MFCO_2$ laser therapy applied during the menopausal period on VVA. In these studies, the Vaginal Health Index Score (VHIS) was used as the primary outcome measure to evaluate vaginal tissue condition. The meta-analytic results demonstrated a statistically significant improvement in vaginal health among women receiving $MFCO_2$ laser therapy (SMD = 1.437; 95% CI: 0.646–2.228; Z = 3.559; $p < 0.001$).

However, considerable variability was observed across the included studies, as indicated by the heterogeneity analysis (I^2 = 94.933%; $p < 0.001$). This high heterogeneity suggests potential differences in study design, patient characteristics, intervention protocols, or outcome assessment methods among the included trials.

Meta-Analysis of $MFCO_2$ laser Effects on Dyspareunia

Potential publication bias among the included studies was assessed using Egger's regression analysis. The calculated

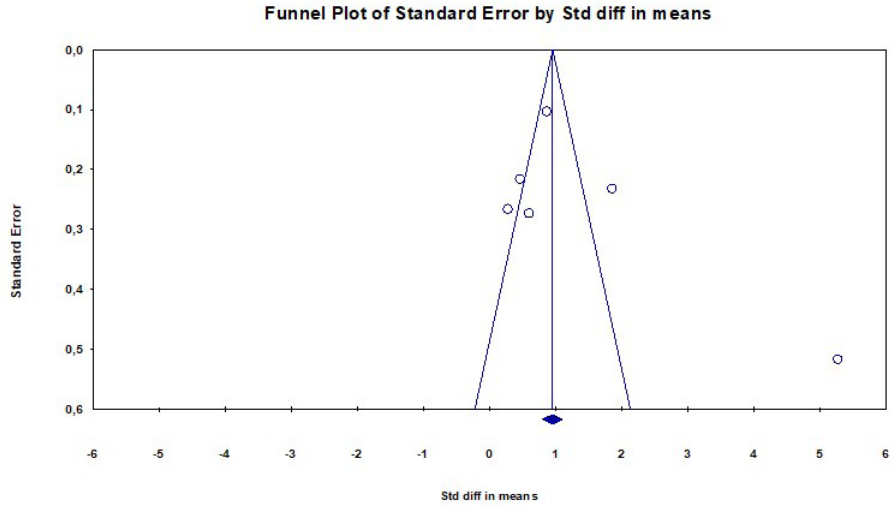

Figure 2 – Funnel plot reporting the results of studies on the effects of $MFCO_2$ laser on VVA

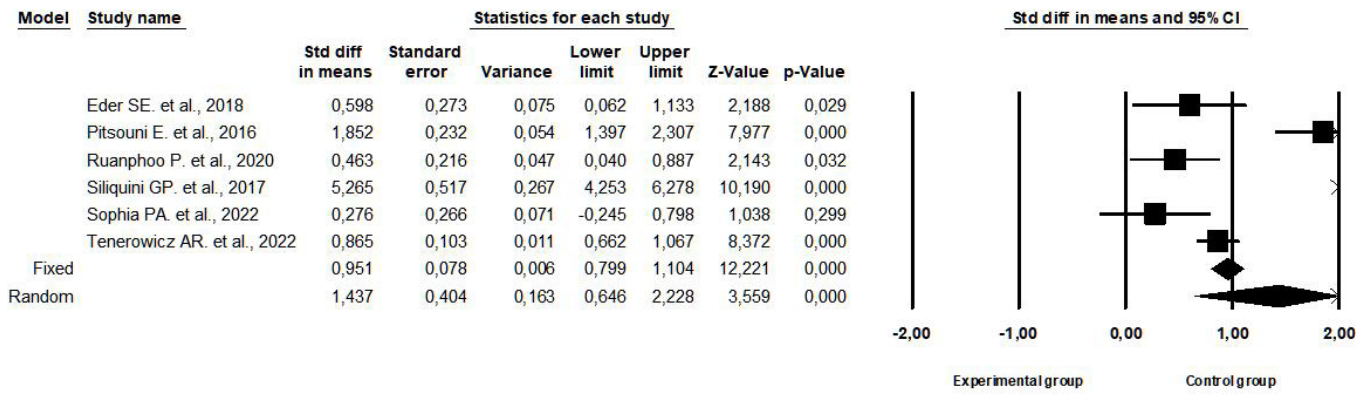

Figure 3 – Forest plot reporting the results of studies on the impact of $MFCO_2$ laser on VVA

