

INNOVATIONS IN THE TREATMENT OF ROSACEA: AN UPDATED REVIEW OF THE SCIENTIFIC LITERATURE

Thais Botini

Instituto Educacional Jaguarly LTDA
(UNIFAJ)
Jaguariúna - SP
<https://orcid.org/0009-0006-6940-9666>

Larissy Gabriely Matos Costa

Universidade Federal de Sergipe (UFS)
Aracaju - SE
<https://orcid.org/0009-0000-9989-892X>

Ana Caroline Andrade de Melo

Universidade Federal de São Paulo
(UNIFESP). São Paulo-SP
<https://orcid.org/0000-0003-0414-1081>

Ana Júlia Pagnan

Centro Universitário Max Planck (UniMAX)
Indaiatuba - SP
<https://orcid.org/0009-0005-0582-5671>

Marielli Antunes Molina

Universidad Maria Auxiliadora (UMAX)
Asunción - PY
<https://orcid.org/0009-0007-5733-1205>

Maria Eduarda Gibbon Oliveira

Maria Eduarda Gibbon Oliveira (FTESM-RJ)
Rio de Janeiro-RJ
<https://orcid.org/0009-0006-7442-377X>

Giovana Calsoni Sorensen

Centro Universitário das Faculdades
Associadas de Ensino (UNIFAE)
São João da Boa Vista - SP
<https://orcid.org/0009-0001-9466-4945>

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Maria Vitória Bezerra Leite Nunes
Centro Universitário Christus
(UNICHRISTUS)
Fortaleza- CE
<https://orcid.org/0009-0008-9603-7102>

Rafaela Fioravanti Cantu
Pontifícia Universidade Católica de
Campinas (PUC-Campinas)
Campinas - SP
<https://orcid.org/0009-0008-1261-3193>

Fernanda Franoso
Universidade Cidade de São Paulo (UNICID)
São Paulo - SP
<https://orcid.org/0009-0003-7608-1134>

Alana de Almeida Corso
Universidade Estácio de Sá- Cittá (UNESA-
Cittá)
Rio de Janeiro - RJ
<https://orcid.org/0009-0006-0001-1342>

Luccas Dias Alves
Universidad Nacional de Rosario (UNR)
Rosario - Argentina
<https://orcid.org/0009-0005-8329-0756>

Abstract: Objective: Explore and synthesize the most recent scientific evidence on innovations in the treatment of rosacea, aiming to understand their impact on the clinical management of this dermatological condition. Method: This systematic study followed the PVO strategy and used 11 articles collected in the PubMed database, dated from 2014 to 2024. Results: Among the therapies evaluated, the highlights were combined topical therapy, therapy with oral antibiotics, and innovative therapies with different antibiotics and monoclonal antibodies. For ocular symptoms, oral antibiotics and topical eye drops are effective, but corneal ulcers require ophthalmologic treatment. Botanical agents and vitamins have shown effectiveness against inflammation. Advances in procedural therapies, such as combined laser therapy, produce superior results in the treatment of telangiectasias and erythema. Final considerations: Despite the therapeutic options available, there is still no effective treatment for all rosacea phenotypes nor preventive treatments to stop its progression. Future research and therapeutic trials are essential to improve the clinical management of rosacea and mitigate its impact on patients' health.

Keywords: rosacea, treatment, innovations, topical therapy, oral antibiotics, monoclonal antibodies, laser therapy.

INTRODUCTION

Rosacea is a chronic dermatological disease of an inflammatory nature, characterized by skin symptoms such as facial erythema, telangiectasias (spider veins) and papulopustular lesions. Predominantly affecting the forehead, nose, cheeks and chin, this condition is frequently observed in individuals with light skin types and is associated with chronic sun exposure (Semenescu et al., 2024). Although its multifactorial etiology is not

completely understood, it is recognized that the underlying mechanisms involve vascular and neurocutaneous aspects (Picardo, Eichenfield, Tan, 2017).

