

BLUE LIGHT EMITTING DIODE IN TREATMENT OF RECURRING VULVOVAGINAL CANDIDIASIS: A CASE REPORT

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Introduction: Recurring vulvovaginal candidiasis (RVVC) is an infectious disease of the lower genitourinary tract, that occurs at least 4 times per year. Drug treatment can last months and favor the appearance of adverse effects and increase the chances of recurrence. Blue Light Diode (LED) is an electromagnetic spectrum light, with antimicrobial functions. **Case Report:** A case report was made of a patient with RVVC whose treatment consisted of three sessions of 60-minutes each, of application of blue LED in intervals of 15 days. Evaluation was carried out before, at the end of third application and three months after the last session by means of fungal culture, cervical cytology; analysis of patient's clinical condition; and measurement of vaginal pH. After the third session, there was a reduction in fungal load and vaginal pH; absence of symptoms (pruritus, burning and dyspareunia) and vulvovaginal edema, but there were no alterations in the cytology and microflora, which remained with inflammatory markers. Three months after the end of the treatment, there was no *Candida* in vaginal secretion, neither signs nor symptoms of candidiasis, and vaginal pH was normal. As for cytology and microflora, cellular alterations associated with cytolysis and presence of lactobacilli was observed. **Conclusion:** The blue LED 401±5 nm may be a promising alternative to treat RVVC by eliminating signs and symptoms in women.

INTRODUCTION

Vulvovaginal candidiasis (VVC) is an infection of the vagina and vulva caused by numerous species of *Candida*, where *Candida albicans* is responsible for 85% of the cases¹. It is characterized by intense vulvar pruritus, dyspareunia and vaginal discharge in lumps. In addition, the vulva and vagina become swollen and hyperemic, often followed by dysuria and burning sensation².

This infection is one of the most common diagnoses in gynecological practice, being considered the second most prevalent genital infection in Brazil, preceded only by bacterial vaginosis. It is estimated that 75% of adult women present at least one episode of VVC during their lifetime, of which 5% present recurrence, i.e. four or more VVC episodes per year².

The factors that lead to the development of recurrent vulvovaginal candidiasis (RVVC) are still uncertain. However, it is believed that intrinsic factors linked to women, i.e. changes in the immune response of the vaginal epithelium may facilitate the emergence of new disease outbreaks. In some cases, stressful situations could also lead to the onset of fungal infection, because cortisol, considered a powerful anti-inflammatory, can be responsible for triggering an important suppression of the vaginal immune system³. The use of broad-spectrum antibiotics, personal hygiene, *diabetes mellitus* and immunosuppression are also considered possible risk factors for cases of recurrence².

The treatment of RVVC initially includes drug therapy, aiming to achieve clinical and microbiological remission of the infection. Frequent use of oral antifungal for 7 to 14 days followed by maintenance with oral antifungal is also used for a period of six months. Alternative treatments, such as the use of oral yoghurts, lactobacillus therapies and low-carbohydrate diets are described in the literature, but there is a lack of evidence of their actual efficacy⁴.

It is hypothesized that Light Emitting Diode (LED) irradiation may be a therapeutic alternative for VVC, based on its proven antimicrobial effect in other studies⁵. The LED consists of semiconductor diodes that when subjected to an electric current emits light. This light is part of the electromagnetic

spectrum and wavelength varies from 405 to 940 nm, which leads to differentiation of the color and of effects obtained⁶.

At shorter wavelengths, between 400 and 425 nm, LED is blue and has antimicrobial effects confirmed by studies. The highest capacity of destruction of microorganisms has been found at 405 nm. Even with the germicidal action of the blue LED, this is considered safe for humans because it does not cause cellular damage when used in adequate irradiance⁷.

Most of the studies use the light associated with photosensitizer because it believes that this initiates the process of photochemical reaction for consequent cellular destruction⁸. However, it is known that the plasma membrane and mitochondria of fungi have endogenous porphyrins that allow photoactivation and cause singlet oxygen production when in contact with blue light, which is highly reactive and causes cellular destruction, without allowing any mechanism of resistance⁹.

