

# Treatment of erythemato-telangiectatic rosacea with brimonidine alone or combined with vascular laser based on preliminary instrumental evaluation of the vascular component

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**Abstract** The purpose of this study is to evaluate the outcome of a series of patients with erythematotelangiectatic rosacea (ETR) affected by persistent erythema and varying degree of telangiectasias being treated with brimonidine alone or combined with a vascular laser based on the type of vascular components preliminarily evaluated by clinical and instrumental observation. Ten patients affected by ETR were enrolled in a pilot, open study. Instrumental evaluation included erythema-directed digital photography by VISIA-CR™ system and X10 dermoscopy. Those patients showing marked background erythema and minimal telangiectasias (group A) were treated with a single application of brimonidine 0.33% gel, while patients showing both marked background erythema and marked telangiectasias (group B) were treated with a session of Nd:YAG laser and reevaluated 1 month later after a single application of brimonidine. An Investigator Global Assessment (IGA) of treatment outcome was performed at the end of treatment in both groups. In group A, 6 h after brimonidine application, a marked reduction of the background erythema was observed in all patients, and IGA was rated as excellent. In group B, 6 h following the application of brimonidine, a marked reduction of the background erythema was observed in all cases, while telangiectasias remained unchanged. A further treatment with brimonidine 1 month after the Nd:YAG laser session determined complete clearing of facial erythema, and IGA was rated as excellent. In

conclusion, a preliminary evaluation of the vascular component by erythema-directed digital photography and dermoscopy in ETR may be helpful to select the most appropriate therapeutic strategy.

**Keywords** Rosacea · Brimonidine · Vascular laser · Treatment · Dermoscopy · Digital photography

## Introduction

Rosacea is a chronic inflammatory disease that can manifest with different cutaneous signs, such as flushing, erythema, telangiectasias, edema, papules, pustules, rhinophyma, and ocular symptoms. Based on the presence of these signs, four main subtypes have been identified: erythematotelangiectatic rosacea (ETR), papulopustular rosacea, phymatous rosacea, and ocular rosacea [1, 2].

ETR is initially characterized by transient erythema (flushing) followed by persistent erythema presenting with a variable combination of background erythema and telangiectasias. The management of persistent erythema of ETR is challenging. The recent introduction in the market of topical brimonidine for its treatment has proved to be effective in a majority of patients. Brimonidine is a  $\alpha_2$ -adrenergic receptor agonist with potent vasoconstrictive activity. In two randomized, double-blind, and vehicle-controlled clinical trials, brimonidine 0.33% gel once-daily has demonstrated to provide significantly greater efficacy compared to vehicle for the symptomatic treatment of moderate to severe erythema of ETR, as early as 30 min after application [3]. A certain percentage (~30%) of patients, however, showed minimal or no response [3].

In a previous study, we used erythema-directed digital photography and dermoscopy in order to better identify the

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presence/degree of the different vascular components of erythema in ETR [1]. Erythema-directed photography was particularly useful to show the deep vascular component clinically corresponding to background erythema, while dermoscopy highlighted the characteristic presence of linear vessels arranged in a polygonal network (vascular polygons), which clinically corresponded to superficial telangiectasias [4]. For an optimal therapeutic management, based on these findings, we proposed the following: persistent erythema characterized mainly by background erythema is better managed by topical brimonidine; for background erythema associated with marked telangiectasias, a combined approach with topical brimonidine and vascular laser is recommended; in case of predominant telangiectasias with minimal background erythema, the suggested approach is vascular laser only [1].

The aim of this study is to evaluate the outcome of a series of ETR patients affected by persistent erythema and varying degree of telangiectasias being treated with brimonidine alone or combined with a vascular laser based on the type of vascular components preliminarily evaluated by clinical and instrumental observation.

