Evidence for the Use of Photobiomodulation in Sexual Dysfunction in Women with Breast Cancer Undergoing Hormone Therapy: Literature Integrative Review

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Evidências para o Uso da Fotobiomodulação para Disfunção Sexual em Mulheres com Câncer de Mama em Uso de Hormonioterapia: Revisão Integrativa da Literatura

Evidencias sobre el Uso de la Fotobiomodulación para la Disfunción Sexual en Mujeres con Cáncer de Mama en Tratamiento con Hormonoterapia: Revisión Integradora de la Literatura

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ABSTRACT

Introduction: Hormone therapy is one of the main strategies in the adjuvant treatment of women with hormone receptor-positive breast cancer. Despite its oncological benefits, it is associated with significant side effects, especially sexual dysfunction resulting from prolonged hypoestrogenism. Photobiomodulation has been proposed as a non-hormonal and non-pharmacological alternative for the treatment of female pelvic disorders, although its use in this population remains limited. **Objective:** Analyze, through an integrative literature review, the available evidence on the use of photobiomodulation in female pelvic disorders, considering its potential applicability in women undergoing hormone therapy for breast cancer. **Method:** Search at national and international databases following PRISMA guidelines. Studies involving photobiomodulation interventions for pelvic dysfunctions were included regardless of language, publication year, or study type. A total of 38 studies were identified, with 25 analyzed in greater detail. **Results:** The results indicated positive outcomes in pain reduction, vaginal lubrication, sexual function, vaginal stenosis, and quality of life. However, protocol heterogeneity and the lack of controlled clinical trials limit the generalization of the findings. **Conclusion:** Although current evidences on the use of photobiomodulation for sexual dysfunction in women with breast cancer undergoing hormone therapy remains limited and does not yet allow robust clinical recommendation, this review compiles relevant information that expands the available knowledge by identifying gaps and highlighting potential physiological mechanisms and clinical outcomes for the use of photobiomodulation in oncological female sexual health.

Key words: Breast Neoplasms/complications; Antineoplastic Agents, Hormonal/adverse effects; Atrophic Vaginitis/chemically induced; Sexual Dysfunction, Physiological/chemically induced; Low-Level Light Therapy/methods.

RESUMO

Introdução: A hormonioterapia é um dos pilares do tratamento adjuvante em mulheres com câncer de mama com receptores hormonais positivos. Apesar de sua eficácia oncológica, está associada a efeitos colaterais significativos, especialmente disfunções sexuais decorrentes do hipoestrogenismo prolongado. A fotobiomodulação (FBM) tem sido proposta como alternativa não hormonal e não farmacológica para o tratamento de disfunções pélvicas femininas, mas sua aplicação nesse público ainda é incipiente. **Objetivo:** Avaliar as evidências sobre o uso da FBM em disfunções pélvicas femininas, com vistas à sua aplicabilidade em mulheres com câncer de mama em hormonioterapia. **Método:** Foi realizada uma busca em bases de dados nacionais e internacionais, seguindo as diretrizes PRISMA. Foram incluídos estudos com intervenção em disfunções pélvicas utilizando FBM, independentemente do tipo de estudo, idioma ou ano de publicação. Foram selecionados 38 estudos, sendo 25 incluídos. **Resultados:** Os estudos demonstraram efeitos positivos da FBM sobre dor, lubrificação vaginal, função sexual, estenose vaginal e qualidade de vida. A diversidade de protocolos e a escassez de ensaios clínicos controlados limitam a generalização dos resultados. **Conclusão:** Embora as evidências atuais sobre o uso da FBM para disfunção sexual em mulheres com câncer de mama em hormonoterapia ainda sejam limitadas e não permitam uma recomendação clínica robusta, esta revisão reúne informações relevantes que ampliam o conhecimento disponível sobre o tema, uma vez que identifica lacunas e aponta potenciais mecanismos fisiológicos e desfechos clínicos para o uso da FBM na saúde sexual feminina oncológica.

Palavras-chave: Neoplasias da Mama/complicações; Antineoplásicos Hormonais/efeitos adversos; Vaginite Atrófica/induzido quimicamente; Disfunções Sexuais Fisiológicas/induzido quimicamente; Terapia com Luz de Baixa Intensidade/métodos.