Initial management of rosacea involves avoiding triggers and adopting a sensitive skin care routine, which includes regular use of sunscreen. These measures may be sufficient to control symptoms in some patients, but others may require more individualized treatments. Medications such as azelaic acid, isotretinoin, ivermectin, metronidazole, and procedures such as intense pulsed light have shown effectiveness when adapted to the specific needs of each case (Picardo, Eichenfield, Tan, 2017).

According to Semenescu et al. (2024), rosacea affects more than 5% of the global population, with symptoms that tend to appear early in women between 30 and 50 years old. Light-skinned individuals are most affected, followed by Asian ethnicities and, lastly, dark-skinned individuals. Furthermore, more than half of patients with rosacea present ocular involvement, manifesting symptoms such as dry eyes, foreign body sensation, photophobia, conjunctivitis and blepharitis, which highlights the epidemiological relevance of this disease (Zuuren et al., 2021).

Given the clinical importance and prevalence of rosacea, this study aims to address innovations in the treatment of this condition, including topical and systemic therapies that use anti-inflammatory, antimicrobial and immunomodulatory agents. In addition, advanced medical procedures and devices such as lasers, intense pulsed light, microneedling and radiofrequency will be explored (Semenescu et al., 2024).

Therefore, the aim of this research is to explore and synthesize the latest scientific evidence on innovations in the treatment of rosacea, aiming to provide a comprehensive overview of emerging therapeutic strategies

and their impact on the clinical management of this complex dermatological disease.

METHODOLOGY

The methodology used in this study consisted of a systematized bibliographic review, guided by the PVO strategy, which refers to: Population or problem, Comparison (optional) and Outcome (outcome). This methodology was chosen to frame the central research question: "What are the most recent innovations in the treatment of rosacea and how do these approaches influence the clinical management of this dermatological condition?"

For data collection, a comprehensive search was carried out in the PubMed - MEDLINE (Medical Literature Analysis and Retrieval System Online) database, using combinations of relevant search terms linked by Boolean operators, particularly "AND". The publication period was limited between 2014 and 2024, covering articles in all languages available in full.

The defined inclusion criteria were: articles that directly addressed the topics of interest and specifically, innovations in the treatment of rosacea. The exclusion criteria eliminated articles only available in summary format, and those that did not directly align with the proposed themes or that did not meet the other inclusion criteria.

Initially, 21 potential articles were identified. After meticulous application of the inclusion and exclusion criteria, the number was refined to 11 relevant articles. Of these, seven articles were selected to compose the final bibliographic review, based on the PubMed database. This systematic method allowed for a rigorous and detailed analysis of recent publications, providing a comprehensive and up-to-date overview of innovations in rosacea treatment and their implications for clinical practice.

DISCUSSION

EVOLVING TOPICAL AND SYSTEMIC THERAPIES FOR ROSACEA

Rosacea is a complex dermatological condition, characterized by a diversity of clinical manifestations, which include persistent erythema, telangiectasias, flushing, papules, pustules and phymatosis. According to Marson and Baldwin (2020), erythema, telangiectasias and flushing are believed to result mainly from vasodilation induced by inflammatory processes. Topical treatments, such as 0.33% brimonidine gel and 1% oxymetazoline cream, have been shown to be effective in reducing this vasodilation, significantly improving the appearance of the skin. In addition, laser and light-based therapies, including pulsed dye (PDL) and potassium titanyl phosphate (KTP) lasers, as well as intense pulsed light (IPL), also have benefits in alleviating erythema and removing telangiectasias.

Although there is no cure, the objective of current therapies is to control the disease and alleviate symptoms. Recommendations published in the Journal of the American Academy of Dermatology in 2020 by a group of global experts highlight the importance of oral and topical treatments, such as doxycycline, metronidazole and azelaic acid, in a combined treatment regimen, although there is still a need for more research to confirm the long-term benefits of these combinations (Semenescu et al., 2024).