## Methods

Ten patients (4M, 6F; age range, 22–64 years; mean age, 43.8 years) affected by ETR were enrolled in a pilot, open study after giving their informed consent. Patient data are summarized in Table 1. The evaluation included erythema-directed digital photography by VISIA-CR™ system (Canfield, USA) equipped with technology to enable separation of the unique color signatures of red skin components (RBX™ system) and X10 dermoscopy (DermLite hybrid®, 3 Gen, San Juan Capistrano, CA, USA). The protocol study included a preliminary instrumental evaluation in order to

assess the presence/degree of background erythema through VISIA-CR™ evaluation as well as the presence/degree of telangiectasias using dermoscopy. Patients affected by predominant telangiectasias with minimal background erythema were excluded from the study. Based on the prior evaluation, two groups were identified: group A (5 cases, 2M/3F; age range, 22–54 years; mean age, 38 years) included those patients presenting with marked background erythema and minimal telangiectasias, and group B (5 cases, 2M/3F; age range, 43–64 years; mean age, 54.2 years), those patients with both marked background erythema and marked telangiectasias. Treatment of group A consisted of a single application of a thin film of brimonidine 0.33% gel on the entire face followed by a further instrumental evaluation 6 h later. Patients of group B, in addition to a single application of brimonidine 0.33% gel, were treated 6 h after application with a session of 1064-nm neodymium-doped, yttrium-aluminum-garnet (Nd:YAG) laser (Synchro FT, DEKA M.e.l.a., Florence, Italy) using a 2.5-mm spot size handpiece, a fluence ranging from 105 to 110 J/cm<sup>2</sup> and a pulse duration of 7 ms. One month later, group B patients were reevaluated (by digital photography and dermoscopy) before brimonidine treatment and 6 h after. An Investigator Global Assessment (IGA) of treatment outcome, rated by a 5-point scale (excellent, good, moderate, mild, and absent response), was performed at the end of treatment in both groups (Fig. 1).

## Results

In group A, 6 h after treatment with brimonidine, both digital photography and dermoscopy showed a marked reduction of the background erythema in all patients. The minimal telangiectasias observed at baseline persisted, but the overall IGA was rated as excellent (Fig. 2).

**Table 1** Patients data

| PTS     | Sex | Age (years) | Duration of disease (years) | Previous treatments                 |
|---------|-----|-------------|-----------------------------|-------------------------------------|
| Group A |     |             |                             |                                     |
| 1       | F   | 22          | 3                           | None                                |
| 2       | F   | 34          | 8                           | Topical brimonidine 0.33% gel       |
| 3       | F   | 54          | 5                           | Topical anti-inflammatory cosmetics |
| 4       | M   | 24          | 1                           | None                                |
| 5       | M   | 33          | 3                           | Sunscreens                          |
| Group B |     |             |                             |                                     |
| 1       | F   | 64          | 10                          | Topical anti-inflammatory cosmetics |
| 2       | F   | 61          | 4                           | Topical brimonidine 0.33% gel       |
| 3       | M   | 51          | 6                           | None                                |
| 4       | F   | 43          | 6                           | Sunscreens                          |
| 5       | M   | 52          | 12                          | Topical brimonidine 0.33% gel       |