RESUMEN

Introducción: La hormonoterapia es una de las principales estrategias en el tratamiento adyuvante del cáncer de mama en mujeres con receptores hormonales positivos. A pesar de su eficacia oncológica, se asocia a efectos adversos importantes, especialmente disfunciones sexuales derivadas del hipoestrogenismo prolongado. La fotobiomodulación ha sido propuesta como una alternativa no hormonal y no farmacológica para el tratamiento de disfunciones pélvicas femeninas, aunque su uso en esta población aún es limitado. **Objetivo:** Analizar, mediante una revisión integradora de la literatura, la evidencia disponible sobre el uso de la fotobiomodulación en disfunciones pélvicas femeninas, considerando su aplicabilidad en mujeres con cáncer de mama en tratamiento hormonal. **Método:** Búsquedas en bases de datos nacionales e internacionales, siguiendo las directrices PRISMA. Se incluyeron estudios con intervención de fotobiomodulación para disfunciones pélvicas, sin restricciones de idioma, año o tipo de estudio. Se identificaron 38 estudios, de los cuales 25 fueron analizados en profundidad. **Resultados:** Los resultados mostraron efectos positivos de la fotobiomodulación sobre el dolor, la lubricación vaginal, la función sexual, la estenosis vaginal y la calidad de vida. Sin embargo, la heterogeneidad de los protocolos y la falta de ensayos clínicos controlados limitan la generalización de los resultados. **Conclusión:** Aunque la evidencia actual sobre el uso de la fotobiomodulación para la disfunción sexual en mujeres con cáncer de mama en tratamiento con hormonoterapia sigue siendo limitada y aún no permite una recomendación clínica sólida, esta revisión reúne información relevante que amplía el conocimiento disponible sobre el tema, ya que identifica vacíos y señala posibles mecanismos fisiológicos y resultados clínicos para el uso de la fotobiomodulación en la salud sexual femenina oncológica.

Palabras clave: Neoplasias de la Mama/complicaciones; Antineoplásicos Hormonales/efectos adversos; Vaginitis Atrófica/inducido químicamente; Disfunciones Sexuales Fisiológicas/inducido químicamente; Terapia por Luz de Baja Intensidad/métodos.

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INTRODUCTION

Breast cancer is the most common neoplasm among women worldwide accounting for one quarter of all cancer cases in this population[1]. Thanks to the advance of early detection and adjuvant therapy – chemotherapy, radiotherapy, hormone therapy and immunotherapy – survival has been increasing significantly, which poses challenges to maintain the quality of life, particularly regarding psychosocial and sexual aspects[1,2]. Nearly 70% of the cases of breast cancer are hormone-dependent and treated with endocrine therapy as tamoxifen and aromatase inhibitors; although effective to reduce relapse and mortality, these drugs induce accentuated and prolonged hypoestrogenism leading to what today is called genitourinary syndrome of menopause (GSM) which provokes vaginal dryness, dyspareunia, mucosa atrophy, urinary urgency, vulvar burning and recurring urinary infections[1,3].

Studies[3] demonstrate that around 74% of the women in hormone therapy reported signs and symptoms associated with GSM and more than half suffers with pain or discomfort in sexual relations, self-image changes and harms in affectionate relationships. Although some local hormone alternatives as vaginal estrogens have been proven effective for GSM, its use is controversial in women with history of breast cancer due to fear of tumor relapse, which usually leads to treatment neglect or palliative and ineffectual measures as vaginal lubricants[2,4].

Given this scenario, photobiomodulation (PBM) stands out as a non-hormonal, safe and promising therapeutic approach, consisting in the therapeutic use of low-level light therapy (laser or LED, wavelength between 600 and 1000 nm) without promoting thermal or ablative effect[5,6]. The main mechanisms of photobiomodulation involve the absorption of mitochondrial chromophores, especially cytochrome c oxidase resulting in a cascade of intracellular biochemical effects. This process leads to the increase of the production of adenosine triphosphate (ATP), promoting more effective cellular metabolism. Simultaneously, nitric acid is released, inducing vasodilation and improvement of local microcirculation. In addition, the therapy modulates the inflammatory response through reduction of pro-inflammatory cytokines release, contributing to pain relief and control of the inflammatory process. At last, there is stimulation of tissue regeneration, increasing cellular proliferation, collagen synthesis and neo-angiogenesis, favoring the repair of the tissues treated[6,7].

Studies indicate that intravaginal PBM can increase lubrification, reduce pain, restore the elasticity of the vaginal mucosa and improve significantly the overall sexual function in post-menopausal and oncologic women[4,8]. An observational, multicenter cohort showed consistent improvement of pain and quality of life of women with chronic pelvic pain submitted to transvaginal PBM[8]. Another study reported increase of the epithelial thickness and local vascularization after use[7].

