A Review of the Current Modalities for the Treatment of Papulopustular Rosacea

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KEYWORDS

• Doxycycline • Metronidazole • Azelaic acid • Ivermectin • Topical • Management • Papulopustular • Rosacea

KEY POINTS

- Rosacea is an inflammatory skin disorder that is characterized by a wide variety of clinical manifestations.
- Topical and oral antimicrobials are the mainstay of therapy for the treatment of papulopustular rosacea.
- This article highlights the current literature surrounding the treatment of papulopustular rosacea and aims to help clinicians in making treatment decisions in clinical practice.

INTRODUCTION

Rosacea is a common inflammatory skin disorder. It is classically seen in patients with lighter skin types, and the National Rosacea Society Expert Committee divides rosacea into 4 subtypes.[1,2] The papulopustular subtype of rosacea is characterized by the presence of persistent central facial erythema, in addition to inflammatory papules and pustules, which are transient in nature.[2] Phymatous changes and ocular manifestations may exist alone or in conjunction with papulopustular rosacea (PPR). In addition to these findings, patients often complain of dryness, burning, and stinging sensations in affected areas.[3,4] Topical and oral antimicrobials are the mainstay of therapy for the

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treatment of PPR, and numerous clinical trials comparing efficacy, tolerability, and quality of life measures have been performed. The primary objective of this article is to review the current literature pertaining to the treatment of PPR and to provide evidence-based recommendations regarding the appropriate management of rosacea.

METHODS

A PubMed search of articles published from 1980 to 2015 was performed using the following MeSH terms: rosacea and clinical trial. EMBASE and the Cochrane (Central) databases were searched using the keywords, "rosacea" and "clinical trial." After the initial search was performed, additional searches were performed to include rosacea and each treatment modality used. The abstracts of each article were screened; studies on erythematotelangiectatic, phymatous, and ocular rosacea were excluded. Trials with fewer than 10 subjects, and those not in English were excluded. The remaining articles were reviewed for objective measures of efficacy. Articles that studied steroid rosacea or non–efficacy-related outcomes were excluded. Studies primarily assessing patient perspective quality of life and not objective measures of improvement were excluded. Articles with primary and secondary endpoints related to the Investigator's Global Assessment (IGA), Physician's Global Assessment, erythema severity, and inflammatory lesion count (ILC) were included in the review (**Fig. 1**). A table including trials meeting criteria was developed and scored based on the JADAD criteria.[5]

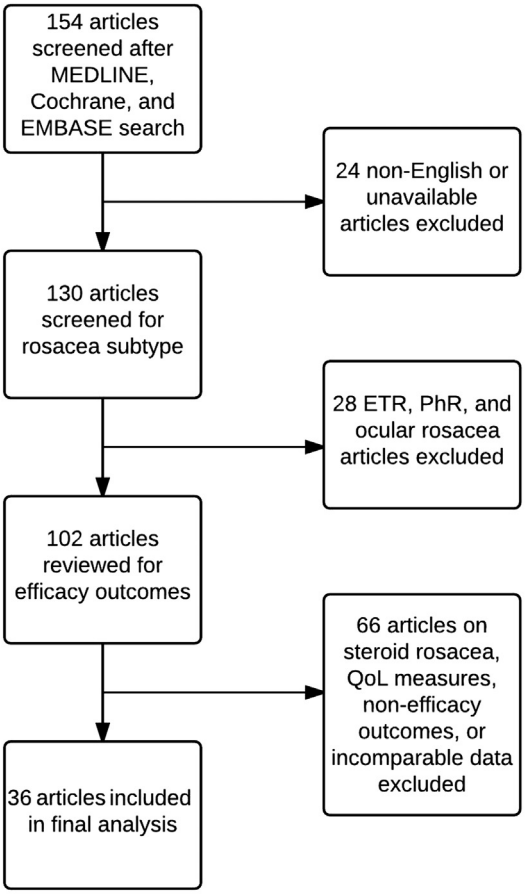

Fig. 1. Results of literature search regarding papulopustular rosacea. ETR, erythematotelangiectatic rosacea; PhR, phymatous rosacea; QoL, quality of life.

RESULTS

A total of 154 articles were identified after the initial search. A total of 52 articles were excluded owing to non-English language or subject matter. A total of 102 articles were reviewed in entirety, 66 articles that studied steroid rosacea, quality of life, non–efficacy-related outcomes, or had incomparable data were excluded (see **Fig. 1**, **Table 1**). A total of 36 articles were included in the final analysis. Owing to the lack of standardization among clinical trial results, we were unable to develop a true comparative statistical analysis. Variation with regard to ILC reduction and/or change in IGA was reported in some trials (see **Table 1**). Most trials either reported the percent reduction in ILC or the true reduction in ILC without a standard deviation or 95% confidence interval.

Doxycycline

Tetracycline antibiotics have been used for more than 60 years, and modified-release doxycycline 40 mg orally once daily is the only systemic agent approved by the US Food and Drug Administration for the treatment of PPR.[41,42] In PPR, the goal is to achieve subantimicrobial dosing and antiinflammatory effects that reduces the number of inflammatory lesions and limits adverse effects. Cost and individual patient pharmacokinetics may preclude the exclusive use of modified-release doxycycline. Doxycycline is the most well-studied tetracycline antibiotic for the treatment of PPR, and its efficacy is well-documented in clinical trials.[8–12,21] Doses of 40 to 200 mg daily are routinely used in clinical practice. Higher doses of doxycycline may be devoid of additional benefit and are accompanied by an increased risk of adverse effects.[10] A study that compared doxycycline 40 mg daily with 100 mg daily found no difference with regard to overall benefit, but an increased risk of nausea, vomiting, diarrhea, and abdominal pain associated with higher doses.[10] The risk of phototoxicity and pill esophagitis increase when using