The blue light with short wavelengths (400-425 nm) has been already used in humans for the purpose of destroying bacteria. There are studies performed in gastric mucosa and skin for the treatment of *Helicobacter pylori* and acne, respectively^{5,10}. The use of this therapy also at a shorter wavelength (405 nm) for fungal destruction has already been proven in *in vitro* and in studies with animals; however, there are no reports of its use in isolation in humans^{9,11}.

Considering the fungicidal effect of the blue LED at shorter wavelengths, this may be an alternative for the treatment of VVC, especially in recurrent cases, since it has a mechanism of action that inhibits resistance chances. In addition, this phototherapy is effective and safe¹⁰.

This study aims to report the microbiological and clinical effects of the blue LED with wavelength length ranging between 401 ± 5 nm in a patient with RVVC, in addition to verifying the adverse effects of the technique.

CASE REPORT

A 33-year-old female patient, married, with a clinical diagnosis of RVVC arrived at the doctor's office

located in the city of Salvador/Bahia with a history of *Candida* infection higher than 4 times per year, abundant vaginal secretion and pruritus in a region of external genitalia. She used fluconazole 150 mg in weekly applications for the past six months and clotrimazole 2% vaginal cream, one tube per day for 3 days, during periods of worsening of symptoms. The study was conducted from February to June 2017 and has been approved by the Research Ethics Committee of the Federal University of Recôncavo Baiano (UFRB), CAAE: 56391416.1.0000.0056 and is registered in the *Clinicaltrial* under number NCT03075046 as this is a study that will continue through a randomized clinical trial.

The participant was instructed by her gynecologist to seek alternative treatment with the use of blue LED because resolution of the pathology was not achieved with conventional therapy.

The treatment took place in the OGYC (Obstetrics and Gynecological Care) office located in a medical center in the city of Salvador/BA and before starting the study, the participant signed the Free and Informed Consent Term as this is was a new modality therapy never previously tested in the human vaginal region.

Initially the patient was interviewed by a physiotherapist to obtain clinical data (Table 1) and questioned about the presence or absence of the following symptoms: pruritus, burning, dysuria and dyspareunia. These symptoms are common in patients with CVV, but are not exclusive of this pathology. The questioning about the presence or absence of this symptoms was based on the FEBRASGO's manual about vulvovaginites¹².

Table 1. Clinical characteristics of the patient with RVVC diagnosis treated with Blue LED.

Variable	YES	NO
Diabetes		X
Regular menstrual cycle	X	
Oral contraceptive		X
Condom use	X	
Sexually active	X	
Fixed sexual partner	X	
Daily intimate protector		X
Intimate hygiene product		X
Drying of intimate clothing in an airy place	X	
Hygienization in vagina-anus direction	X	

The participant then underwent a gynecological clinical examination by the OGYC physician, where the presence or absence of the following signs was checked: leukorrhea, edema, erythema and excoriations in the vulva and uterus. In addition, cervico-vaginal and microflora cytology, pH evaluation and vaginal fluid specific culture were performed to confirm the infection and to determine the types of *Candida* involved. After collection, the material was sent to the clinical analysis laboratory located in the same building.

It was used a prototype of blue LED, developed by study surveyors, with wavelight length ranging between 401 ± 5 nm, with irradiance of $0,000773$ W/cm², and with a total energy of $2,7828$ J/cm². The light was applied for 60 minutes, with the apparatus statically tripped, 5 cm away from the vulva and vagina region. The LED device consists of three light units and it has 3,5 cm in diameter at the location of the light output. Light emission was performed using a speculum in the vaginal canal for 30 min, and the rest of the time without the use of any intracavitary

material. The number of sessions was based on the report of the clinical condition of the patient, since there are no previous studies using LED in the vaginal region that could support the protocol. After the use of light, vaginal secretion was collected to determine the number of colony forming units (CFUs). In addition, the apparatus was sanitized with moist gases soaked in 70% alcohol.