Addressing sexual dysfunction of women survivors of breast cancer goes beyond the gynecologic spectrum. Sexual function has been understood as one of the main components of health-related quality of life, influencing self-esteem, emotional well-being and treatment adherence[1,3]. Ignore these complaints can aggravate depression, anxiety, isolation and even therapeutic abandonment.

Therefore, PBM appears as a relevant and safe alternative of oncologic physiotherapeutic care by providing regenerative, analgesic and modulating effects to inflammation without direct hormone action, specifically indicated to estrogen-sensitive oncologic populations as women in breast cancer hormone therapy.

The objective of this study is to analyze the existing evidences of PBM use to treat female pelvic functions through an integrative literature review to evaluate the feasibility and therapeutic potential of this approach for women with breast cancer in use of hormone therapy.

METHOD

Integrative literature review to find scientific evidences on the application of PBM in pelvic dysfunctions according to the recommendations of Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)-ScR[9]. A comprehensive and structured search based on the combination of terms previously established was conducted to identify the studies at national and international databases PubMed, LILACS, MEDLINE, Cochrane Library, EMBASE, SciELO and Google Scholar. The descriptors photobiomodulation, laser, sexual and pelvic dysfunctions, pelvis and LED originally in Portuguese and in English combined through Boolean operators (AND, OR) were applied to expand the search at international databases.

The descriptors DeCS/MeSH were selected based on their relevance for the theme and frequency they are utilized in specialized scientific publications that help the standardization of the terms across different databases.

Studies addressing directly the theme in any language or methodological design were considered. There were no publication time restraints in order to favor the chronologic analysis and expand the inclusion of relevant studies, given the reduced number of publications available. Systematic and integrative literature reviews

were excluded, only original studies that met the objectives proposed remained.

The platform Rayyan[10] was utilized to organize the articles selected and submitted to two blind independent reviewers; duplicates were removed and the remaining studies were selected after reading the titles, abstracts and full texts. Analysis criteria included methodological quality, intervention and outcomes observed, discrepancies between the reviewers were decided upon consensus (Flowchart 1).

Each article selected was read thoroughly by two investigators simultaneously with critical interpretation and identification of core concepts. The data extracted were organized in a chart containing sample size, study type, intervention, instruments of evaluation utilized, main results, efficacy of the intervention and technical specifications of the equipment. The variables were analyzed through content evaluation, based on the characterization of the sample, methods utilized and main results reported.

RESULTS

Upon application of the eligibility criteria and analysis of full content, 25 studies which utilized PBM as therapeutic intervention for different female pelvic dysfunctions were included. As methodological robust studies on the theme were not identified and the available studies utilized different equipment, parameters and association with other resources, it was opted to present the findings as descriptive analysis. The main information reported in the articles are depicted in Chart 1[8,11-34].

The analysis of the studies showed that, in despite of few investigations about the use of PBM for sexual dysfunction in women with breast cancer in hormone therapy, the available articles for pelvic dysfunction by different dysfunctions gather information that contribute to expand the knowledge on the theme.

The literature identified is highly heterogeneous in regard to clinical conditions, parameters of application and types of equipment utilized, which hampers direct comparisons among studies. For vaginal alterations and sexual dysfunctions, a few reports and case series indicate clinical benefits. Barros et al.[12] noticed good tolerability and potential of use in long-term sequelae in cancer survivors with seemingly low toxicity. Dias et al.[16] reported that the application facilitated the use of vaginal dilators, reducing pain and bleeding and reducing the duration of recovery. Forret et al.[17], in a prospective cohort, found self-reported global improvement in 72% of the participants with vulvovaginal disorders with median of symptomatic improvement of 65%.

