Anais Brasileiros de Dermatologia
Print version ISSN 0365-0596*On-line version* ISSN 1806-4841

An. Bras. Dermatol. vol.84 no.5 Rio de Janeiro Sept./Oct. 2009

http://dx.doi.org/10.1590/S0365-05962009000500003

INVESTIGATION

A prospective, randomized, open and comparative study to evaluate the safety and efficacy of blue light treatment versus a topical benzoyl peroxide 5% formulation in patients with acne grade II and III

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ABSTRACT

BACKGROUND: Many acne patients improve after exposure to sunlight and there are many reports about the efficacy of blue light phototherapy on acne lesions.
OBJECTIVES - The purpose of this study was to evaluate efficacy and safety of blue light treatment versus topical benzoyl peroxide 5% formulation in patients with acne grades II and III.
METHODS - Sixty volunteers with facial acne were included and evaluated in 5 visits: the first one for screening, another 3 held on days 7, 14 and 28 of treatment, and the last one after 14 days of the end of treatment. Thirty of them were irradiated with Blue Light (8 times, twice a week) and the other thirty were treated with topical Benzoyl Peroxide 5% formulation, auto-applied twice a day, every day. We assessed the severity of acne by counting the lesions and analyzing the photographs.
RESULTS - The improvement achieved by the blue light was the same as the one with benzoyl peroxide, regardless of the type of lesion (p> 0.05). Otherwise, the side effects were less frequent in the group treated with blue light.
CONCLUSIONS - Blue light irradiation was as effective as Benzoyl Peroxide in acne treatment grades II and III but

there were fewer side effects.

Keywords: Acne vulgaris; Benzoyl peroxide; Phototherapy

INTRODUCTION

Acne is a chronic inflammatory disease of pilosebaceous unit and affects approximately 80% of the young population. Abnormalities to the formation and differentiation of pilosebaceous follicle cells result in hyperkeratinization of the duct, with consequent accumulation of lumen cells, which associated with retention of sebaceous secretion forms the comedones, which are the initial acne lesions. This medium becomes prone to the development of bacteria, especially *Propionibacterium acnes (P. acnes)*, which modifies the lipid composition of the sebum. Moreover, immune response of *P. acnes* and hyperseborrheia with its proinflammatory lipids seem to be involved in the formation of the inflammatory process that cause papules, pustules and nodules[1,2].

The classical treatment advocated for acne seems to correct one or more factors involved in the genesis of the process. The choice will depend on the severity and extension of the disease. Poorly inflammatory and non-extensive clinical presentations are treated in general with topical medication: benzoyl peroxide, retinoid acids or azelaic acid. For more severe and extensive cases systemic drugs are used: antibiotics, anti-androgens or isotretinoin [3-7]. All these modalities are well known and have precise indications for inhibition and regulation of sebaceous production; however, they may occasionally trigger non-tolerable adverse effects such as severe dryness of the mucosa and the skin, increase in levels of triglycerides and cholesterol and teratogenesis induced by isotretinoin. Another important aspect is the onset of bacterial resistance in the presence of erythromycin and tetracycline and its derivates [8], which limit its use, in addition to refusal to use some of these drugs by the patient.

Many patients, regardless of the treatment, describe clear improvement of acne when they are exposed to sunlight [9,10]. Thus, many studies have demonstrated that visible light is an alternative and effective way to treat acne [11-15]. This result may be explained by the production of porphyrins, specially uroporphyrins, coproporphyrins and protoporphyrins IX [16] by *P. acnes*. Protoporphyrins may absorb light and thus promote a photodynamic reaction that induces to bacterial destruction. Within this context, Blue Light, which has 407 to 420 nm wave length, can also activate these porphyrins and produce the same photodynamic reaction [17]. Therefore, treatment with light can be effective in acne, because it causes selective damage to pilosebaceous unit and destruction of *P. acnes*, without producing visible damage around it. Recently, it has been demonstrated that *P. acnes* radiation with UVA rays and Blue Light can modify transmembrane proton inflow of the bacteria, and induce cell damage by modifying intracellular pH [18]. An important aspect of Light Blue is that differently from ultraviolet radiation from the sun, it is not carcinogenic.