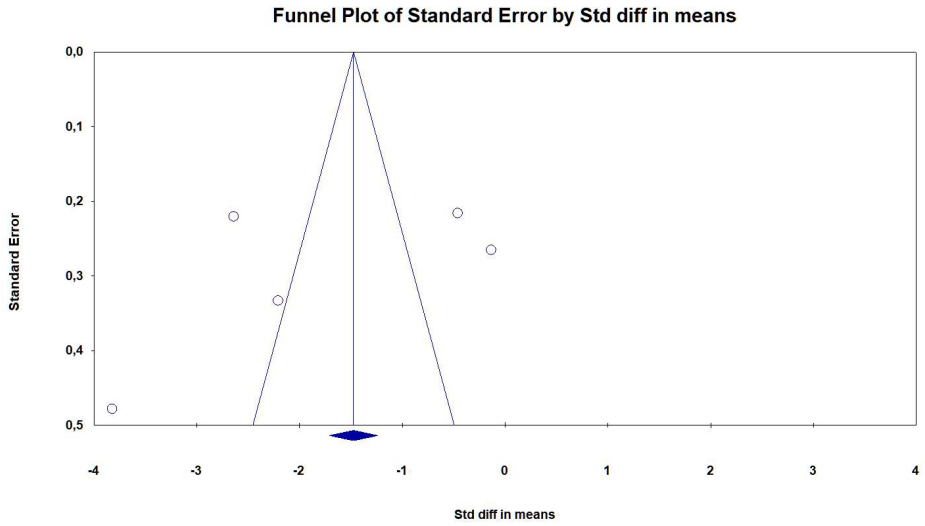

Figure 4 – Funnel plot reporting the results of studies on the effects of $MFCO_2$ laser on dyspareunia

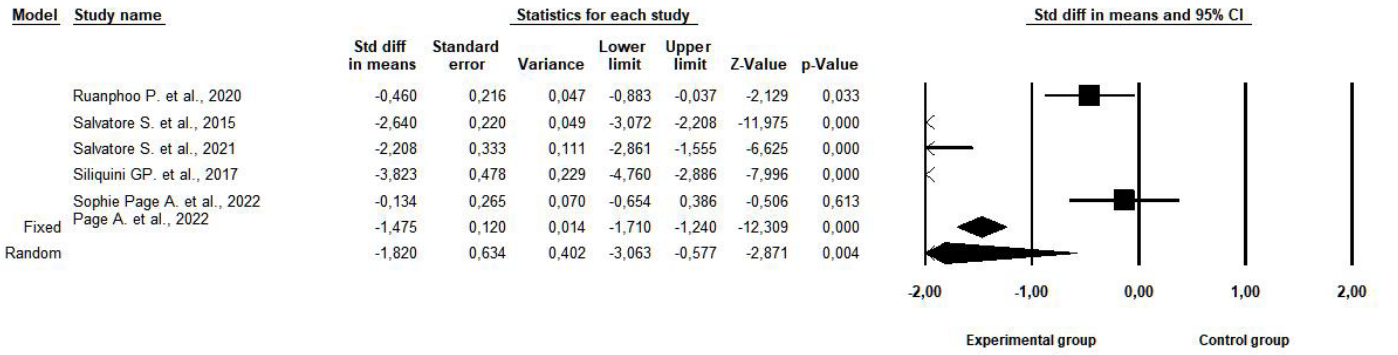

Figure 5 – Forest plot reporting the results of studies on the effect of $MFCO_2$ laser on dyspareunia

intercept (B0) was −7.96890 with a 95% confidence interval ranging from −37.18128 to 21.24349 (t = 0.86815, df = 3). The two-sided p-value was 0.44919, suggesting that there was no statistically significant evidence of publication bias within the analyzed dataset.

Figure 5 illustrates the pooled results of five studies evaluating the effects of $MFCO_2$ laser therapy administered during menopause on dyspareunia. Pain intensity in these studies was assessed using the Visual Analog Scale (VAS). Meta-analytic synthesis of the available data demonstrated a statistically significant reduction in dyspareunia following $MFCO_2$ laser treatment (SMD = −1.820; 95% CI: −3.063 to −0.577; Z = −2.871; p = 0.004).