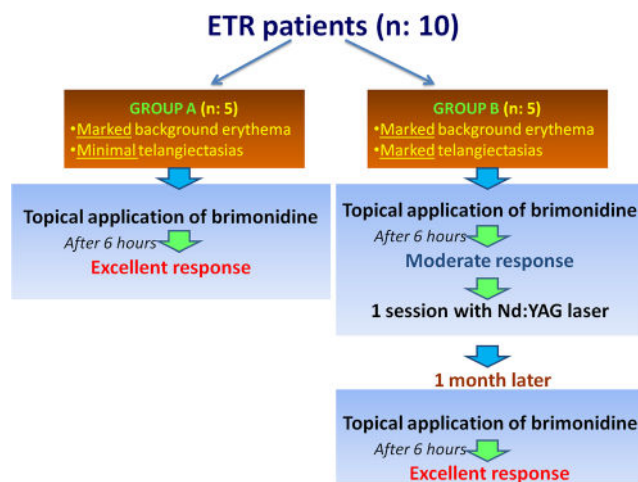


**Fig. 1** Study design

In group B, 6 h following the application of brimonidine, both digital photography and dermoscopy showed a marked reduction of the background erythema in all cases, while telangiectasias remained unchanged. IGA was rated as moderate in all five cases. As planned, a session of Nd:YAG laser was performed targeting the telangiectasias that were clearly visible after suppression of background erythema by brimonidine. One month later, instrumental evaluation of such patients showed, as expected, the presence of marked background erythema but minimal telangiectasias. After a further treatment with brimonidine, at 6 h, a marked reduction of the

background erythema was observed in all cases, and IGA was rated as excellent (Fig. 3).

## Discussion

ETR is one of the most common forms of presentation of rosacea being characterized by confluent and diffuse background erythema, telangiectasias, or a combination thereof. The background erythema in ETR is due to increased cutaneous blood flow, especially of the subpapillary plexus. Because of the deep localization and/or the small diameter of the blood vessels involved, no laser (or light-based treatments) is really effective [1]. Brimonidine 0.33% gel, which targets  $\alpha$ -adrenergic receptors located in the smooth-muscle layer of the horizontal plexuses of the skin, is recommended for symptomatic treatment [5, 6].

Telangiectasias are superficial, dilated blood vessels typical of ETR, although they may be often observed in subjects with sun-damaged facial skin [6, 7]. As these vessels do not contain a fully formed smooth-muscle layer, they are not responsive to  $\alpha$ -adrenergic receptor stimulation [6]. The treatment of telangiectasias is currently based on the use of laser and light-based therapies, with a variety of devices targeting hemoglobin reported to be effective, among these the 595-nm pulsed dye laser, the 532-nm potassium titanyl phosphate or lithium triborate laser, the 1064-nm Nd:YAG laser, and 500 to 1200-nm non-coherent intense pulsed light sources [1, 8].

In our study, a preliminary evaluation of the vascular component by erythema-directed digital photography and dermoscopy was undoubtedly helpful to select the most appropriate approach: patients of group A, showing marked background erythema and minimal telangiectasias, experienced clearing of erythema after brimonidine therapy and were fully satisfied. Patients of group B, presenting with both marked background erythema and marked telangiectasias, experienced clearance of the deep vascular component after brimonidine therapy, but the superficial dilated vessels remained unchanged and were clearly visible, causing patient concern. Treatment with one session of Nd:YAG laser was then performed targeting telangiectasias. A further treatment with brimonidine 1 month after the laser session showed complete clearing of facial erythema leading to complete patient satisfaction. Patients of group B were informed that in case of new telangiectasias, an additional laser session would be advisable.

Patients from both groups were followed up for 4 months, and the results were unchanged. They were instructed to continue to use daily application of brimonidine along with daily SPF 50 + sunscreens in order to prevent sun-induced aggravation/recurrence.

