

Low level Laser therapy in radiation-induced vaginal stenosis after cervical cancer treatment: Case Report

Terapia a laser de baixa potência na estenose vaginal induzida por radiação após tratamento do câncer cervical: relato de caso

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ABSTRACT

Background and objective: Low Level Laser Therapy (LLLT) has been widely studied to relieve pain and accelerate the wound healing process. Considering the occurrence of radiation-induced vaginal stenosis due to the treatment of cervical cancer, as well as the pain and tissue injury that ionizing radiation therapy causes, this study discusses the use of LLLT as a therapeutic resource to complement the recommended therapy of dilation of the vaginal canal. Methods: Case report of a woman with radiation-induced vaginal stenosis after brachytherapy cervical cancer treatment, complaining of pain and local bleeding. Results: LLLT favored vaginal dilation therapy, reducing vaginal pain and bleeding, reducing recovery time. Conclusions: LLLT can be a resource to be considered in the treatment of radiation-induced vaginal stenosis. Implications for Cancer Survivors: The use of this technique demonstrates improving the patient's quality of life after

treatment, leads to a decrease in pain, improves adherence to physical therapy treatment, facilitates sexual intercourse and follow-up exams.

Keywords: low level laser therapy, pelvic radiotherapy, vaginal stenosis, oncology, case report.

RESUMO

Justificativa e objetivo: A terapia a laser de baixo nível (LLLT) tem sido amplamente estudada para aliviar a dor e acelerar o processo de cicatrização de feridas. Considerando a ocorrência de estenose vaginal induzida por radiação devido ao tratamento do câncer cervical, bem como a dor e lesão tecidual que a radioterapia ionizante provoca, este estudo discute o uso da LLLT como recurso terapêutico para complementar a terapia de dilatação recomendada de o canal vaginal. **Métodos:** Relato de caso de mulher com estenose vaginal induzida por radiação após tratamento com braquiterapia para câncer de colo do útero, com queixa de dor e sangramento local. **Resultados:** a LLLT favoreceu a terapia de dilatação vaginal, reduzindo a dor e sangramento vaginal, reduzindo o tempo de recuperação. **Conclusões:** a LLLT pode ser um recurso a ser considerado no tratamento da estenose vaginal induzida por radiação. **Implicações para Sobreviventes de Câncer:** O uso dessa técnica demonstra melhora na qualidade de vida do paciente após o tratamento, leva à diminuição da dor, melhora a adesão ao tratamento fisioterapêutico, facilita a relação sexual e os exames de acompanhamento.

Keywords: terapia a laser de baixo nível, radioterapia pélvica, estenose vaginal, oncologia, relato de caso.

1 INTRODUCTION

Chemotherapy (CT) and Radiotherapy (RT) treatment of gynecological cancer is associated with progression-free survival¹. However, late treatment-related toxicities are frequent and have a major impact on quality of life¹, such as changes in the gastrointestinal and genitourinary systems resulting in diarrhea, vaginal or rectal bleeding, dysuria, urinary and fecal incontinence, hematuria, symptoms related to menopause, decreased vaginal lubrication, sexual interest and vaginal stenosis².

Radiation-induced vaginal stenosis (RIVS) is defined as narrowing of the vaginal canal resulting from an accumulation of scar tissue, due to an increase in the production of collagen in connective tissue³. It is considered a subacute effect of radiotherapy, but it can appear up to 5 years after the end of treatment^{4,5}.

Late RT reactions are those that occur three months after the end of treatment³, as a consequence, microcirculation changes leading to damage to the basal cells of the epidermis, endothelial and vascular components, resulting in atrophy of the vaginal mucosa^{3,4}. In vaginal stenosis, the changes are due to the tissue repair process^{5,6,7}. Clinically, the mucosa evolves with the development of telangiectasias, pallor reaction,

adhesions, loss of elasticity, fragility and atrophy^{5,7,8,9}. In fact, the formation of abnormal superficial vessels can trigger bleeding in gynecological exams and during sexual intercourse¹⁰.

Several authors cite vaginal dilation as the major therapeutic strategy to prevent and treat RIVS^{11,12,13,14}. Management combines perineal massage and vaginal dilators, which can cause discomfort, leading to the difficulty of adhering to therapy^{11,12,14}. However, vaginal dilatation device often traumatizes mucosa, probably due to rupture of the epithelium. Therefore, trauma may induce greater tissue inflammation and therefore an increase in fibroblasts, generating a healing disorder. Consequently, greater difficulty in the preventive approach¹³.

