

# Low-Level Laser Therapy in Vulvovaginal Symptoms Induced by Graft-Versus-Host Disease: Case Report

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*Terapia a Laser de Baixa Potência nos Sintomas Vulvovaginais Induzidos pela Doença do Enxerto contra o Hospedeiro: Relato de Caso*

Terapia con Láser de Baja Intensidad en los Síntomas Vulvovaginales Inducidos por la Enfermedad de Injerto contra Huésped: Informe de Caso

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## ABSTRACT

**Introduction:** In the literature, vulvovaginal graft versus host disease (GVHD) has an incidence that varies between 24.9 and 69% and there are not many studies addressing this topic. Photobiomodulation (PBM) for vulvovaginal GVHD has not been described in the literature to date, but there is evidence of its effectiveness in oral GVHD and in the prevention of cancer-related oral mucositis. The objective of this study was to describe the evaluation and physical therapy treatment with PBM of a patient diagnosed with vulvovaginal GVHD. **Case report:** Woman with vulvovaginal GVHD complaining of moderate pain when urinating, difficulty performing intimate hygiene, burning sensation in the vulva and severe discomfort when wearing underwear. PBM favored the improvement of pain and tissue repair of vulvar injuries, relieving symptoms and facilitating the performance of vaginal dilation exercises. **Conclusion:** PBM was appropriate and effective in reducing pain, burning sensation and discomfort, providing an anti-inflammatory and tissue regenerating effect. This resulted in a perceived improvement in other complaints related to the use of underwear and intimate hygiene. However, for the laser to become a strongly recommended resource in this scenario, more robust studies are needed, with longer intervention and follow-up times, as randomized and controlled clinical trials.

**Key words:** Genital Diseases, Female/radiotherapy; Hematopoietic Stem Cell Transplantation/adverse effects; Host vs Graft Reaction/immunology; Low-Level Laser Therapy/methods.

## RESUMO

**Introdução:** Na literatura, a doença do enxerto contra o hospedeiro (DECH) vulvovaginal possui uma incidência que varia entre 24,9 e 69% e não há muitos estudos que abordem essa temática. A fotobiomodulação (FBM) para a DECH vulvovaginal não foi descrita na literatura até o presente momento, mas há evidências da sua eficácia na DECH oral e na prevenção de mucosite oral relacionada ao câncer. O objetivo do estudo é descrever a avaliação e o tratamento fisioterapêutico com FBM de uma paciente diagnosticada com DECH vulvovaginal. **Relato do caso:** Mulher com DECH vulvovaginal com queixa de dor moderada para urinar, dificuldade para realizar a higiene íntima, ardência na vulva e desconforto severo ao utilizar roupas íntimas. A FBM favoreceu a melhora da dor e a reparação tecidual das lesões da vulva, aliviando os sintomas e facilitando a realização dos exercícios de dilatação vaginal. **Conclusão:** A FBM foi apropriada e eficaz na redução da dor, sensação de ardência e desconforto, proporcionando um efeito anti-inflamatório e regenerador tecidual. Isso resultou em uma percepção de melhora de outras queixas relacionadas ao uso de roupas íntimas e higiene íntima. No entanto, para que o *laser* se torne um recurso fortemente indicado nesse cenário, são necessários estudos mais robustos, com tempo de intervenção e acompanhamento mais longos, como ensaios clínicos randomizados e controlados.

**Palavras-chave:** Doenças dos Genitais Femininos/radioterapia; Transplante de Células-Tronco Hematopoéticas/efeitos adversos; Reação Enxerto-Hospedeiro/imunologia; Terapia com Luz de Baixa Intensidade/métodos.

