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REVIEW ARTICLE

Rosacea and its management: an overview

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ABSTRACT

Background Rosacea is a chronic inflammatory disorder that affects 10% of the population. The prevalence of rosacea is highest among fair-skinned individuals, particularly those of Celtic and northern European descent. Since a cure for rosacea does not yet exist, management and treatment regimens are designed to suppress the inflammatory lesions, erythema, and to a lesser extent, the telangiectasia involved with rosacea.
Objectives This review outlines the treatment options that are available to patients with rosacea.
Methods Published literature involving the treatment or management of rosacea was examined and summarized.
Results Patients who find that they blush and flush frequently, or have a family history of rosacea are advised to avoid the physiological and environmental stimuli that can cause increased facial redness. Topical agents such as metronidazole, azelaic acid cream or sulfur preparations are effective in managing rosacea. Patients who have progressed to erythematotelangiectatic and papulopustular rosacea may benefit from the use of an oral antibiotic, such as tetracycline, and in severe or recalcitrant cases, isotretinoin to bring the rosacea flare-up under control. Treatment with a topical agent, such as metronidazole, may help maintain remission. Patients with ocular involvement may benefit from a long-term course of an antibiotic and the use of metronidazole gel. A surgical alternative, laser therapy, is recommended for the treatment of telangiectasias and rhinophyma. Patients with distraught feelings due to their rosacea may consider cosmetic camouflage to cover the signs of rosacea.
Conclusions With the wide variety of oral and topical agents available for the effective management of rosacea, patients no longer need to feel self-conscious because of their disorder.
Key words: azelaic acid, isotretinoin, management, metronidazole, rosacea, tetracycline

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Background

Rosacea is a chronic disorder, involving the mid facial region, and occasionally the neck and scalp and eyes.[1] It may progress from inflammatory lesions and/or erythema, to telangiectasia and rhinophyma, and sometimes also cause ocular involvement. The prevalence of rosacea is highest among fair-skinned individuals, especially those of Celtic and northern and eastern European heritage.[2] The onset of rosacea is usually between the ages of 20 and 50 years, with females more often affected than males; however, males more frequently progress to the end-stages of severe rosacea. Rosacea has been described as having four subtypes, erythematotelangiectatic rosacea, papulopustular rosacea, phymatous rosacea, and ocular rosacea, with one variant, granulomatous rosacea.[3]

Presently there is no cure for rosacea; management and treatment may provide only a method of suppressing its signs and symptoms. The choice of treatment is dependent primarily on the severity of the disorder and ranges from avoiding the factors that can trigger a flare-up, to the use of surgery for correcting the hypertrophied soft tissue of the nose (rhinophyma). This paper will discuss the treatment options rosacea patients have for managing their disorder.

Pre-rosacea (episodic erythema)

Avoidance policy

The earliest manifestation of rosacea includes frequent flushing and blushing, or episodic erythema. Patients, who experience

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Table 1 Rosacea trigger factors and management techniques

Rosacea triggering factors	Management factors
Foods: Meat: liver Dairy products: yogurt, sour cream, cheeses (not including cottage cheese) Vegetables: eggplant, tomatoes, spinach, lima and navy beans, peas Fruits: avocados, bananas, red plums, raisins, figs, and citrus fruits Condiments/flavoring: chocolate and vanilla, soy sauce and vinegars Other: hot and spicy foods, yeast extraction	Identify and avoid any foods that aggravate the condition
Beverages: Alcohol and hot beverages	Avoid alcoholic beverages, especially red wine, beer, bourbon, gin, vodka or champagne Avoid hot drinks, e.g. Tea, coffee, hot cider or hot chocolate
Emotional: Stress and anxiety	Practice stress management techniques, e.g. Yoga or breathing exercises
Weather: Sun, strong winds, cold, humidity	Use ski masks, scarves to protect from cold and windy conditions Use sunscreens (min. SPF 15)
Temperature: Any hot environment: saunas, hot baths, simple overheating	Avoid any hot or humid environment
Skin Care Products: Cosmetics and hairsprays especially those containing alcohol, witch hazel or fragrances Hydro-alcoholic or acetone substances Any substance that causes redness or stinging	Resist using skin products that are listed as irritating
Medications: Vasodilators, and topical steroids	If avoidance is not possible, they should not be taken for long periods of time
Medical Conditions: Menopause, caffeine withdrawal syndrome, chronic cough, frequent flushing	Not avoidable; however, avoiding other factors minimizes these conditions
Physical Exertion: Exercise, heavy lifting	Avoid long strenuous exercising and heavy lifting Use cool-down techniques: chewing on ice, or covering face with cool cloth after the workout