Low level laser therapy (LLLT) is a safe, low-cost strategy. Besides that, LLLT has been widely used for pain relief and tissue regeneration^{15,16,17,18}, and associated to promote tissue repair, analgesia and process modulation inflammatory. LLLT use in the prevention and treatment of radiodermatitis.^{19,20,21}. Additionally, LLLT has been used for different dysfunctions of the pelvis²². However, there are no publications on its intracavitary use in RIVS. This study discusses the use of LLLT as a therapeutic resource to complement perineal massage and vaginal dilators for the treatment of RIVS, which may reduce pain and local bleeding.

2 CASE REPORT

R.M., 43 years old, diagnosed with cervical adenocarcinoma, stage IIIB (FIGO), performed six cycles of chemotherapy (CDDP) and pelvic radiotherapy (teletherapy at a dose of 50.4Gy and 4 fractions of high dose rate brachytherapy - HDRB, 28Gy). One month after completion of HDRB, during an evaluation with a physiotherapist, reported not having been sexually active for four years and presence of urinary incontinence. During the pelvic evaluation, it was observed that the vaginal walls were intact, a vaginal depth of 9 cm, and pelvic floor muscle contraction grade 3 (Oxford scale). There was no shortening or narrowing of the vaginal canal, however, reported pain (VAS 4). She was instructed to use the vaginal dilator to prevent RIVS (3 times per week, for 20 minutes).

Four months after completion of HDRB, RMM reported not using the dilator due to feel pain and bleeding. In the physiotherapeutic reassessment, a shortening of the vaginal canal was noticed - eight centimeters deep and signs of RIVS in the vaginal fornix, grade 1 (CTCAE v.4)²³.

Grade 3 RIVS (CTCAE v.4)²² was seen six months after completion of treatment. RMM reported occasional urinary and fecal losses, and no sexual activity. Upon examination, a vaginal depth of 3 centimeters was noted, with significant narrowing and shortening of the vaginal canal. There was bleeding on vaginal touch and RMM reported pain 8 on the visual analog scale (VAS) used to assess pain. The strength of the pelvic floor muscles remained constant. The patient was instructed about the LLLT and a free informed consent form was obtained from her.

LLLT was performed with a InGaAlP diode laser (indium phosphide, gallium, and aluminum) (DMC, São Carlos, São Paulo, Brazil). LLLT parameters wavelength of 660 nm (emitting continuous light), power of 100mW, energy of 2J, density of energy 71.4J/cm², applicator beam 0.028 cm² was used in the following points: lateral vaginal walls (two points), vaginal fornix (1 point), wall posterior vaginal (2 points). (Figure 1A; 1B)

FIG 1A. points of application of LLLT on the vaginal wall

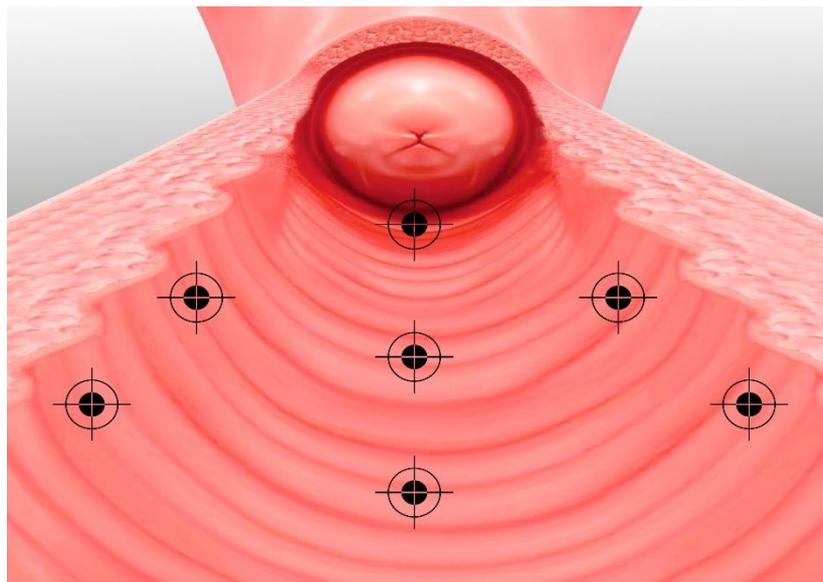


FIGURE 1B: intracavitary application of LLLT in patient with vaginal stenosis



After LLLT, digital perineal massage was performed and the use of mechanical massagers and dilators, aiming to increase the vaginal depth and elasticity. After the session, there was an important improvement in bleeding and pain (perception of pain from 8 to 2 in VAS). Eight sessions for the treatment of RIVS were carried out following the same protocol, and at the end there was an increase in depth from 3 to 8 centimeters.