Concerning topical medication, benzoyl peroxide 5% is a classical formulation to treat inflammatory acne. It may be used as monotherapy or as combined therapy with other drugs, both topical and systemic, at concentrations that range from 5% to 10%. The concentration of 5% produces less local irritation and may be applied twice a day. In these concentrations, benzoyl peroxide has anti-inflammatory and antibacterial action and for this reason, it is used to treat inflammatory acne grades II or III. [3-6]

In view of this knowledge, the authors decided to carry out a study to check safety and efficacy of Blue Light as a treatment modality of inflammatory acne grades II or III, comparing it to treatment with Benzoyl peroxide at 5%.

MATERIAL AND METHODS

The study was open prospective randomized comparative and included patients with inflammatory acne lesions grades II or III, according to the classification of the Brazilian Group of Acne, seen consecutively between November 2006 and September 2007. The protocol was submitted and approved by the Clinical Research Ethics Committee, PUC Campinas (N.491/06).

The 60 subjects selected to start the study had taken no specific acne medication for at least 15 days. They were randomly divided into two groups, in which 30 patients used Blue Light and 30 used 5% Benzoyl Peroxide. Subjects of GL group (Blue Light) underwent 8 sessions of light therapy for 15 minutes each, twice a week, within minimum intervals of 48 hours, for 4 weeks. All patients in both groups used facial hygiene soap and sun protection lotion SPF15, used daily and during the whole studied period.

Blue Light emission was obtained using a specific light source that illuminated a 55mm circular area, which was externally protected by a spherical non-transparent globe, manufactured for this specific purpose. The device is named Soret Blue Light® and was developed by companies EVTECH and Komlux Fibras Ópticas. It produces high intensity light in the range 407 to 420 nm in medium power in the lighted area of 40-40 mW/cm2 distance. This

light length is efficient for the photostimulation of porphyrins, as provided by *in vitro* and *in vivo* studies.[12-17] The penetration of this light is approximately 1mm into the skin, and it reaches *P. acnes* that is on the surface and inside the ducts. Patients received eye protection with dark lenses swimming goggles *Speedo*® during the sessions. Benzoyl peroxide 5% was prepared as topical cream, provided in 20g tubes, manufactured by the reference laboratory of the Service of Dermatology.

Patients' follow up was divided into 4 visits as follows: (V0) - Recruitment visit, for instructions and selection of cases one week before the beginning of treatment; (V1) - Visit for randomization and inclusion of patients capable of starting treatment; (V2) - First assessment visit after two weeks of treatment; (V3) - Second assessment visit after four weeks of treatment; (V4) - Third assessment visit two weeks after the end of treatment.

Quantification of acne improvement was made by counting the total number of inflammatory lesions (papules and nodules) and non-inflammatory lesions (comedones) observed between the initial visit V0 and visit V3, shown on the face and documented by photos. Photos were taken with camera HP Photosmart 735 digital, 3.3 MPixel, with 3X optical magnification.

Concerning safety and tolerability, we asked patients about the occurrence of erythema, dryness, desquamation and burning during treatment in all visits.

To meet the objectives of the study, we calculated the descriptive measures of each type of lesions (mean and standard deviation) and designed charts with the means and the respective standard errors to illustrate the results found [19]. We carried out normal range tests of Kolmogorov-Smirnov[20] for lesions, grouped as non-inflammatory and inflammatory and we assumed the normal distribution of data. To compare both treatment options concerning the types of lesions, we compiled the number of detected lesions in visits V0 and V3, observed for each patient, who demonstrated the variation between the beginning and end of treatment. The visits performed between V0 and V3 were control visits, to check patient compliance to treatment and adverse events. The comparisons were tested with non-paired t-student test [19].