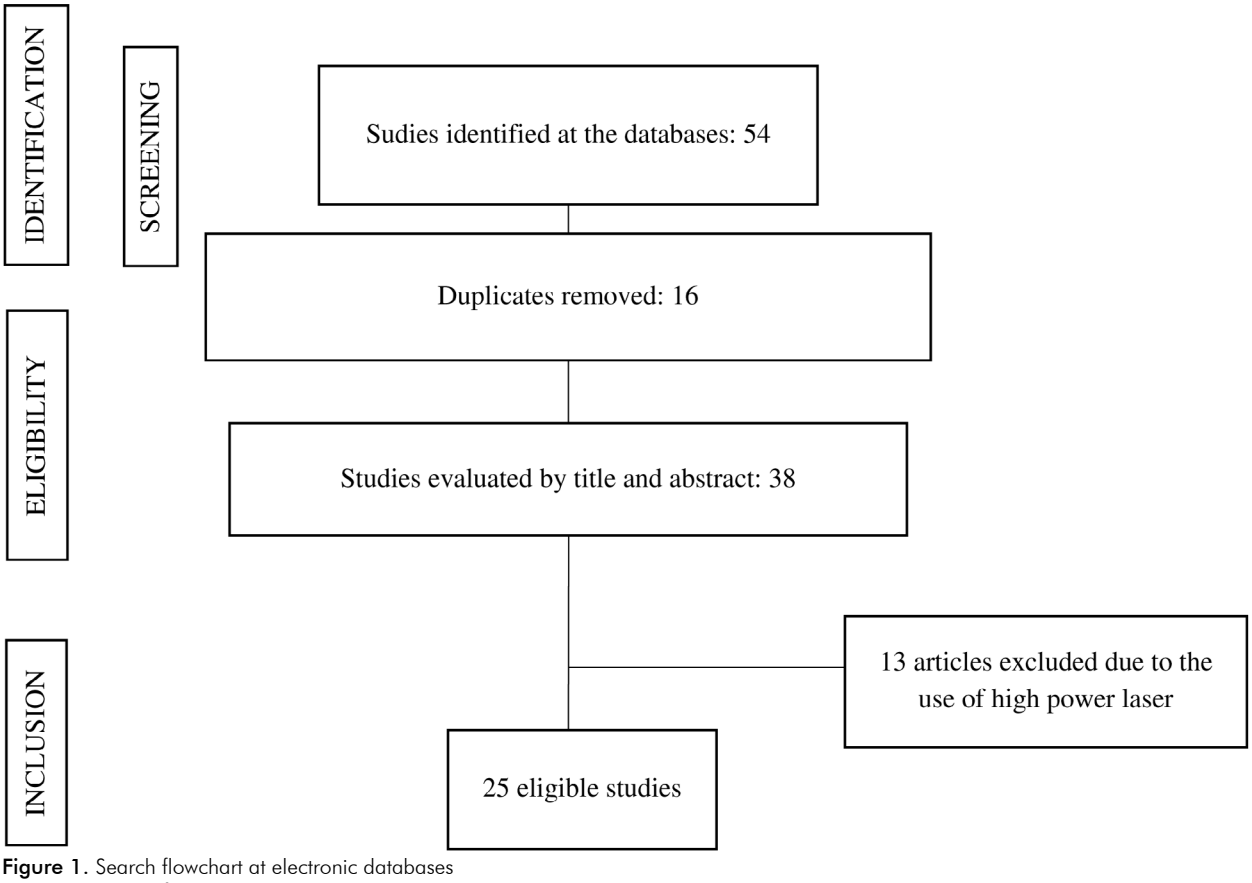

Figure 1. Search flowchart at electronic databases
Source: Adapted from PRISMA[9].

Chart 1. Articles selected according to the use of PBM in pelvic dysfunctions

Author	Study design	Sample	Instrument of evaluation	Dysfunction evaluated	Intervention
Kohli et al.[8]	Observational	128 women with chronic pelvic pain	VAS	Pain at rest and while practicing exercises, seating and standing, urinating, evacuating, during sexual relations and vulvar pain	SoLá Pelvic Therapy Laser diode, 15 W, 810 and 980 nm, through exclusive, sterile and disposable vaginal probe 9 sessions – 3 to 4 weeks
Arjmand et al.[11]	Narrative review about PBM but tangentially addressing Er:YAG and CO_2				
Barros et al.[12]	Case report	Two women with vaginal stenosis post-radiotherapy of endometrium cancer	Physical exam, maturation cell index, vaginal health index, VAS, FSFI and Likert-scale of satisfaction	Moderate vaginal stenosis with severe dyspareunia: genitourinary syndrome	10 8-minute blue LED sessions (405 ± 5 nm, 30 W, 0.000773 W/cm3 of irradiance) intra and extravaginal. Model Energy, DGM®
Butrick e Lamvu[13]	Cohort follow up study pre and post intervention	140 women with rigidity of the muscles of the pelvic floor and syndrome of painful bladder/ interstitial cystitis 125 – 4 sessions 83 – 8 sessions	VAS, clinical evaluation	Pain while urinating, practicing exercises, seating, standing, evacuating, during sexual relations and vulvar pain	15 W diode laser, wavelength 810 and 980 nm – sterile, disposable vaginal probe
Silva et al.[14]	Double-blind, placebo-controlled randomized clinical trial	22 women with effort urinary incontinence: group 1 (PBM + strengthening) and group 2 (PBM placebo + strengthening)	Quality of life, strength and resistance of contraction of muscles of the pelvic floor	Effort urinary incontinence	Infrared laser (808 nm, 100 mW) and 3 J/point – flow of 107.1 J/cm^2. Applied in three points at vaginal introduction and in another three points inside the cavity of vaginal canal
Marchi et al.[15]	Double-blind randomized clinical trial	33 women with effort urinary incontinence	———	———	———
Dias et al.[16]	Case report	Women with vaginal stenosis post-radiotherapy due to cervical adenocarcinoma	Clinical follow-up	Vaginal stenosis	Diode laser InGaAlP (aluminum gallium, indium, phosphide) (DMC®) Parameters: wavelength 660 nm, 100mW, 2J energy, density of energy 71,4J/cm^2, beam of applicator of 0.028 cm^2 Following sites: lateral vaginal walls (two spots), vaginal fornix (1 spot), posterior vaginal wall (2 spots)

