

Pathogenetic Method of Complex Treatment in Erythematotelangiectatic Rosacea Patients.

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ABSTRACT

Introduction

Rosacea is a wide-spread dermatosis which a multifactorial disease. The clinical efficiency of wideband light emission in treatment of rosacea provides excellent results during long-term treatment courses. The minimal course should include 5-8 sessions. In the modern settings, it is necessary to develop combined effective treatment methods to achieve the clinical effect in a shorter time. We have designed the pathogenetic combined treatment method that includes a combination of wideband impulse light emission with topical application of 0.5% brimonidine tartrate gel in patients with erythematotelangiectatic rosacea (ETR).

Material and Methods

We have monitored a group of female patients (18 subjects) aged from 32 to 46 years with diagnosed ETR. To control the morphological changes and the functional status of the microcirculation within the skin, we used skin polyspectral analysis with the aid of Antera 3D scanning device before and after treatment in the patients of the monitored group. Such equipment allows for real-time evaluation of morphological patterns of pathological processes in cases of rosacea at the epidermal and dermal levels, creating a map of hemoglobin distribution and measuring its concentration within the rosacea foci. 0.5% brimonidine gel neutralizes the background erythema, making telangiectasis more susceptible to phototherapy, and the energy applied by wideband light treatment becomes actively absorbed by hemoglobin within the telangiectatic blood vessels. As a result of this, its obliteration develops, and a significant clinical effect is achieved.

Results

Means of polyspectral dermal analysis evaluated the hemoglobin concentration parameters within the selected skin area using Antera 3D scanning device. Significant clinical manifestations before and after treatment were exhibited. In all of the 18 female patients undergoing applications of such a combined treatment technique, the mean total hemoglobin level before treatment was 2.1 ± 0.3 and after two sessions of combined therapy (three months) it was 1.5 ± 0.2 ; the hemoglobin deviation value before treatment was 0.5 ± 0.2 , while after treatment it was 0.2 ± 0.09 ; the relative hemoglobin distribution after treatment was $55 \pm 5\%$. Thus, hemoglobin level decrease in the tissues (as a result of treatment) is $45 \pm 5\%$ (where $p < 0.05$). Further monitoring procedures during three months revealed no recurrences.

Discussion

Thus, the proposed method of combined pathogenetic therapy for cases of ETR that includes, on the one hand, applications of 0.5% brimonidine tartrate gel (as a product that affects the intensity of erythema) and, on the other hand, exposure to wideband light emission (affecting the permanent telangiectatic dilation of the vessels), is not only efficient, but allows for shortening the time to expected visible clinical effect. To achieve the significant clinical effect in treatment of ETR, we recommend undergoing sessions of such combined therapy. Brimonidine removes background erythema, leaving the telangiectatic foci intact; then the energy of wideband impulse light is actively absorbed by hemoglobin in the telangiectatic vessels, causing its obliteration. Therefore, combined therapy

using brimonidine (for erythema) and wideband impulse light (for telangiectasia) is an efficient and rapid treatment option for symptoms of ETR.

Rosacea is a wide-spread dermatosis which a multifactorial disease characterized by the chronic recurrent course with the lesion foci located predominantly on the facial skin and associated with the development of transient or permanent erythema, telangiectasia, papulopustular elements, and nodes [1]. Rosacea is a common skin disease, people of middle and old age suffer more often [2]. The morbidity of rosacea is 165/100 000 per year, the prevalence depends on the country - from 1% to 22%. [3,4]. In 2002, the members of National Rosacea Society (USA) have published a classification system which helps standardize the diagnostics of rosacea and break in down into four main subtypes based in the primary and secondary characteristics. These are erythematotelangiectatic rosacea, papulopustular rosacea, phymatous rosacea, and ocular rosacea [5].