## RESUMEN

**Introducción:** En la literatura, la enfermedad de injerto contra huésped vulvovaginal (EICH) tiene una incidencia que varía entre 24,9% y 69% y no existen muchos estudios que aborden este tema. La fotobiomodulación (FBM) para la EICH vulvovaginal no se ha descrito en la literatura hasta la fecha, pero existe evidencia de su eficacia en la EICH oral y en la prevención de la mucositis oral relacionada con el cáncer. El objetivo de este estudio fue describir la evaluación y el tratamiento de fisioterapia con FBM de una paciente diagnosticada de EICH vulvovaginal. **Informe del caso:** Mujer con EICH vulvovaginal que refiere dolor moderado al orinar, dificultad para realizar la higiene íntima, sensación de ardor en la vulva y malestar severo al usar ropa interior. La FBM favoreció la mejora del dolor y la reparación tisular de las lesiones de la vulva, aliviando los síntomas y facilitando la realización de ejercicios de dilatación vaginal. **Conclusión:** La FBM fue apropiada y eficaz para reducir el dolor, la sensación de ardor y el malestar, proporcionando un efecto antiinflamatorio y regenerador de tejidos. Esto resultó en una mejora percibida en otras quejas relacionadas con el uso de ropa interior y la higiene íntima. Sin embargo, para que el láser se convierta en un recurso muy recomendable en este escenario se necesitan estudios más robustos, con tiempos de intervención y seguimiento más prolongados, como ensayos clínicos aleatorizados y controlados.

**Palabras clave:** Enfermedades de los Genitales Femeninos/radioterapia; Trasplante de Células Madre Hematopoyéticas/efectos adversos; Reacción Huésped-Injerto/inmunología; Terapia con Láser de Baja Intensidad/métodos.

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## INTRODUCTION

The graft-versus host disease (GVHD) is the major cause of late mortality and morbidity affecting 40% to 70% of the patients after allogeneic hematopoietic stem-cells transplantation (HSCT)<sup>1</sup>. Inflammation-mediated donated cells results in tissue damage and fibrosis of the organ affected<sup>2,3</sup>.

The diagnosis is challenging because clinical presentation may mimic and overlap other vulvovaginal dermatosis and atrophy due to estrogen insufficiency. Most of premenopausal women submitted to allogeneic HSCT will enter menopause and many of vulvovaginal GVHD may coexist with vulvovaginal atrophy. The main symptoms included dryness, irritation, vaginal discharge, dyspareunia, sinusorrhagia, erythematous-like vulvar lichen planus, redness, erosive areas and teleangiectasias, vulvar fissures, vulval synechia and vaginal stenosis<sup>3,4</sup>.

Diagnosis is based on signs and symptoms, some scales guide professionals on how to identify the severity of the disease, being essential to differentiate primary ovarian insufficiency and vulvovaginal GVHD. Biopsy may be necessary and treatment of different pathological processes can be similar<sup>5-7</sup>. There are no evidences of specific treatment for GVHD, but vulvovaginal hygiene, sexual education, estrogen replacement, immunosuppressor agents, anti-inflammatory and vaginal dilators are recommended<sup>3</sup>.

So far, photobiomodulation (PBM) for vulvovaginal GVHD has not been described in the literature but there are evidences of its efficacy for oral GVHD and preventing cancer-related oral mucositis<sup>8</sup>.

PBM is a non-ionizing optical radiation within the red and infrared wavelength absorbed by the cytochrome C oxidases (found in mitochondria) and by the transforming growth factor beta 1 (TGF- $\beta$ 1). These proteins mediate biological cascades producing effects in the modulation of the pain, inflammation, healing and regeneration of tissues<sup>9</sup>.

The objective of this study is to describe the evaluation and physiotherapeutic treatment with PBM of a patient with vulvovaginal GVHD. The electronic chart was reviewed upon approval by INCA's Institutional Review Board, number 6004756 (CAAE (submission for ethical review): 68792623.0.0000.5274) and signature of the Informed Consent Form in compliance with Directive number 466/2012<sup>10</sup> of the National Health Council.

## CASE REPORT

Female, 46-years old patient submitted to related donor allogeneic HSCT following the protocol

cyclophosphamide – total body irradiation – antitumocytes globulins (Cy-TBI-ATG) in November 2021. After five months of HSCT, the first signs of vulvovaginal changes appeared: vaginal burning, occasional pruritus and redness, discomfort and dryness. The vulvovaginal GVHD diagnosis was confirmed after ten months.