To be continued

Chart 1. Continuation

Author	Study design	Sample	Instrument of evaluation	Dysfunction evaluated	Intervention
Forret et al.[17]	Prospective cohort	25 oncologic patients with sexual dysfunction	Patient Global Impression of Improvement FSFI	Female sexual response: desire, arousal, sexual activity and function Vaginal lubrication, orgasm, sexual satisfaction and pain	Six sessions of PBM, one 25-session/week with the device Milta of laboratory Physioquanta® 5 minutes, application on femoral shafts (337 Hz red and infrared, later 50 Hz and 17 Hz) Use with external device on perineum or endovaginal (according to the patient option) with program of vaginal dryness (50 Hz red and infrared, later 5 Hz) and universal (1,000 Hz red and infrared and later 50 Hz and 5 Hz), 10 minutes each
Frederice et al.[18]	Randomized clinical trial	100 women with myofascial pelvic pain	VAS Muscular function of pelvic floor: Oxford scale and surface electromyography Urinary symptoms: ICIQ-OAB and ICIQ-SF, intestinal constipation, ROME criteria	Urinary symptoms and myofascial pelvic pain	10 sessions for two weeks - 100 mw - DMC - 12 J at surface, intravaginal - 808 nm - 4J in three spots) Group sham PBM Associated with vaginal stretching
Frederice et al.[19]	Randomized clinical trial	103 women with myofascial pelvic pain	VAS FSFI	Pain during sexual intercourse and sexual dysfunction	10 sessions for two weeks - 100 mw – DMC – 12J at surface, intravaginal - 808 nm - 4J in three spots Group sham PBM Associated with vaginal stretching
Garcia et al.[20]	Prospective randomized clinical trial	20 women with vaginal dryness	Dryness, burning, dysuria, dyspareunia, bleeding at intercourse VHIS: Elasticity, secretion/fluid volume, vaginal pH, integrity of epithelium and lubrication/humidity of vaginal tissue FSFI	Did not use PBM alone. Not possible to evaluate the result achieved	12 PBM sessions (one 5-minute session/week for 12 weeks) Follow up: one and twelve months post the last session MILTAPLUS intravaginal Physioquanta®
Hottz et al.[21]	Case report	Man with anus cancer and annal canal – invasive squamous cell carcinoma – in chemo/radiotherapy treatment	VAS and questionnaire of symptoms	Peri-annal radiodermatitis grade 3	Low-level laser (DMC) Power: 100 MW, beam area: 0.03 mm), 660nm, 2 J per spot at perineum and anus irradiated twice a week, 48 hours interval between sessions during radiotherapy treatment