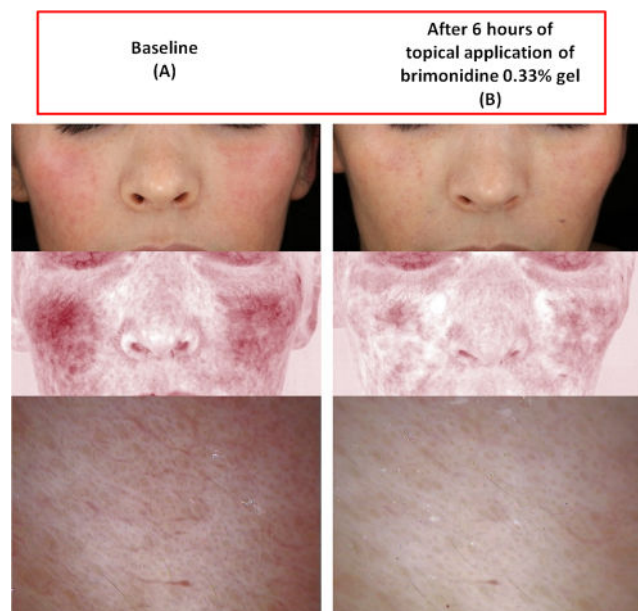
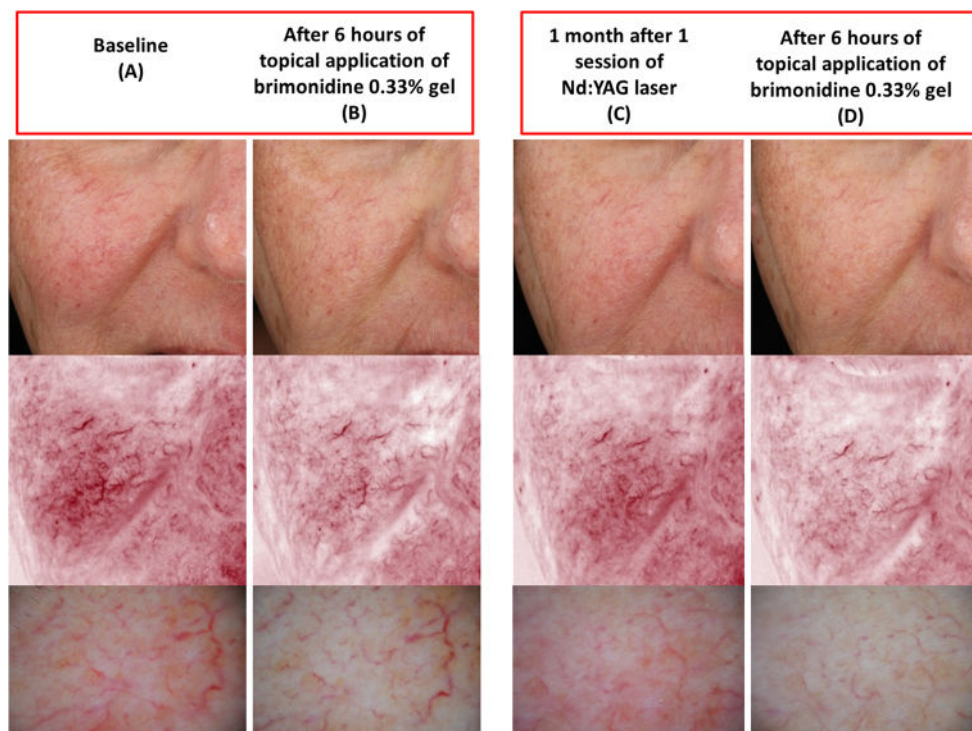


**Fig. 2** Clinical, digital photography, and dermoscopy evaluation of a patient of group A presenting at baseline with marked background erythema and minimal telangiectasias (a). Excellent response 6 h after topical application of brimonidine 0.33% gel, with marked reduction of background erythema and persistence of minimal telangiectasias (b)

**Fig. 3** Clinical, digital photography, and dermoscopy evaluation of a patient of group B presenting at baseline with marked background erythema and marked telangiectasias (a). Moderate response 6 h after topical application of brimonidine 0.33% gel, with reduction of the background erythema but persistence of telangiectasias (b). One month after one session of Nd:YAG laser, disappearance of most of the telangiectasias (c). Further topical application of brimonidine at 6 h determined marked reduction of background erythema (d)



In conclusion, our study showed that persistent erythema of ETR should be carefully evaluated to select the most appropriate therapeutic strategy.

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**Compliance with ethical standards**

**Conflict of interest** The authors declare that they have no conflict of interest.

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