The patient was assisted by the physiotherapy of “Hospital do Câncer II” complaining of moderate pain, score 7 of the visual numerical scale (VNS) and burning on the labia majora (upper right and left), vaginal introitus and perineal body. Dysuria, vaginal dryness, moderate difficulty to perform intimate hygiene and severe discomfort while wearing underwear. She felt less attractive sexually after the onset of the disease and treatment and her self-image was impacted.

At physical examination, two vulval superficial lesions were detected, one on the upper right and another on the upper left side (Figure 1). Unidigital vaginal palpation was performed causing discomfort with exacerbation of symptoms. Vaginal canal was measured with red dilator, brand Dell (118.5 mm x 023.5mm) reaching 11.0 cm.

The disease was graded 3 according to the scale of Spinelli *et al.*<sup>6</sup> (Chart 1).

Treatment was initiated with laser DMC – THERAPY EC – red (660 nm  $\pm$  10 nm) and infrared (808 nm  $\pm$  10 nm), 100mW, four Joules twice a week weekly on the spots marked in Figure 2.

The patient was guided to apply coconut oil daily at evening to hydrate the vulva. At the third visit, improvement of pain was reported, and at the seventh visit, no more burning and she was able to put on underwear.

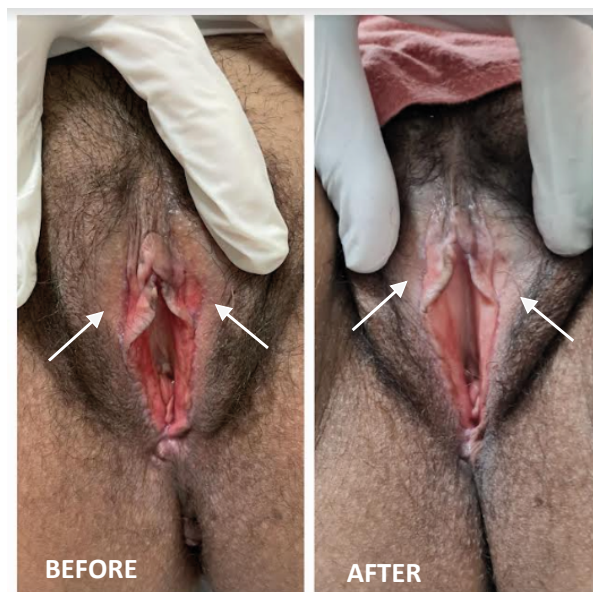


Figure 1. Vulvar superficial lesions before and after laser treatment

Chart 1. Vulvovaginal GVHD grading system

GRADING	SIGNS
GRADE 0	No signs
GRADE 1	General erythema and edema of the vulvar structure; irregular erythema of the mucous and glandular structures of the vulvar vestibule; erythema around the opening of the vestibular glands
GRADE 2	Grade 1 findings plus mucosa erosions on vulvar surface; fissures in vulvar folds
GRADE 3	Grade 2 findings plus agglutination of clitoral hood; introitus stenosis; vaginal synechia; hematocolpos or complete vaginal occlusion; levator ani syndrome