frequent blushing, have a family history of rosacea, or both may be entering prerosacea; these patients are advised to consider changing their lifestyle to control their blushing. The best approach to preventing the blushing and flushing associated with the stages of rosacea is the avoidance policy,[4] where nonspecific physiological and environmental stimuli are avoided, and thus increased facial redness is lessened. One study reported 78% of rosacea patients felt that avoiding the factors that aggravate their rosacea was effective or at least somewhat effective in controlling their condition.[5] The most common triggers of blushing include alcohol ingestion, spicy food, sun exposure, or stress. However, the causes may vary from patient to patient, and therefore it is important for a patient to avoid these causative agents as much as possible during their daily routine. Physicians of rosacea patients must be aware that rosacea is a recognized and controllable disorder; they should educate and monitor their patients for possible triggers and try to establish an individual risk factor profile.[6] Table 1 outlines some common factors that may trigger and aggravate rosacea flare-ups.

Drug therapy

Drug treatment trials for decreasing the flushing associated with rosacea have primarily been unsuccessful. Two drugs, clonidine and nadolol have been tried against rosacea flushing; neither was effective. One study demonstrated that twice-daily treatment with clonidine hydrochloride, 0.05 mg, taken for 2 weeks was unable to suppress the flushing reactions provoked with hot water (60 °C), red wine and chocolate in 23 of 24 patients with erythematotelangiectatic rosacea.[7] Similarly, treatment with 40 mg of nadolol once or twice daily had no apparent effect on flushing induced by hot water (60 °C), ethanol, and niacin in 15 patients with erythematous telangiectatic rosacea.[8] However, one double-blind study showed that 10-minute pretreatment with naloxone 0.8 mg in 2 mL saline

injected subcutaneously completely inhibited alcohol induced facial flushing in all five subjects.[9] The mean forehead skin temperature increased by 1.1 ± 0.6 °C during flushing after saline administration, but by only 0.4 ± 0.2 °C after naloxone administration. Currently, there are no effective long-term drug therapies to control the flushing associated with rosacea.

Erythematotelangiectatic and papulopustular rosacea

Rosacea is a progressive disorder, and although not all patients necessarily pass through all stages, early diagnosis and management will prevent or lessen the chances that the rosacea will worsen. A variety of oral and topical treatments, with the ability of suppressing the disorder, are available for patients suffering with rosacea.

Systemic therapy

Several oral agents have been used in the treatment of rosacea. Table 2 summarizes the clinical trials evaluating the efficacy of these systemic drugs.

Oral antibiotics

Oral antibiotics have long been accepted as safe and effective treatments for rosacea, and are thought to exert their therapeutic effects primarily via anti-inflammatory rather than antibacterial methods. Antibiotic therapy is most effective against inflammatory papules and pustules, with minimal effects on erythema and telangiectasia.[26]

Tetracycline has historically been the antibiotic of choice for treating rosacea, as it has been shown to be successful in reducing the number of papules and pustules. High doses are initially recommended until the disorder is brought under control, and then lower doses are used to maintain control. Total daily doses of up to 1000 mg, taken two to four times a day are recommended for up to 4 weeks, and then reduced by half for an additional 5 months.

Tetracycline has proven to be successful in treating patients diagnosed with rosacea. In one randomized, double-blind study, 78% of patients treated with tetracycline 250 mg twice daily for 1 month experienced the disappearance of pustules, the flattening of papules and the diminution of erythema.[11] In another randomized, double-blind clinical trial, compared with ampicillin, tetracycline 250 mg taken three times daily for the first week and then twice daily for the subsequent 5 weeks, did not significantly differ in the reduction of papules and pustules; however, post-treatment evaluation revealed that both treatments were effective in decreasing the mean number of papules and pustules in comparison with the pretreatment means ($P < 0.05$).[12]

The effects of doxycycline, 100 mg twice daily for 4 weeks, then once daily for another 4 weeks were compared with clarithromycin, 250 mg twice daily for 4 weeks, then once daily for another 4 weeks in patients with mild and moderate rosacea.[13] The overall results of the treatment provide evidence of a higher clarithromycin efficacy profile in comparison with doxycycline. Significant differences were seen in erythema in favour of the clarithromycin group at weeks 4 and 6 ($P < 0.05$); however, after 8 weeks of treatment, no significant differences were seen in erythema. A significant difference between the mean values of the numbers and dimensions of telangiectasia in the two groups of patients was observed after 4 weeks of treatment. After 6 and 8 weeks of treatment, there were no significant differences between the two groups. A significantly faster decrease ($P < 0.0005$) of the mean number of papules and pustules was observed in the clarithromycin-treated patients, when compared with the doxycycline-treated patients after 4 and 6 weeks of therapy; however, after 8 weeks there was no significant difference in these two parameters between the two groups.