Despite the observed therapeutic effect, heterogeneity analysis revealed considerable variability among the included studies (I^2 = 96.172%; p = 0.004). This elevated heterogeneity may reflect differences in treatment protocols, participant characteristics, follow-up duration, or methodological approaches used across the studies.

Discussion

GSM is a condition affecting the genital and lower urinary tract after menopause, primarily due to estrogen deficiency, which leads to VVA and related symptoms [31].

In the literature, there are some concerns regarding the safety of CO2 lasers, especially after the FDA's warning against their inappropriate use in the treatment of symptoms related to "vaginal rejuvenation" and sexual function, several important findings regarding the use of energy-based devices have been reported [32]. However, although the findings of the present study suggest that vaginal fractional CO_2 laser treatment is generally well tolerated and no serious complications were reported in the included studies, it should be noted that this meta-analysis primarily focused on symptom improvement and did not include a quantitative synthesis of safety outcomes. Therefore, conclusions regarding safety should be interpreted with caution.

In a meta-analysis conducted by Sarmento et al., CO2 laser has been identified as the most commonly used and scientifically proven effective treatment among physical methods, with the ability to improve all GSM symptoms up to 12 months after treatment [33]. In a meta-analysis study by Prodromidou et al. (2021), laser therapy was found to be effective on subjective and objective symptoms [34]. Liu et al. (2022) demonstrated in their meta-analysis that CO_2 laser therapy contributed to reductions in VVA symptoms and improvements in sexual function among postmenopausal women [2]. The consistency of these findings with our results strengthens the evidence supporting the therapeutic role of CO_2 laser treatment in GSM management. Nevertheless, variations in laser parameters, treatment sessions,

and follow-up durations among studies highlight the need for standardized treatment protocols.

Vulvovaginal atrophic changes may negatively affect women's quality of life and sexual function, highlighting the importance of effective management strategies for GSM symptoms [35,36]. These pathophysiological alterations emphasize the clinical importance of early identification and effective management of GSM symptoms, as untreated conditions may negatively influence not only physical health but also psychosocial well-being and intimate relationships.

In this meta-analysis, it was determined that $MFCO_2$ laser treatment applied during menopausal period has a generally significant effect on dyspareunia. The studies included in this meta-analysis used VAS to assess dyspareunia in most cases. In the systematic review and meta-analysis conducted by Filippini and colleagues, improvement in GSM symptoms before and after laser treatment was found [37]. The improvement in dyspareunia observed in our analysis may be explained by laser-induced stimulation of collagen remodeling, increased vascularization, and restoration of vaginal epithelial integrity. These biological mechanisms may contribute to improved tissue elasticity and lubrication, which are essential factors for reducing pain during sexual intercourse. In contrast to our study findings, Ni and Lian (2024) meta-analysis revealed that CO2 laser treatment did not make a significant difference in terms of dyspareunia, dryness, burning, itching, and dysuria scores on criteria such as GSM, FSFI, VHIS, and VAS [4]. This discrepancy may be related to methodological differences such as sample characteristics, intervention protocols, and outcome assessment methods. Additionally, differences in baseline symptom severity and patient selection criteria across studies may have influenced treatment responsiveness. Salvatore and colleagues' meta-analysis also found that Fractional CO2 laser improved sexual function and reduced pain in menopausal women affected by GSM [38]. In Mension and colleagues' (2022) meta-analysis, it was found that vaginal laser improved VAS and FSFI scores [13]. Taken together, the available evidence suggests that fractional CO_2 laser therapy may positively influence both pain-related and sexual function outcomes; however, the high heterogeneity observed across studies indicates that treatment outcomes may vary depending on clinical and methodological factors. The substantial heterogeneity ($I^2 > 90\%$) observed in this meta-analysis may be attributed to several factors, including differences in study design, variation in $MFCO_2$ laser treatment protocols (e.g., energy settings, number of sessions, and application techniques), heterogeneity in follow-up durations, and differences in outcome assessment methods across studies. These factors may have contributed to variability in the magnitude of the reported effects. Furthermore, although short- and medium-term results appear promising, there remains limited evidence regarding long-term effectiveness and safety. Additionally, the inclusion of both randomized controlled trials and quasi-experimental studies may have contributed to variability in the pooled results, as differences in study design, methodological rigor, and risk of bias can influence the magnitude and consistency of observed effects. Therefore, this methodological diversity should be considered when interpreting the findings.