Tests were carried out at significance level of 5%.

To analyze the adverse events we used chi-square test.

RESULTS

After signing the Free Informed Consent Term, the 60 patients were randomly divided into two groups, out of which 30 underwent treatment with benzoyl peroxide (GP) and the other 30 underwent Blue Light application (GL). Within such 60 patients, 51 completed the study and 9 did not (3 in the GP and 6 in the GL groups). We did not carry out sensitivity or adversity treatment tests. They were all healthy and had no other comorbidities or used any medication that could have interfered in the progression or patient compliance to treatment.

There 26 female and 34 male patients - in GP there were 12 women and 18 men, and in GL there were 14 women and 16 men. Eleven were mixed Brazilians, 47 were Caucasian, and two had no reference to race in the chart. The mean age at the onset of study was 17.3 years. Out of the total, 39 had undergone some kind of treatment before, from topical to systemic drugs, including oral isotretinoin. As to acne severity, 3 were classified as having acne grade III and 57 as acne grade II.

Out of the total, in the GP group, the mean number of non-inflammatory lesions at V0 was 128.67 and at visit 3, it was 93.50, which amounts to 27.3% reduction. As to the inflammatory lesions, the mean number of inflammatory lesions was 35.37 at V0 and 19.14 at V3 (reduction of 45.8%). By adding up inflammatory and non-inflammatory lesions (total of lesions), we detected reduction of 31.32% after treatment (from 164.03 at V0 to 112.64 at V3.

In the GL group, the mean number of non-inflammatory lesions at V0 was 111.60 and at visit 3 it was 85.92 (23% reduction), whereas for inflammatory lesions it was 27.87 at V0 and 23.33 at V3 (reduction of 16.28%). Upon analyzing the mean total of lesions we observed reduction of about 21.66% after the use of benzoyl peroxide (from 139.47 at V0 to 109.25 at V3) (Table 1).

Table 1: Distribution of cases concerning gender, age, location, size, diagnosis and immune-histochemical markers

Case	Gender	Age	Location(*)	Size (cm)	DIAG	PCNA[1]	Ki67[2]	p53[3]	Bcl2[4]
1	M	44	Nose	1.8 X 0.7	AK	4 +	1+	4+	1+
2	M	77	L Hand dorsum.	0.6 X 0.3	AK	4+	3+	4+	1+
3	F	71	Nasal dorsum	0.5 X 0.3	AK	4+	1+	4+	1+
4	F	92	Temporal-frontal	2.3 x 0.9	AK	4+	1+	2+	0
5	F	60	L Nasal Dorsum	0.8 x 0.5	AK	3+	2+	3+	0
6	M	62	R arm	0.6 X 0.4	AK	3+	0	4+	1+
7	F	78	R Glabella region	0.4 X 0.3	AK	3+	2+	4+	2+
8	F	81	Dorsum	1.2 x 0.7	AK	4+	3+	3+	0
9	F	75	R Eyelid	0.5 x 0.2	AK	4+	0	3+	2+
10	M	59	R Forearm	0.4 diam.	AK	4+	3+	3+	0
11	M	59	L Clavicle	0.1 x 0.1	SCC	4+	1+	4+	0
12	F	44	L Mandible	0.6 X 0.3	SCC	4+	0	2+	0
13	M	75	R Hemiface	0.6 x 0.3	SCC	4+	2+	1+	0
14	M	87	Temporal	1.2 diam.	SCC	4+	2+	2+	0
15	M	88	Scalp	0.9 x 0.5	SCC	4+	2+	2+	0
16	F	44	R Upper lip	0.8 x 0.4	SCC	3+	2+	2+	0
17	M	88	R Chest region	3.0 x 1.5	SCC	2+	0	1+	0
18	F	81	R neck	1.3 x 0.7	SCC	4+	3+	4+	0
19	F	86	R hand	3.5 x 1.0	SCC	4+	1+	4+	0
20	M	60	L Supraclavicular	3.6 x 2.5	SCC	4+	4+	4+	0