The etiology of rosacea is not fully known, but in the literature there are suggestions of causality of this disease. First of all, the development of diseases is associated with changes in the immune system. Due to an impaired permeability barrier in the stratum corneum, the release of various cytokines such as tumour necrosis factor α (TNF- α), IL-1 and IL-6 is triggered, leading to cutaneous inflammation, perhaps in an attempt of the epidermis to initiate self-repair [6]. Elevated epidermal serine protease activity occurs in rosacea and causes the deposition of cathelicidin-derived peptides in the skin [7]. These peptides have the ability to cause inflammation when injected in the skin [8]. Flushing and erythema are vascular components and represent increased numbers of erythrocytes in mildly inflamed vasculature. Chronic extravascular fluid accumulation in the superficial dermis causes damage to the lymphatic vessels and subsequent inflammatory edema [9]. In addition, neutrophil elastase released at the site of inflammation degrades the extracellular matrix and Type IV collagen in the capillary walls reducing the integrity of blood vessels. Reduction in the integrity of the upper dermal connective tissue allows passive dilation of vasculature causing the telangiectatic component [11].

Triggers of rosacea are conventionally divided into two main groups: endogenous and exogenous. Endogenous: diseases of the digestive tract associated with *H. pylori* infection, immune system disorders, the presence of microorganisms, in particular *Demodex folliculorum* (although it is present) not in all patients: the frequency of its detection from 40 to 95%); the pathology of the sebaceous-hairy apparatus, neuroendocrine disorders in the perimenopause, in addition, some women note the occurrence of symptoms of rosacea during pregnancy, before menstruation, when taking oral contraceptives; activation of kallikrein-kinin system with increase in bradykinin production; disbalance of cellular and humoral immunity with a reliable increase CD3 and CD4 on the background of a decrease in CD8, the presence of antinuclear antibodies, the formation of autoimmune reactions. Exogenous: physical factors (insolation, strong wind, temperature changes, ionizing radiation, active physical exercises, irritating cosmetic procedures, long-term topical application of glucocorticosteroid preparations; the use of irritating and hot food, alcohol [12].

The main reactions of the erythematotelangiectatic rosacea are redness (short-term erythema), permanent central facial erythema (background erythema), and progressive development of telangiectasia of the facial skin. Treatment of rosacea patients is a complex task; the treatment options depend on multiple etiological and pathogenetic factors, stages, and clinical forms of dermatoses [5]. The clinical efficiency of wideband light emission in treatment of rosacea provides excellent results during long-term treatment courses [13]. The minimal course should include 5-8 sessions. The main chromophore for IPL-therapy is oxyhemoglobin of blood vessels. After absorption by oxyhemoglobin, light energy is converted into thermal energy, which heats the blood vessel, causing photocoagulation, mechanical damage and, finally, occlusion [14].

In the modern settings, it is necessary to develop combined effective treatment methods to achieve the clinical effect in a shorter time. We have designed the pathogenetic combined treatment method that includes a combination of wideband impulse light emission with topical application of 0.5% brimonidine tartrate gel in patients with erythematotelangiectatic rosacea. The method is expected to shorten the phototherapy treatment courses and to achieve the significant clinical effect.

Objective: the aim of our study was to develop a pathogenetic combined treatment method of erythematotelangiectatic rosacea that includes a combination of the wideband impulse light emission with topical application of 0.5% brimonidine tartrate gel (Mirvaso Derm®) and to evaluate its efficiency with the aid of polyspectral skin analysis that allows for real-time evaluation of the morphological structure of the pathologically affected skin area, as well as to create hemoglobin distribution map and to evaluate its concentration in the lesion foci.

Materials and Methods:

We have monitored a group of female patients (18 subjects) aged from 32 to 46 years with diagnosed erythematotelangiectatic rosacea. The disease history varied on average from 1 to 8 years.

To control the morphological changes and the functional status of the microcirculation within the skin, we used skin polyspectral analysis with the aid of Antera 3D scanning device before and after treatment in the patients of the

monitored group. Such equipment allows for real-time evaluation of morphological patterns of pathological processes in cases of rosacea at the epidermal and dermal levels, creating a map of hemoglobin distribution and measuring its concentration within the rosacea foci (Fig.1). Combined effects of 0.5% brimonidine tartrate gel (Mirovaso Derm®) and phototherapy potentiate each other. Thus, 0.5% brimonidine gel neutralizes the background erythema, making telangiectasis more susceptible to phototherapy, and the energy applied by wideband light treatment becomes actively absorbed by hemoglobin within the telangiectatic blood vessels. As a result of this, its obliteration develops, and a significant clinical effect is achieved.