Treatment with antibiotics must be long-term, lasting a minimum of 6 months. Treatment failure with antibiotics is most commonly the result of patient noncompliance, particularly resulting from side-effects including nausea, and also because some antibiotics, such as tetracycline must been taken on an empty stomach; food and milk restrict its absorption.

Oral metronidazole

Oral metronidazole is a treatment alternative for rosacea patients who do not respond well to tetracycline. Two double-blind, randomized controlled trials assessed the efficacy of oral metronidazole.[14,15] Metronidazole 200 mg, taken twice daily for 12 weeks proved to be as effective as oxytetracycline 250 mg taken twice daily in improving the papulo-pustules related to rosacea.[14] In addition, 6 weeks of therapy with metronidazole 200 mg taken twice daily in combination with 1% hydrocortisone, applied twice daily produced 'definite improvement' in the overall clinical severity of the rosacea condition in 10 of 14 patients.[15]

Isotretinoin

Another effective therapy in the treatment of rosacea is isotretinoin. However, this treatment is suggested for patients with severe or recalcitrant rosacea. Patients may benefit from a trial with systemic tetracycline, metronidazole or topical metronidazole before the use of isotretinoin. Daily doses of isotretinoin usually range from 0.5 mg/kg to 1.0 mg/kg. The advantage of isotretinoin is that it has an immediate effect on papules and pustules. Four studies have shown isotretinoin to significantly decrease the mean number of papules and pustules compared to baseline[17–20] within as little as 1 month of therapy.[18] Isotretinoin also produces considerable improvement in erythema,[17,20] however, the effects may be slow and

Table 2 Systemic therapies used in the treatment of rosacea

Study design	Regimen	Efficacy parameters Inflammatory lesions	Erythema	Telangiectasia	Physician assessment	Patient assessment	Other	Reference
DB, R 1% clindamycin phosphate lotion vs. oral tetracycline $N = 43$; 12 weeks	1% clindamycin lotion b.i.d. + placebo or 250 mg tetracycline q.i.d. + placebo lotion for 9 weeks	Clindamycin: facial lesions decreased from baseline ($P < 0.05$) tetracycline: facial lesions decreased from baseline ($P < 0.05$)	No significant difference	No significant difference	Improvement in clindamycin: 94.7% of patients tetracycline: 94.4% of patients	Improvement seen in 81.8% of patients treated with clindamycin and 90.5% of tetracycline	N/A	Wilkin 1993[10]
DB, R Tetracycline vs. placebo $N = 78$; 4 weeks	Tetracycline 250 mg b.i.d. or placebo tablets b.i.d. for 4 weeks	N/A	N/A	N/A	N/A	N/A	Improvement in disappearance of pustules, flattening of papules, and diminution of erythema: Tetracycline: 78% Placebo: 45%	Sneddon 1966[11]
DB, R Tetracycline vs. ampicillin $N = 56$; 6 weeks	t.i.d. for the first week then b.i.d. for 5 weeks	Tetracycline: decreased from 21.05 to 4.6 ampicillin: decreased from 21.06 to 9.53	No significant difference	N/A	N/A	Ampicillin marginally better than tetracycline	N/A	Marks 1971[12]
Clarithromycin vs.doxycycline $N = 40$; 8 weeks	Clarithromycin 250 mg b.i.d. for 4 weeks then q.i.d. for 4 weeks or doxycycline 100 mg b.i.d. for 4 weeks then q.i.d. for 4 weeks	No significant difference between treatments after 8 weeks	No significant difference between treatments after 8 weeks	No significant difference between treatments after 8 weeks		No significant difference between treatments after 8 weeks	N/A	Torresani 1997[13]
DB, R Metronidazole vs. oxytetracycline $N = 38$; 12 weeks	Metronidazole 200 mg b.i.d. or oxytetracycline 250 mg b.i.d. 12 weeks	N/A	N/A	N/A	Mean independent opinion of patient and 2 doctors No significant difference between groups; both improved from baseline ($P < 0.05$)		N/A	Saihan 1980[14]
DB, R Metronidazole vs. placebo $N = 27$; 6 weeks	Metronidazole 200 mg b.i.d. + 1% hydrocortisone cream daily or placebo + 1% hydrocortisone for 6 weeks	N/A	N/A	N/A	10 patients in metronidazole and 2 patients in placebo group showed good results ($P < 0.02$)	N/A	N/A	Pye 1976[15]

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