(*) R - right; L - Left;
AK Actinic Keratosis; SCC Squamous cell carcinoma

The statistical analysis of the results of treatment was performed by comparing the number of lesions seen at visit V0 with the number observed after 30 days of treatment (V3), using non-paired t-student test. The last visit (V4) was carried out just for follow-up purpose after the end of treatment, and we did not use it to analyze efficacy by counting the number of lesions. Visits V1 and V2 served as a control to check patients' compliance and adverse events.

As to adverse events, we observed that 28 patients using benzoyl peroxide, that is, 93.3% of them, had some symptom related with use of the product, and only two patients did not have any complaints. The reported signs and symptoms were some level of erythema, desquamation, dryness or burning. In some patients, there was the need to reduce the frequency of product use to once a day, which led to improvement of symptoms. Conversely, among the patients who used Blue Light treatment, only 23.3% reported some unexpected events, characterized by desquamation and/or dryness, but they were all of mild intensity. In this group, it was not necessary to interrupt the treatment in any of the patients owing to such effects. Thus, considering the result of the chi-square test, the percentage of effects is statistically higher in the group that used Benzoyl peroxide ($p < 0.001$).

DISCUSSION

Despite the reports of clinical improvement of acne when exposed to low intensity sun exposure, the medical literature had no scientific paper that explained and confirmed the improvement caused by light exposure in its entire visible spectrum, or in some fractions of the spectrum such as Blue Light or Red Light. Tzung12, in a study with 31 patients, reported improvement of acne grade II in 52% of the cases when treated in one of the sides of the face with Blue Light, and in the other as control. In that paper, based on the participation of porphyrins, the author related pre and post-intensity treatment of fluorescence with Wood lamp and did not find any difference in effectiveness of treatment with the change in intensity of fluorescence. Shalita 13, in a study with 35 patients, showed mean reduction of 60% of the number of inflammatory lesions and improvement in clinical presentation in 80% of the patients with application of Blue Light for one month. The study, however, was not controlled with any other acne treatment.

Papageorgiou [15] compared 107 patients in four groups of acne treatment: isolated exposure to Blue Light, exposure to combined Blue and Red Light, exposure to White Light, and treatment with benzoyl peroxide at 5%. The authors noticed improvement in 76% of the inflammatory lesions and 58% of the comedones in the group treated with Blue and Red Lights, which was significantly higher than in the groups of Blue Light and Benzoyl peroxide in isolation. The results of the groups treated with isolated Blue Light and benzoyl peroxide were similar. The mean improvement of Blue Light group was 45% for comedones and 63% for inflammatory lesions, using an accumulated dose of 320J/cm2. Thus, Papageorgiou[15] noticed that the association between the two types of radiation, Blue and Red Light, provided better results than other isolated treatments. Our study observed

significant improvement in acne presentation in both treatment options, both for Blue Light and benzoyl peroxide (Figure 1 and 2).