3 DISCUSSION

Vaginal stenosis present high prevalence women undergoing pelvic radiotherapy treatment, around 3 to 33%, interfering with quality of life^{1,3}. Currently, the best approach to prevention and treatment is unclear. Early management was described as an important prognostic factor.

Adverse events usually reported at the end of the RT was pain, mucositis and radiodermatitis. Recent guideline recommended early intervention, mainly with the use of vagina dilators associated with perineal massage¹². However, the early use of vaginal dilators is often accompanied by reports of pain and bleeding, which can cause additional discomfort to the patient. In fact, the irradiation injury mechanism can last for months after the end of radiotherapy. The tissue repair process dysfunction predisposes the

disordered deposition of extracellular matrix and, consequently, the formation of fibrosis and tissue adhesions.

LLLT is a non-invasive, low-cost and safe therapy to assist in the treatment of toxicities of patients undergoing cancer therapy^{24,25}. In addition, there is an increasing number of clinical trials on its application in the treatment and prevention of adverse effects related to cancer therapy^{18,19}.

Although its benefits are well established, the literature still lacks clinical trials to better understand dosimetry in vaginal walls. It is worth mentioning the important similarity described between the vaginal and oral mucosa²⁴. In addition, the safety of using this device in cancer patients for mitigation and even prevention of oral mucositis in patients undergoing treatment of head and neck cancer is one of the greatest recommendations. Therefore, it is plausible to think of the approach as a complementary therapy for the prevention and treatment of RIVS²⁷.

Currently, scientific evidence showed LLLT mitigated adverse events have similar conditions involved in the etiology of vaginal stenosis²⁷. Indeed, application for pain relief and acceleration of the tissue repair process for complications arising from CT and RT has strong evidence in the literature when it comes to the oral mucosa^{24,25,29}. Similar situations with the vaginal mucosa can be better seen in studies that used LLLT in the oral mucosa^{24,25,29}.

Late effects improve chronification of the tissue repair process predisposes the disordered deposition of extracellular matrix and, consequently, the formation of fibrosis and tissue adhesions^{29,30,31,32,33}. LLLT contributes largely to the tissue repair process, enabling the modulation of this process. Hamblin demonstrated LLLT enables the repair of the epithelium in an orderly manner¹⁷. In addition, it contributes to pain reduction. In the systematic review conducted by Paglioni et al., demonstrated the effectiveness of LLLT in relieving pain in head and neck cancer, presenting 15 studies that resulted in better pain control with this therapy and greater use of analgesics for control groups versus LLLT³⁴.

Following this proposal, as demonstrated in this case report, where there was a contribution from the LLLT in order to make the treatment with dilators for vaginal stenosis more bearable, since some studies such as that by Berger & Echols et al., 2019, bring that many women they struggle to maintain the treatment, as they report difficulty in tolerating emotions, physical discomfort. In addition, they showed that the anticipated fear of feeling pain or blood loss during dilation³⁵.

LLLT mechanisms has been indicate a positive effect on tissue regeneration, modulating the inflammatory phase and in the proliferative phase it enhances the fibroblast synthesis, aids in the mobility of the cells involved in this repair process and also by dissociation of nitric oxide, which is an important vasodilator^{17,37} Remodeling phase, it has an effect on collagen deposition and reconstitution of the extracellular matrix³⁸.

Pre-clinical studies have shown that LLLT increases the bioavailability of ATP^{16,39,40} and assists in the tissue healing process inducing the local release of cytokines, chemokines and other biological response modifiers, increasing the production and activity of fibroblasts and macrophages, improving the mobility of leukocytes, promoting the formation of collagen and inducing neovascularization²⁷. Thus, LLLT performance seems to promote cell proliferation⁴¹, better healing after tissue lesions caused by vaginal dilation, and the patient progresses with less pain and bleeding after completion of therapy, as observed in this case report.

LLLT treatment effectiveness has great variability and is dependent on physical parameters, with upper and lower thresholds. Below this threshold, the light is too weak to have an effect or above it may have inhibitory effects⁴². Therefore, in order to be effective, treatment must use irradiation parameters within therapeutic windows of bio-stimulation dose^{20,43}.

4 CONCLUSION

LLLT decreased pain and bleeding and facilitated vaginal dilation in this case report. However, randomized clinical trials should be performed in order to have higher levels of evidence on the use of LLLT in RIVS.

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