To be continued

Chart 1. Continuation

Author	Study design	Sample	Instrument of evaluation	Dysfunction evaluated	Intervention
Lanzafame et al.[22]	Presentation of the equipment vSculpt (class IIa) based on a review, safety analysis and presentation of preliminary data	48 women self-reported effort urinary incontinence and sexual dysfunction	UDI-6 IIQ-7 FSFI FSDS-R Muscular strength of pelvic floor VHIS Histological analysis	Safety and efficacy of vSculpt for sexual function and bladder	Every other day for 45 days. Total photonic power output of the devices ranges between 1.2 and 1.4 W, with delivered energy density of 16-24J/cm^2, vibration of 75-100hz Heat generated: 40-42ºC (10min) and 40-44ºC (12min) vSculpt contains nine LEDs placed circumferentially and disposed radially within a 2.5 cm section of the body of the device (Figs. 1 and 2). Six LEDs emit red light (662 – 20 nm,15mW, 125_ viewing angle) and three LEDs emit NIR light (855 – 30 nm, 15 mW, 130_ viewing angle). The total power output of the vSculpt device is 1.4 W, with delivered energy densities of 12 J/cm^2 at 6 min, 17 J/cm^2 at 8 min, 22 J/cm^2 at 10 min, and 24 J/cm^2 at 12 min. The average power density is 34 mW/cm^2
Modesto et al.[23]	Prospective clinical trial	62 drug-resistant women with candidiasis: Group I: 16 women with 3–4 episodes/year; Group II: 21 women with 5–11 episodes/year; Group III: 25 women with uninterrupted episodes	Absence of symptoms at least for two weeks during treatment and/or when submitted to triggering factor and absence of development of symptoms after one treatment period and/or after 6-month period follow up	Vulvovaginal candidiasis	10 sessions of blue LED of 405 nm (DGM Eletrônica®), energy emission of 240 J, irradiance of 21.71 mW/cm^2, energy density of 26.63 J/cm^2 and one cumulative dose of 79.89 J/cm^2
Pavie et al.[24]	Case series	10 women with healthy vaginal mucosa	Before and after 21 or 28 days (depending on the menstrual cycle): oncotic cytology and measurement of vaginal pH and presence of symptoms: pruritus, pain, burning, dysuria, erythema, fissure, edema, bruises on vulva and uterus and leukorrhea	Safety study	Blue LED 401±5 nm, 30 W and average irradiance of 0.000773 W/cm^2 - 30 min

To be continued

Chart 1. Continuation

Author	Study design	Sample	Instrument of evaluation	Dysfunction evaluated	Intervention
Pereira e Silva et al.[25]	Case series	8 women with vulvovaginitis	FSFI and the WHOQOL-bref	Vulvovaginitis	Blue LED 401±5 nm, 30 W and average irradiance of 0.000773 W/cm^2 – three weekly sessions
Robatto et al.[26]	Case report	Menopausal 52- year woman, with pruritus and lumpy discharge at external genitalia	Before and after 21 days: Microbiological evaluation, cervicovaginal cytology and microflora, clinical manifestations	Lumpy vaginal discharge with pruritus	Ultraviolet A/blue LED of 401± 5 nm, irradiance of 3.01 W/cm^2 Three sources of LED displayed in a circular area of 3.5 cm parallel among themselves, 0.6 cm distant and adjusted for a single power utilized in one session alone: initially, the light was applied for 30 minutes in the vaginal canal with a 10-cm transparent disposable speculum, 1.353 J/ cm^2. Immediately after, the light was applied at a 5cm distant from the vulva for 30 minutes with exposed internal vulvar region and vaginal introitus, 5,418 J/cm^2
Santos et al.[27]	Animal model	15 male Wistar rats submitted to induction of anal fistula and after 30 days Two groups with five rats: control and intervention group, observation for more 30 days			4J applied on the external orifice of the fistula of the animal's anus and between these two points utilizing the following configurations: model Foton Laser III, 100 mw, beam area of 0.028 cm^2, energy density 4J/cm^2, power density 3.57W/cm^2, time of application of 1.12s per point, visible emitter of wavelength 660 nm InGaAlP (aluminum + gallium + indium + phosphide)
Santos et al.[28]	Review about the mechanism of action of PBM on vaginal mucosa	Narrative review	_____	_____	_____
Sarveazad et al.[29]	Animal model	35 healthy male rabbits	Manometry Histological analysis Mallory trichrome stain and quantitative essay of collagen Extraction of RNA cDNA synthesis Real-time PCR Electromyography	External and internal anal sphincter and laceration of the anal mucosa	660 nm and power of 100 mW (model Heltschl, model ME-TL10000-SK The laser irradiation device was mounted on a metal height-adjustable stand (2 cm to the lesion site) to stabilize the laser's irradiation point