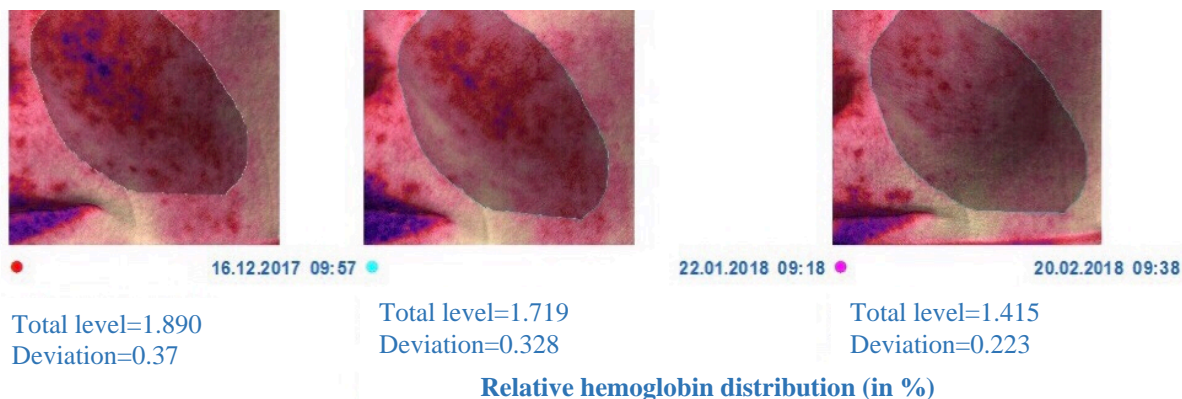


Fig. 1. Patient M. Treatment results based on the changes in hemoglobin absorption within the telangiectatic blood vessels and its occlusion detected by skin polyspectral analysis using the Antera 3D scanning device.

Red color – before treatment;

Blue color – one month after a single combined treatment session;

Violet color – one month after two combined treatment sessions.

Results and discussion.

Means of polyspectral dermal analysis evaluated the hemoglobin concentration parameters within the selected skin area using Antera 3D scanning device. Significant clinical manifestations before and after treatment were exhibited.

1. The total hemoglobin levels (mean concentration of hemoglobin within the selected area) were reduced from 1.890 units to 1.415 units.

2. The deviation parameter for hemoglobin (hemoglobin homogeneity degree within the selected area) has decreased (average values) from 0.37 units to 0.223 units. The closer this parameter is to zero, the more homogeneous is the hemoglobin distribution, and the better is the skin color, which, in this case, indicates the presence of positive changes in the patients.

3. Relative hemoglobin distribution (percentage).

This parameter defines the total hemoglobin and the hemoglobin deviation level ratio. It provides information on the distribution homogeneity and the hemoglobin content decrease. Thus, the parameter value has decreased from 100% to 60.3% in the patients, which indicates the presence of significant positive changes (Fig. 1).

In all of the 18 female patients undergoing applications of such a combined treatment technique, the mean total hemoglobin level before treatment was 2.1 ± 0.3 and after two sessions of combined therapy (three months) it was 1.5 ± 0.2 ; the hemoglobin deviation value before treatment was 0.5 ± 0.2 , while after treatment it was 0.2 ± 0.09 ; the relative hemoglobin distribution after treatment was $55\% \pm 5\%$. Thus, hemoglobin level decrease in the tissues (as a result of treatment) is $45\% \pm 5\%$ (where $p < 0.05$). Further monitoring procedures during three months revealed no recurrences.

Treatment was well tolerated by all the patients with no registered cases of adverse effects.

Conclusions:

Thus, the proposed method of combined pathogenetic therapy for cases of erythematotelangiectatic rosacea that includes, on the one hand, applications of 0.5% brimonidine tartrate gel (as a product that affects the intensity of erythema) and, on the other hand, exposure to wideband light emission (affecting the permanent telangiectatic dilation of the vessels), is not only efficient, but allows for shortening the time to expected visible clinical effect. To achieve the significant clinical effect in treatment of erythematotelangiectatic rosacea, we recommend undergoing sessions of such combined therapy.