For the papules and pustules typical of rosacea, several therapeutic options are available, including topical agents such as 1% ivermectin, 15% azelaic acid, and 0.75% metronidazole. A double-blind, randomized study revealed that the foam formulation of azelaic acid provides a better treatment adherence rate due to its rapid absorption and

lower incidence of adverse effects compared to the gel version (Wollina, 2014).

Oral antibiotics, such as doxycycline and minocycline, are also commonly prescribed, although antibiotic resistance represents a growing concern, especially in chronic cases. In advanced stages of the disease, characterized by phymatosis, procedures such as the ablative CO₂ or erbium laser are indicated to remove excessive tissue and remodel the affected areas (Marson; Baldwin, 2020).

Furthermore, the combination of therapies also proves to be effective, such as the association of topical metronidazole with 40 mg oral doxycycline, which improves mild to moderate rosacea lesions. However, topical metronidazole as monotherapy was also shown to be efficient, equivalent to the efficacy of azelaic acid, available in different concentrations (Wollina, 2014).

Innovative therapies are also being explored, including the use of minocycline and benzoyl peroxide in topical forms, which have demonstrated a significant reduction in rosacea lesions with minimized adverse effects. Studies also indicate the effectiveness of secukinumab, a monoclonal antibody that binds to IL-17A, showing promising results in treating papules in patients with rosacea (Zuuren et al., 2021).

In addition to conventional treatments, azithromycin has been used for both ocular and cutaneous rosacea, presenting superior safety compared to tetracyclines, especially in pregnant women. Alternatively, topical azithromycin eye drops are successfully used to reduce ocular symptoms, although they cause mild burning after application (Wollina, 2014). The therapeutic approach to rosacea continues to evolve with the development of new formulations and treatment combinations, aiming for efficacy and minimization of adverse effects.

Ocular rosacea, which affects approximately half of patients with cutaneous rosacea, can manifest independently of skin symptoms. Initial management for mild to moderate cases may include topical use of azithromycin and calcineurin inhibitors. In more severe situations, oral doxycycline may be indicated. Cases that develop complications, such as corneal ulcers or intense inflammation, require specialized evaluation and intervention by ophthalmologists (Marson; Baldwin, 2020).

The combination of different therapeutic agents is a common practice in the treatment of rosacea and is not contraindicated. Studies have shown that combining medications such as ivermectin and brimonidine can accelerate therapeutic success. Furthermore, there is a growing interest in the use of complementary and alternative therapies. Botanical agents and vitamins, including niacinamide, green tea and vitamin C, have demonstrated anti-inflammatory, antioxidant and moisturizing properties, contributing to the repair of the skin barrier (Marson; Baldwin, 2020).

As Dall'Oglio, Nasca and Micali (2021) point out, despite the wide range of therapeutic options available, there is still no single effective treatment for all rosacea phenotypes, and preventive treatments capable of stopping the progression of the disease have not yet been identified. The management of rosacea, therefore, remains a clinical challenge that requires individualized approaches and the consideration of multiple factors to achieve the best results for each patient.

Significant advances have been achieved with the US FDA approval of new agents such as brimonidine and ivermectin, which act through distinct mechanisms to reduce facial erythema and inflammatory lesions. Brimonidine, an alpha-adrenergic receptor agonist, promotes vasoconstriction, reducing erythema, while ivermectin combats the proliferation of Demodex mites, often

associated with rosacea (Rosso, 2014).

Growing interest in gentler, more natural therapies has led to the use of botanical substances in the treatment of rosacea. These products, rich in antioxidants, vasoprotectors and anti-inflammatory properties, are considered promising for the management of erythema and papules. However, it is important to be aware that mild side effects such as burning or itching may occur. Combining conventional methods with botanicals offers a promising comprehensive approach to treating rosacea, with the potential to improve long-term outcomes and provide patients with a greater variety of therapeutic options (Semenescu et al., 2024).