To be continued

Chart 1. Continuation

Author	Study design	Sample	Instrument of evaluation	Dysfunction evaluated	Intervention
Sarveazad et al.[30]	Animal model	35 healthy male rabbits	Manometry Histological analysis Mallory trichrome stain and quantitative essay of collagen Extraction of RNA cDNA synthesis Real-time PCR Electromyography	External and internal anal sphincter and laceration of the anal mucosa	660 nm and power of 100 mW (model Heltschl, model ME-TL10000-SK The laser irradiation device was mounted on a metal height-adjustable stand (2 cm to the lesion site) to stabilize the laser's irradiation point. The location of the laser irradiation was three points (each point 5 mm wide). The first and second points included the border between the lesion and the healthy tissue of the sphincter (both sides of the lesion) and the third point was the center of the lesion. The irradiation time at each point was 30 s (total of three points 90 s). Immediately after sphincterotomy, the lesion site was irradiated. Laser irradiation was performed every day for 14 days
Starzec-Proserpio et al.[31]	Narrative review about the use of ablative laser and PBM for vaginal dysfunctions	_____	_____	_____	_____
Zipper e Lamvu[32]	Narrative review on ablative laser use and PBM in vaginal dysfunctions	_____	_____	_____	_____
Zipper e Pryor[33]	Animal model	Healthy vaginal mucosa of an adult Suffolk/Dorset sheep	Test of feasibility and irradiance of the equipment	_____	Near-infrared laser class IV and transvaginal applicator SoLá Pelvic Therapy Laser System – 5W in different moments
Zipper et al.[34]	Observational study	13 women with chronic pelvic pain (completed nine sessions) and 6-month 10 follow-up	SF-MPQ: evaluation one week, three and six months post intervention CGI	All ACOG criteria for diagnosis of chronic pelvic pain	Near-infrared laser class IV and transvaginal applicator SoLá Pelvic Therapy Laser System - 5 to 8 W, 3000 to 3500J Two consecutive days and later, quarterly up to nine sessions

Captions: PBM: Photobiomodulation; FSFI: Female Sexual Function Index; VAS: Visual analogue scale; ICIQ-OAB: Incontinence Questionnaire Overactive Bladder; ICIQ-SF: International Consultation on Incontinence Questionnaire - Short Form; ACOG: American College of Obstetricians and Gynecologists; SF-MPQ: Short Form-McGill Pain Questionnaire; CGI: Clinical Global Impression; VHIS: Vaginal Health Index Scale; UDI-6: Urogenital Distress Inventory-Short Form; 1IIQ-7: Incontinence Impact Questionnaire-Short Form (IIQ-7); FSDS-R: Female Sexual Distress Scale-Revised 2005; WHOQOL-bref: World Health Organization Quality of Life..

The randomized clinical trial by Silva et al.[14] found significant improvement of the quality of life, strength and resistance of the muscles of the pelvic floor (p<0.05) while Marchi et al.[15] did not find positive results, possibly for not evaluating PBM alone. The study of Lanzafame et al.[22], utilizing the device vSculpt, reported consistent clinical changes in post-menopausal women with GSM and/or effort urinary incontinence without adverse effects.

Under painful pelvic conditions, Butrick and Lamvu[13] reported reduction of pain in diverse activities with improvement ≥ 1 point in the visual analogue scale in 73.5% of women and ≥ 2 points in 63.9% after eight sessions, in addition to expressive reduction of severe or moderate pain (p<0.001). Kohli et al.[8] have also observed significant reductions of pain at rest and during several activities (p<0.000). Zipper et al.[34], in an observational study, reported improvement in 60% of the participants with chronic pelvic pain and 75% of them classified the improvement as significantly "better" or "much better" with mean reduction of 50% of the severity of the pain for six months.

In infection and vaginal inflammation scenarios, Modesto et al.[23] reported complete vulvovaginal remission in 58% of the patients after six months, with significant improvement of symptomatic relief or cure of signs and symptoms of vulvovaginitis for all the participants with increased sexual function and quality of life scores in five of them. Robatto et al.[26] described clinical and lab resolution of infection by *Candida albicans* with 12-month remission. Pavie et al.[24] evaluated the safety of blue LED on vaginal mucosa without adverse events.

Some studies did not show efficacy or methodological limitations. Frederice et al.[18,19] (two clinical trials) found improvement in the groups with and without PBM, suggesting lack of specific effect. Garcia et al.[20] and Marchi et al.[15] did not utilize the technique alone, hampering the attribution of the results to the intervention. Santos et al.[27,28] (animal model) observed reduction of inflammation and vascular congestion in annal fistula but without complete healing of the trajectory.

Sarveazad et al.[29,30] tested PBM in sphincter lesions of rabbits in experimental and pre-clinical setting, including increase of collagen and markers of muscular regeneration, although one of the studies have reached worse results than stem-cells therapy. Other narrative-based studies as those by Arjmand et al.[12], Santos et al.[27,28], Starzec-Proserpio et al.[31], Zipper and Lamvu[32] discussed possible applications of the technique, especially for vaginal dysfunctions but without robust clinical evidence.