Conclusion

In conclusion, fractional CO_2 laser therapy appears to be a promising non-hormonal intervention for the management of genitourinary syndrome of menopause, particularly in reducing dyspareunia among postmenopausal women. The findings of this meta-analysis indicate significant improvements in symptoms; however, the presence of substantial heterogeneity and the limited number of included studies warrant cautious interpretation. From a clinical perspective, this approach may be especially relevant for women who cannot or prefer not to use hormonal therapies. Nevertheless, further well-designed randomized controlled trials with larger sample sizes and longer follow-up periods are needed to confirm long-term efficacy, establish standardized treatment protocols, and support its integration into evidence-based clinical practice.

Limitations

Interpretation of the present meta-analytic results requires consideration of certain methodological constraints. In particular, the inclusion of studies with relatively small sample populations and quasi-experimental study designs may reduce the overall reliability and generalizability of the synthesized evidence. Additionally, although the inclusion of studies published within the last decade was intended to reflect contemporary clinical practice, this restriction may have limited the number of eligible studies and potentially excluded relevant earlier research. Another important limitation is the high level of heterogeneity observed among the included studies. Variations in study design, participant characteristics, treatment protocols, laser parameters, follow-up duration, and outcome measurement tools may have contributed to the observed heterogeneity. These differences may affect the comparability of study results and should be considered when interpreting the pooled effect sizes.

Furthermore, the diversity of assessment instruments used to evaluate outcomes such as vaginal health, dyspareunia, and sexual function may have influenced the consistency of the reported findings. Differences in subjective outcome measures may introduce variability related to patient perception and reporting bias. Although publication bias was not statistically significant, the relatively limited number of included studies may reduce the sensitivity of bias- detection methods. Moreover, for certain outcomes, such as dyspareunia, the number of included studies was particularly small, further limiting the robustness of the pooled estimates. In such cases, statistical tests for publication bias (e.g., Egger's test) should be interpreted with caution, as their reliability is reduced when the number of studies is limited. Therefore, the possibility of undetected publication bias cannot be completely excluded. Finally, the lack of long-term follow-up data in several studies restricts the ability to fully evaluate the sustainability of treatment effects and the long-term safety profile of laser therapy. Further high-quality clinical investigations with larger sample sizes, consistent intervention protocols, and longer observation periods are necessary to strengthen the current evidence. These limitations were carefully considered when interpreting the findings. Although they may influence the precision of the estimated effects, the overall direction and consistency of the results support the main conclusions of the study.

Theoretical Contributions

By integrating available research findings, this study offers theoretical insight into the role of $MFCO_2$ laser therapy as a non-hormonal therapeutic option for GSM. The findings support existing theoretical models suggesting that $MFCO_2$ laser treatment promotes vaginal tissue regeneration through collagen

remodeling, epithelial restoration, and enhanced vascularization, which are associated with improvements in dyspareunia and VVA. Additionally, by integrating heterogeneous research findings, this study strengthens the evidence base and supports the development of standardized, patient-centered therapeutic models for menopausal genitourinary symptom management.

Author Contributions: Conceptualization, A.Ç, H.Ö; methodology, A.Ç. H.Ö, Y.Ç.B; validation, A.Ç, H.Ö, Y.Ç.B; formal analysis, A.Ç. H.Ö; investigation, A.Ç. H.Ö, Y.Ç.B; resources, A.Ç. H.Ö, Y.Ç.B; data curation, A.Ç. H.Ö, Y.Ç.B; writing – original draft preparation, A.Ç. H.Ö, Y.Ç.B; writing – review and editing, A.Ç. H.Ö, Y.Ç.B; visualization, A.Ç. H.Ö, Y.Ç.B; supervision, A.Ç. H.Ö, Y.Ç.B; project administration, A.Ç. H.Ö, Y.Ç.B; funding acquisition, A.Ç. H.Ö, Y.Ç.B. All authors have read and agreed to the published version of the manuscript.

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Data availability statement: The corresponding author can provide the data supporting the study's conclusions upon request. Due to ethical and privacy constraints, the data are not publicly accessible.

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