Three sessions were performed in intervals of 15 days. During the visits, the patient was naked, in a closed room, in the lithotomy position on a gynecological stretcher, in the presence of only one physiotherapist specialized in urogynecology, who applied the light. The patient was advised to attend to the clinic if any new complaint appeared, or in case of persistence or worsening of symptoms in the intervals without treatment.

The microbiological evaluation was performed through a fungal culture test with quantitative analysis of CFUs (secretion collected shortly after the first LED application, immediately after the last session and three months after the conclusion of the treatment) and for specification of *Candida* subtypes present in the area (material collected before the first LED application, after the last session and three months after the end of therapy).

In the analysis performed before the start of the treatment with the use of the blue LED, it was detected infection by *C. albicans*. The vaginal secretion collected after the first application of the LED indicates growth of 15 CFUs of the same species. Immediately after the last application of the light, the result of the fungus culture presented reduced growth of the germ to 5 CFUs of *C. albicans* species. After three months, *Candida* absence was verified, with negative culture result.

In addition, vaginal pH and vaginal cervical cytology and microflora were also performed

before, immediately after therapy, and three months after the completion of therapy. In the case of pH evaluation, tapes were used for this purpose and there was alteration when compared the values before the beginning of treatment (pH = 6.0), immediately after its completion (pH = 5.0) and three months after completion of therapy (pH = 4.0).

The cervical cytology and microflora performed by conventional smear did not present alterations when compared before the beginning of the treatment and immediately after, being observed variation only in the reevaluation after three months of conclusion of the treatment. In the interpretation of the previous evaluation and that performed immediately after therapy, benign reactive cellular changes associated with marked inflammation were seen: cells with discretely increased nuclei and fine chromatin in the medium to numerous neutrophils. As for organisms, fungal elements were found morphologically compatible with *Candida*. In the same exam conducted three months after the end of the treatment, there were no inflammatory signs and it was observed presence of cellular changes associated with cytolysis and common lactobacilli of the healthy vaginal microflora. In addition, the report was negative for intraepithelial lesion or malignancy.

The patient's clinical status was assessed before, immediately after the therapy and three months after completion of treatment. Each sign and symptom was classified as: present or absent. In the reassessments, when the symptoms remained present, they were still classified as: better, worse or unchanged for comparative purposes. There was observed an improvement in most of the signs and symptoms presented, when compared before and immediately after treatment, and in the last reassessment, three months after the therapy, it was detected the resolution of symptomatology (table 2).

Table 2. Clinical picture of patient diagnosed with RVVC before, immediately after and three months after completion of treatment with blue LED.

Variables	Before		Immediately after		Three months after	
	Present	Absent	Present	Absent	Present	Absent
Itching	X			X		X
Burning	X			X		X
Dysuria		X		X		X
Dyspareunia	X			X		X
Leukorrhea	X		X			X
Erythema	X		X			X
Edema	X			X		X
Vulva /uterus excoriations		X		X		X

The patient did not present discomfort, sensation of heat, pain, erythema or any other adverse effect during and/or after the LED application. In addition, she discontinued the use of the antifungal medication after the second therapy session.

Discussion

This study pioneered in the use of blue LED in RVVC, presenting positive results in clinical and microbiological complaints in one patient. The mechanism of action in this case is still unknown. However, it is known that the use of blue light with the objective of evaluating fungal load in *in vitro* studies and bacterial load in humans has also obtained effective results, with significant reduction of microorganisms^{5,9,13}.

The results of fungal load reduction indicated by the number of *C. albicans* colonies in the examination performed before and immediately after the treatment and the negative fungal culture result at three months after treatment conclusion can be explained by the presence of endogenous porphyrins present in the fungi. When these come into contact with blue light, generate singlet oxygen and other reactive oxygen species, leading to cell death¹³.