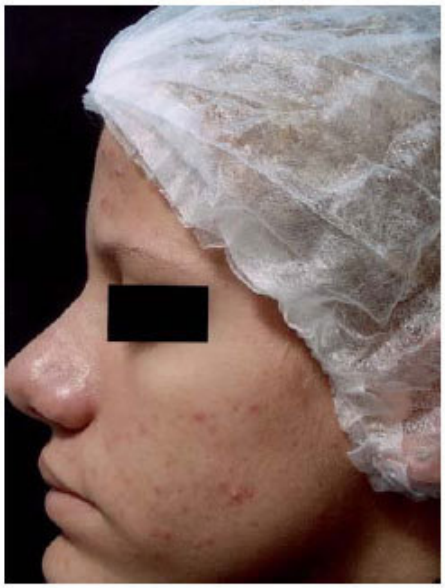

FIGURE 1: Female patient before treatment with Blue Light

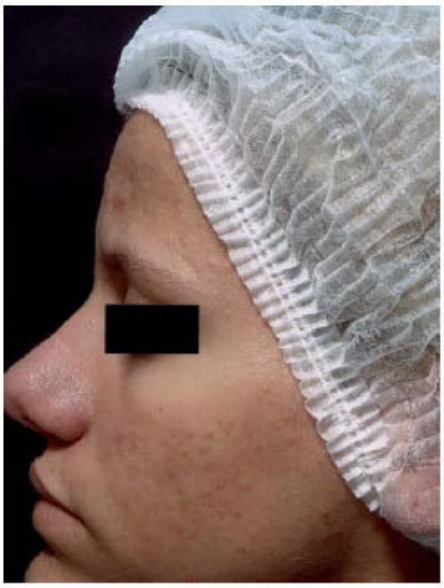

FIGURE 2: Results after 8 sessions with Blue Light

Upon analyzing the isolated number of non-inflammatory and inflammatory lesions during weeks V0 and V3, reduction of non-inflammatory lesions seem to be similar in both groups GP and GL (Chart 1); there seemed to be a trend for better results when counting the inflammatory lesions in the group of benzoyl peroxide when compared to the Blue Light group (Chart 2). However, owing to the analysis of total number of lesions (inflammatory and non-inflammatory) (Chart 3), the mean reduction of the number of lesions is the same for both treatments, regardless of the type of lesion, confirmed by p value in the analysis of inflammatory lesions ($p = 0.500$) or non-inflammatory lesions ($p = 0.177$). This apparent incoherence occurred owing to the major variation of results in the reduction of number of lesions between one patient and the other, within the groups, evidenced by the standard deviation values (Table 1).

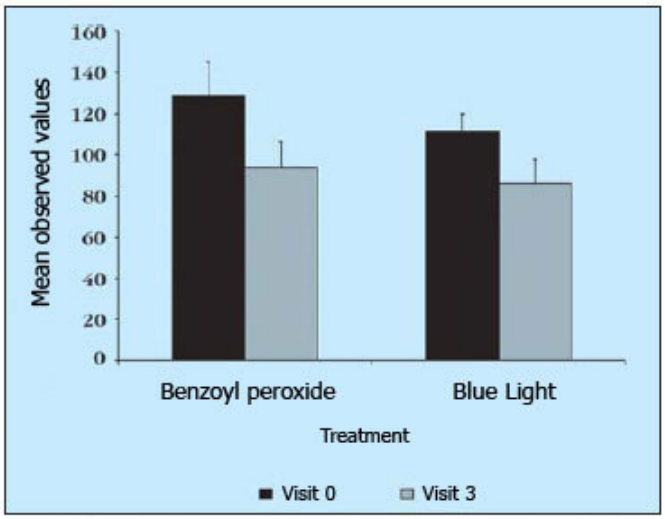

CHART 1: Mean values and respective standard errors of non-inflammatory lesions

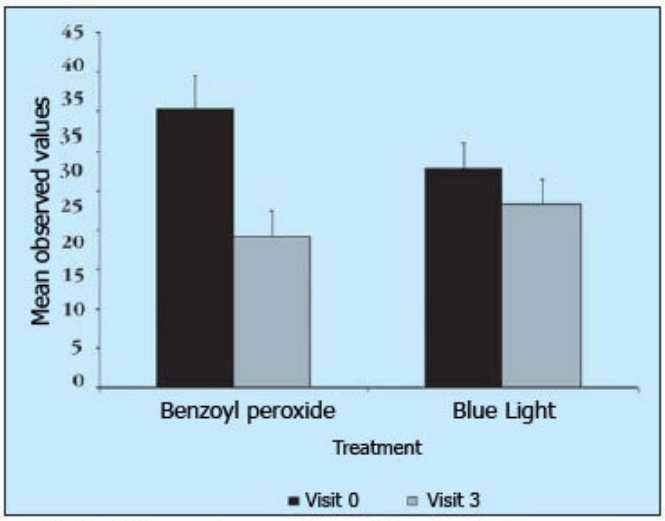

CHART 2: Mean values and respective standard errors of inflammatory lesions.