Therefore, using combined therapy in treatment erythematotelangiectatic rosacea subtype is efficient in 100% of the patients with a further reduction in the clinical values ranging from 40 to 50% and with excellent tolerability and in the absence of significant adverse effects and undesirable events (Fig.2).

Studies conducted in vivo using polyspectral skin tests allow for detecting the patterns of pathological processes in cases of rosacea and controlling its course during treatment. Shortening the duration of treatment is due to combined applications of brimonidine and wideband impulse light emissions in cases of rosacea (erythematotelangiectatic subtype). Brimonidine removes background erythema, leaving the telangiectatic foci intact; then the energy of wideband impulse light is actively absorbed by hemoglobin in the telangiectatic vessels, causing its obliteration. Therefore, combined therapy using brimonidine (for erythema) and wideband impulse light (for telangiectasia) is an efficient and rapid treatment option for symptoms of erythematotelangiectatic rosacea.

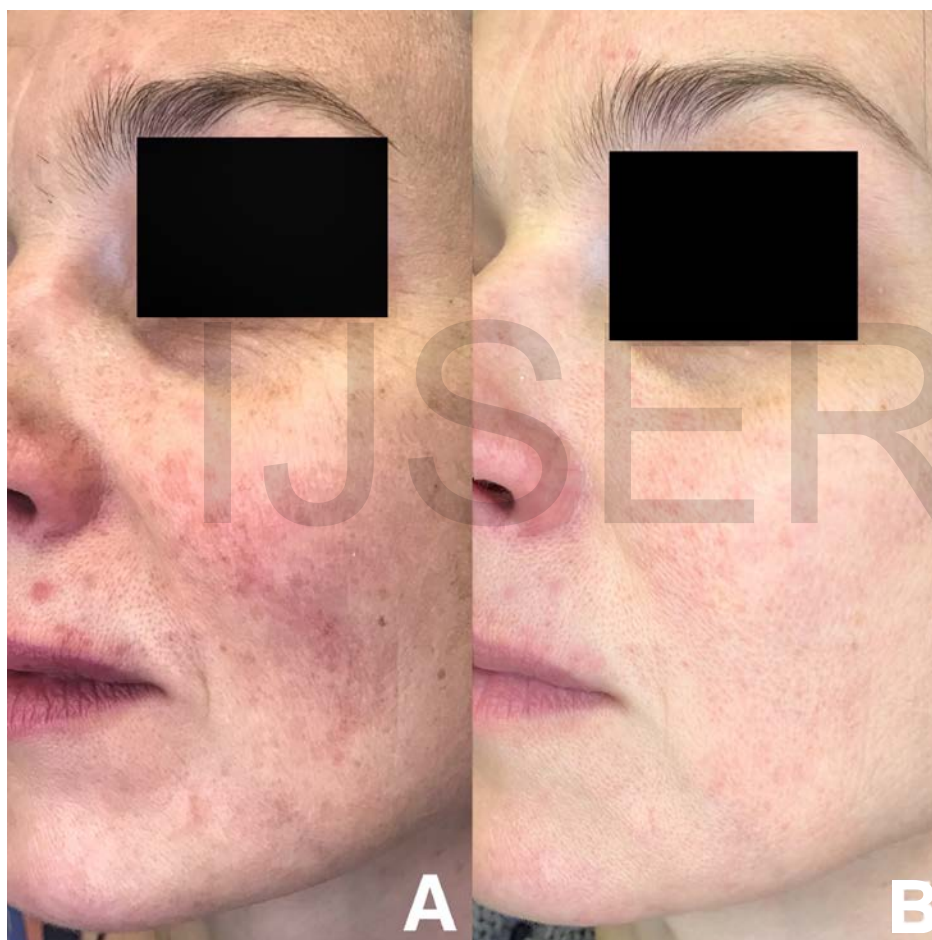


Fig. 2. Patient M. Rosacea, erythematotelangiectatic subtype.
Results of combined therapy including Mirovaso Derm® gel and phototherapy.
a – before treatment; b –one month after two sessions of combined therapy.

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