Inamura et al. (2014) evaluated the effects of 405 nm blue light on pathogenic microorganisms present in the oral cavity, among them *C. albicans*, demonstrating a 90% reduction in fungal load when using a dose of 240J for 20 minutes¹³. This study justifies the use in the vaginal mucosa because of the similar tissue characteristics¹⁴.

Ganz et al. (2005) conducted a clinical trial using 405 ± 2 nm blue light on gastric mucosa of symptomatic patients infected with *Helicobacter pylori* and found a significant bacterial death rate in all treated individuals, with eradication of at least 90% of the bacteria in seven of the nine patients submitted to treatment. According to the authors, this result can be explained by the fact that light at this wavelength induces the photoexcitation of endogenous porphyrins present in *Helicobacter pylori*, resulting in the production of reactive species of singlet oxygen and consequent death of the microorganism⁵.

In this study, the patient's clinical symptoms of pruritus, burning, dysuria, dyspareunia and edema disappeared after application of the blue LED immediately after conclusion of the third session and this result remained in the reassessment three months after treatment conclusion. This finding may be related to the restoration of the vaginal microflora by the significant reduction of fungal load after treatment, as a result of absorption of light by the porphyrins present in the fungi. The molecules, interacting with this light, generate highly reactive singlet oxygen, causing damage to the membrane and mitochondria of fungal species, with consequent selective cell death⁹.

Morton et al. (2005) performed a study in 30 subjects with mild to moderate acne on the face, who received eight treatment sessions with blue light (409-419 nm), at a dose of 48J/cm² and intensity of 40 Mw/cm². According to the authors, despite the variation of clinical response between individuals, there was a 73% improvement in the inflammatory lesions resulting from acne. This result can be explained by

the destruction and inhibition of *Propionibacterium acnes* proliferation due to the absorption of blue light by the endogenous porphyrins, generating singlet oxygen production and subsequent bacteria destruction¹⁰.

Elman et al. (2003) performed a study in patients with acne vulgaris using 405-420 nm blue LED with irradiance between 50 and 200 mW/cm². The research involved a dose response study involving part of the face; a clinical trial involving the whole face; and a double blind controlled study with application of LED in only one hemiface. All three studies found a decrease in inflammatory lesions. According to the authors, *Propionibacterium acnes* produces, as part of its normal metabolism, porphyrin, which when exposed to light generates a chemical reaction with peroxide production that has the potential of destroying the bacteria¹⁵.

In this study, the decrease in vaginal pH, approaching the values considered physiologically normal and protective of genital health, represents a benefit because acid environments are less favorable to the development of pathogens¹⁶. Although *Candida* has a different metabolism from most microorganisms, with better adaptation to this medium¹², there was an improvement in clinical and microbiological conditions, with disappearance of symptoms and absence of fungi.

The persistence of inflammatory signs when comparing the cytology and microflora examination results performed before and immediately after treatment may be explained by the fact that the reassessment was made shortly after the last LED application and, at that moment, not enough time had elapsed for resolution of the inflammatory condition. Furthermore, research shows that the blue LED has no anti-inflammatory effect¹⁵.

The scarcity of studies with the use of blue LED in the female genital region indicates the need for further experimentation in order to explain the possible relationship between this light and its effects on vaginal microflora and pH.

No adverse effects such as hyperemia, irritation or discomfort during and after LED treatment were reported by the patient in this study. The study of Ganz et al (2005) developed in individuals with H.

pylori using the 405 ± 2 nm blue light⁵ is in line with the present research, considering that no adverse reactions were evidenced.

CONCLUSION

We conclude that the blue LED with wavelength length ranging between 401±5 nm may be a promising alternative non-drug therapy, with low cost, easy application and free from adverse reactions in the treatment of RVVC. However, randomized clinical trials are needed to evaluate the efficacy, besides non-inferiority tests in relation to drug treatment.

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