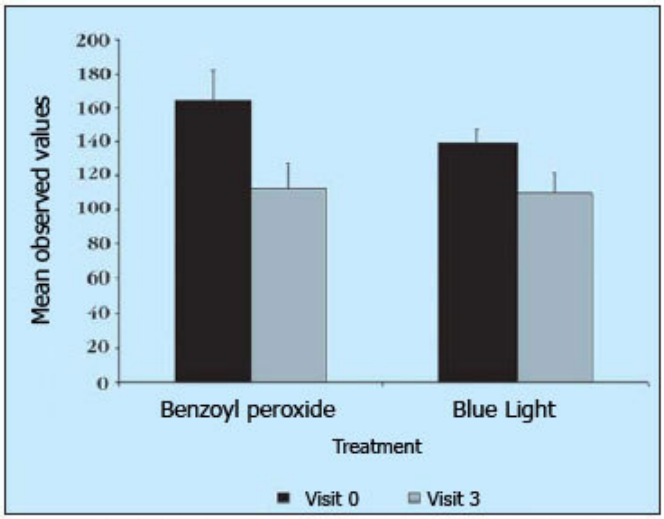

CHART 3: Mean values and respective standard errors of total number of lesions (inflammatory + non-inflammatory lesions)

Therefore, upon analyzing all patients together, through the comparison test (t-student test), results showed that both treatment options presented the same reduction in number of lesions, both in total lesions and in isolated analysis of each type of lesion, either inflammatory or not (p> 0. 05).

In our study, as observed by Papageorgeou[15], the result of Blue Light treatment was similar to that of benzoyl peroxide. Thus, reduction in lesions after four weeks of treatment was similar for the two groups. However, differently from our findings, Shalita [13] showed that Blue Light more significantly improved the inflammatory lesions. We observed that despite the fact that the two treatments had shown similar efficacy, Blue Light was better tolerated, because there were fewer complaints of skin irritability during treatment, differently from benzoyl peroxide, which caused discomfort with two daily applications, causing mild erythema or burning sensation, up to desquamation and dryness of moderate grade. This fact required intervention, changing the initial proposition of two applications a day to reduced frequency of use or interruption of medication for some days. We should consider that these adverse events could have been minimized since the beginning with the application of BP once a day. However, we should emphasize that the application twice a day intended to improve the results and was used as such as monotherapy. Moreover, BP was formulated as cream and not as gel, which produces greater emollient effect, which could have minimized the adverse effects of twice a day application. Despite the need to interrupt the treatment, the authors considered that there was no interference in the results, because the interruption occurred for very short time.

As to Blue Light, the authors observed that there was lower compliance to treatment when compared to BP. This fact was explained by the commuting need - patients had to go to the treatment Center twice a week to undergo Blue Light applications.

CONCLUSION

The authors concluded that Blue Light treatment is as effective as benzoyl peroxide to reduce the number of acne grades II and III and has fewer adverse events when compared to BP in isolation. This fact confirms that Blue Light is a real treatment option, especially for patients with contraindications to other treatment methods. New studies with the association of Blue Light and other treatment options should be performed to maximize the results of combined therapy. The introduction of Blue Light in clinical practice, associated with existing treatment modalities, may shed new light into the future, leading to better results and more treatment options to patients with acne.

ACKNOWLEDGEMENT

We would like to thank Janaina Keyla Cavalcanti Carvalho, Simone C. Furlaneto de Souza and Juliana Gobbo.