Exemplifying the effectiveness of botanical compounds, studies with licorice root and *Chrysanthemum indicum* L. stand out. Licorice root, rich in glabridin and glycyrrhizin, has been shown to reduce skin inflammation and irritation, while *Chrysanthemum indicum* L. improves capillary resistance, beneficial for patients with fragile blood vessels characteristic of rosacea. Furthermore, colloidal oatmeal and chamomile are also recognized for their calming and antioxidant properties, indicated for the treatment of sensitive and inflamed skin (Semenescu et al., 2024). These findings point to the need for additional research to fully understand the modes of action and long-term effectiveness of these natural treatments in managing rosacea.

PROCEDURAL APPROACHES AND INNOVATIVE MEDICAL DEVICES IN THE MANAGEMENT OF ROSACEA

Regarding procedural therapies, Buddenkotte and Steinhoff (2018) indicate that patients with pain sensitivity must avoid laser therapy, but for others, this may be an effective option to treat flushing and erythema. Chen et al. (2023) demonstrate

that the combination of different laser therapies, specifically the sequential use of the neodymium yttrium-aluminum-garnet (Nd: YAG) 532/1064 nm laser and intense pulsed light (IPL), produces superior results in the treatment of facial telangiectasias and erythema compared to isolated treatments. Photodynamic therapy (PDT), comparable to oral antibiotics in the papulopustular form, shows greater efficacy and fewer side effects when combined with treatments such as Danzhi Xiaoyao Powder or 1550 nm fractional laser. For erythematotelangiectatic rosacea (ETR), 577 nm pro-yellow laser and radiofrequency treatments have proven effective in reducing Demodex mite numbers and relieving burning.

Furthermore, the study revealed that the new V-Beam Prima equipment, Syneron-Candela, is superior to the V-Beam Perfecta, with a longer useful life and greater effectiveness in reduced treatments. The 595 nm Pulsed Dye Laser (PDL) treatment, using a dynamic cooling device, proved to be excellent, significantly improving rosacea, including ETR. Monthly PDL sessions have proven effective for both diffuse erythema and linear telangiectasias, with adverse effects limited to edema, erythema and purpura, which are self-limiting, although caution is needed regarding the risk of edema and purpura with different pulse durations (Bernstein et al., 2018).

Botulinum toxin type A is recognized for its multifunctional capacity in modulating cutaneous physiological processes, particularly in dermatological contexts. According to Chen et al. (2023), this compound can inhibit the vasodilator acetylcholine, regulate the activity of neuropeptides, reduce the mast cell count, suppress their degranulation and decrease the expression of certain matrix metalloproteinases (MMPs) in skin fibroblasts. Furthermore, it is capable of

reducing sebum production and improving skin hydration, highlighting its potential as a therapeutic treatment for conditions such as rosacea, where such processes are disturbed.

On the other hand, paroxetine, a selective serotonin (5-HT) reuptake inhibitor, has a potential role in regulating vascular dilation and constriction mediated by the autonomic nervous system. This drug is often prescribed for the treatment of psychological disorders, including anxiety, depression and insomnia, which are commonly experienced by patients with rosacea, as described by Chen et al. (2023). The most common side effects associated with paroxetine include dizziness, lethargy, nausea, dyspepsia, and muscle tremors, which requires careful assessment of its benefit-risk profile in the context of its use for the management of rosacea and its associated psychological comorbidities.

FINAL CONSIDERATIONS

Innovations in rosacea treatment include combination topical therapy and oral antibiotic therapy, which are effective for moderate to severe forms. For ocular rosacea, oral antibiotics and topical eye drops are effective. Botanical agents and vitamins have shown effectiveness against inflammation. Laser therapy is superior in treating telangiectasias and erythema. However, there is still no universal or preventive treatment for rosacea. Future research, including testing monoclonal antibodies and complications such as corneal ulcers, is needed to address gaps in treatment. Rosacea, in 2024, continues to be a chronic inflammatory dermatological disease with open areas of study and the need for more published work.

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