DISCUSSION

The increase of survival of women with breast cancer resulting from improved diagnoses and therapeutic entailed long-term clinical consequences, among them sexual dysfunction. Between 50% and 80% of the patients in hormone therapy presented some type of sexual dysfunction, including pain, dryness, libido reduction and difficulty of arousal[1,2], an impact frequently underestimated in the protocols of oncologic follow-up which compromises the quality of life and adherence to adjuvant treatment, most of the times extended for five to ten years[35]. Hormone therapy, especially with aromatase inhibitors and tamoxifen promotes accentuated estrogenic suppression, resulting in GSM, a condition that affects the vaginal mucosa and pelvic floor, leading to epithelial atrophy, loss of elasticity, local vascular and neurological alteration and persistent inflammation, factors that increase the prevalence of dyspareunia and sexual aversion[36].

It is important to distinguish low-level PBM from ablative technologies as fractioned CO_2 laser and Er:YAG. While ablative devices act by controlled thermal damage to the mucosa with superficial tissue remodeling, PBM utilizes low-level wavelength on red and near-infrared, producing photochemical effects without thermal lesion[32]. Its mechanism involves phototonic absorption by mitochondrial chromophores as cytochrome c oxidase, increasing the production of ATP, releasing nitric oxide with consequential vasodilation, modulating inflammatory processes and stimulating tissue regeneration by cellular proliferation, collagen synthesis and angiogenesis[5,17].

In the oncologic context, the treatment of sexual dysfunctions faces relevant limitations since local hormone therapies as estrogen creams are still controversial or contraindicated even in minimal doses, leading to the adoption of palliative measures of limited efficacy as lubricants and vaginal moisturizers[36]. PBM emerges in this scenario as a non-pharmacological and non-hormone alternative with favorable safety profile and potential application in pelvic rehabilitation[8].

The studies included in this review presented positive and non-expressive results and the differences among them appear to be related to methodological factors, technical parameters and characteristics of the population investigated. Kohli et al.[8] and Forret et al.[17] reported significant improvement of pain, lubrication and sexual functions in women with chronic pelvic pain or sequelae of oncologic treatment, possibly associated with the use of standardized protocols with proper number of sessions, adequate parameters of wavelength and fluency and targeted application on the affected areas, favoring the activation of the biochemical cascade expected for PBM[5]. In addition, the inclusion of symptomatic and refractory patients may have amplified the perception of clinical benefit[8].

On the other hand, the study by Frederice et al.[18,19] did not find superiority of PBM over placebo, which can be related to the association with other interventions, hampering the isolation of the specific effect or utilization of suboptimal parameters as insufficient power and exposure time to trigger consistent tissue alterations. The sample heterogeneity may have contributed too to dilute the benefits in subgroups potentially more responsive.

Encouraging results were observed in specific populations as in the studies of Barros et al.[12] and Dias et al.[16], who applied PBM in women with vaginal stenosis post-radiotherapy, reporting improvement of tissue elasticity, tolerance to the exam and adherence to the use of dilators, probably due to the increase of vascularization and reorganization of collagen fibers in tissues previously fibrotic. Silva et al.[14] and Butrick and Lamvu[13] observed significant reduction of pain and functional improvement of the pelvic floor in standardized protocols, suggesting a relevant rehabilitating effect.

Despite the advances, the available evidence is limited. Most of the studies utilized small samples with up to 141 participants, no control group or double-blinded and short follow-up, which reduces the robustness of the conclusions[4]. Few articles utilized standardized scales to evaluate sexual functions and even for those who do, it is not possible to isolate the effect of PBM from other associated interventions[8,18]. The heterogeneity of the technical parameters, including wavelength, power, fluency, route of application and different number of sessions, hampers direct comparisons and prevents the formulation of definitive clinical recommendations[5,17].

Although low-level PBM is a promising, safe and well-tolerated intervention, especially in patients with contraindication of hormone therapies, the consolidation of its clinical use depends on randomized and controlled clinical trials, preferentially multicenter, with standardized protocols and long-term follow-up, allowing to evaluate its efficacy in a robust manner and establish the dose-response relation in different clinical contexts[4,8].

CONCLUSION

Although the existing evidences on the use of low-level PBM for sexual dysfunctions in women with breast cancer in hormone therapy are still limited and do not warrant definitive clinical recommendations, this review critically integrated and analyzed data that expand the available knowledge. While gathering studies with different designs, parameters and populations, the review identifies important gaps, points out plausible physiological parameters and emphasizes promising clinical outcomes, reinforcing the potential of the technique as non-hormone and safe approach in the oncologic context.

CONTRIBUTIONS

All the authors contributed substantially to the conception and design of the study, acquisition, analysis and interpretation of the data, writing and critical review. They approved the final version for publication.

DECLARATION OF CONFLICT OF INTERESTS

There is no conflict of interests to declare.

DATA AVAILABILITY STATEMENT

All content underlying the text is contained in the article.

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