REFERENCES

1. Zouboulis CC, Eady A, Philpott M, Goldsmith LA, Orfanos C, Cunliffe WC, *et al*. What is the pathogenesis of acne? Exp Dermatol. 2005;14:143-52 [Links]

2. Evans DM, Kirk KM, Nyholt DR, Novac C, Martin NG. Teenage acne is influenced by genetics factors. Br J Dermatol. 2005;152:579-81 [Links]

3. Bikowski JB. Clinical experience results with clindamicin 1% benzoyl peroxide 5% as monotherapy and in combination. J Drugs. 2005;4:164-71 [Links]

4. Dreno B. Topical antibacterial therapy for acne vulgaris. Drugs. 2004;64:2389-97 [Links]

5. Haider A, Shaw JC. Treatment of acne vulgaris. JAMA. 2004;292:726-35 [Links]

6. Leyden JJ. Therapy for acne vulgaris. N Engl J Med. 1997;336:1156-62 [Links]

7. Katsambas A, Papakonstantinou A. Acne: systemic treatment. Clin Dermatol. 2004;22:412-8 [Links]

8. Eady EA, Jones CE, Tipper JL, Cove JH, Cunliffe WJ, Layton AM. Antibiotic resistant propionibacteria in acne: need for policies to modify antibiotic usage. Br Med J. 1993;306:55-6 [Links]

9. Berg M. Epidemiological studies of the influence of sunlight in the skin. Photodermatol. 1989;6:80-4 [Links]

10. Hirsch RJ, Shalita AR. Laser, light and acne. Cutis. 2003;71:353-4 [Links]

11. Sigurdsson V, Knulst AC, van Weelden H. Phototherapy of acne vulgaris with visible light. Dermatology. 1997;194:256-60 [Links]

12. Tzung TY, Wu KH, Huang ML. light phototherapy in the treatment of acne. Photodermatol Photoimmunol Photomed. 2004;20:266-269 [Links]

13. Shalita AR, Harth Y, Elman M. Acne PhotoClearing (APCTM) using a novel, high-Intensity, enhanced, Narrow-band, Blue light source. Clinical Application Notes. [Links]

14. Cunliffe WJ, Goulden V. Phototherapy and acne vulgaris. Br J Dermatol. 2000;142:855-6 [Links]

15. Papageourgiou P, Katsambas A, Chu A. Phototherapy with blue (415nm) and red (660nm) light in the treatment of acne vulgaris. Br J Dermatol. 2000;142:973-8 [Links]

16. Charakida A, Seaton ED, Charakida M, Mouser P, Avgerinos A, Chu AC. Phototherapy in the treatment of acne vulgaris: what is the role? Am J Clin Dermatol. 2004;5:211-6 [Links]

17. Ashkenazi H, Harth Y, Malik Z, Nitzan Y. Eradication of Propionibacterium acnes by its endogenic porphyrins after illumination with high intensity blue light. FEMS Immunol Med Microbiol. 2003;35:17-24 [Links]

18. Futsaether CM, Kjeldstad B, Johnsson A. Intracellular pH changes induced in Propionibacterium acnes by UVA radiation and blue light. J Photochem Photobiol B. 1995;31:125-31 [Links]

19. Bussab WO, Morettin PA. Estatística Básica. 4 ed. São Paulo: Atual; 1987 [Links]

20. Conover WJ. Practical nonparametric statistics. 2nd ed. New York: Wiley; 1980 [Links]

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How to cite this article: Arruda LHF, Kodani V, Bastos Filho A, Mazzaro CB. Estudo clínico, prospectivo, aberto, randomizado e comparativo para avaliar a segurança e a eficácia da luz azul versus peróxido de benzoíla 5% no tratamento da acne inflamatória graus II e III. An Bras Dermatol. 2009;84(5):463-8.

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