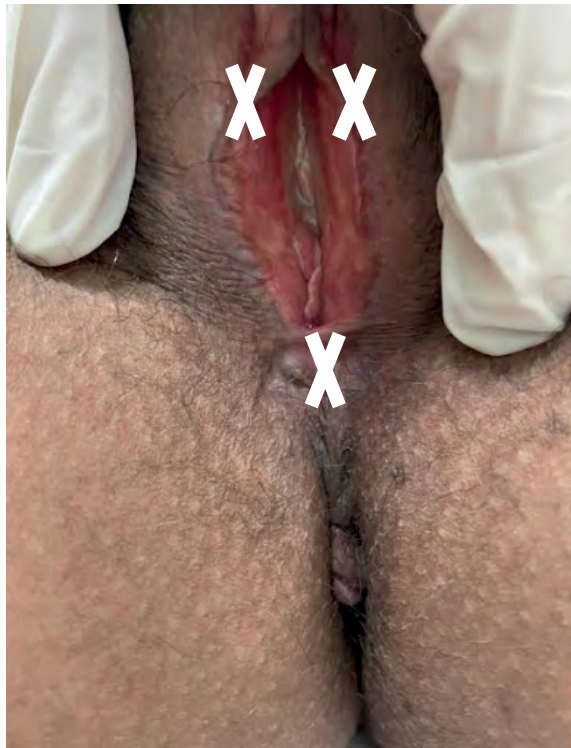


Figure 2. Spots for laser application

Upon reduction of initial symptoms together with earlier interventions, massage was applied at the perineal body to modulate pain and dilators to prevent stenosis were introduced. Initiated exercises of vaginal dilation with blue dilator (134.0 mm x 027.5 mm) and prescribed to continue the use at home to keep vaginal canal open and reduce pain.

She reported improvement of pain at the eighth visit (VNS 0). Coloration and depth of vulvar lesion evolved positively as shown in Figure 1, no adverse effect was noticed.

## DISCUSSION

Vulvovaginal GVHD is highly prevalent (66%), however, women rarely report the symptoms notwithstanding the impacts on quality of life, sexual activities and regular urination which makes the diagnosis difficult<sup>1</sup>. Lubricants, dilators or vibrators for vaginal dilation are recommended, in addition to gradual resumption of sexual activities, although pain may be an obstacle.

The study results indicated expressive improvement of pain (VNS from 7 to 0) and burning (moderate to none), with positive results on daily life after the patient was able to put on her underwear again and felt less discomfort while doing intimate hygiene. PBM has accelerated the process of tissue repair and promoted the reduction of the inflammation, pain and swelling<sup>12</sup>.

With improvement of tissue repair of vulvar lesions, the symptoms reported by the patient reduced.

Comparison with similar population and clinical conditions was not possible because of lack of data, however, PBM is well described for pelvic disorders<sup>13</sup>, also utilized to treat GVHD-related issues in other sites.

A case report of a patient with oral mucosa GVHD treated with PBM in 32 spots found improvement of the pain in four days after the application (VNS 4 to 0). Full repair of the lesions and recovery of oral functions have been noticed<sup>14</sup>. The study of Campos *et al.*<sup>14</sup> corroborates this outcome, with improvement of pain and function.

The first sessions have already resulted in improvement of oral GVHD as reported by Finfter *et al.*<sup>15</sup>, who found pain reduction in more than 50% of the patients soon after the initiation of PBM.

Another report on laser use in gynecological cancer concluded that pain and bleeding reduced during perineal massage and facilitating the use of vaginal dilators. The investigators have also noticed the lack of clinical trials describing dosimetry on vaginal walls, however, they reported that the safe use of this resource to minimize and prevent oral mucositis during treatment of head and neck cancer is a solid recommendation, being plausible to apply on vaginal mucosa given the similarities with oral mucosa<sup>16</sup>.

The use of PBM, therefore, is recommended to treat vaginal GVHD (pain and tissue repair). The results confirmed the literature about the use of this treatment for oral mucosa GVHD.

## CONCLUSION

This is the first report in the literature addressing the use of PBM for vulvovaginal GVHD symptoms, showing



that the technique was appropriate to reduce pain, burning and discomfort (anti-inflammatory effect and tissue repair), leading to the improvement of complaints while wearing underwear and intimate hygiene. Controlled and randomized clinical trials with extended period of intervention and follow-up are necessary to support its indication within this scenario.

### CONTRIBUTIONS

All the authors contributed substantially to the study design, acquisition, analysis and interpretation of the data, wording and critical review. They approved the final version to be published.

### DECLARATION OF CONFLICT OF INTERESTS

There is no conflict of interests to declare.

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None.

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