

JAMA Clinical Evidence Synopsis

Interventions for Rosacea

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CLINICAL QUESTION Which interventions are associated with highest efficacy and fewest adverse events for treating rosacea?

BOTTOM LINE There is high-quality evidence that topical brimonidine, azelaic acid, and ivermectin, as well as oral doxycycline and isotretinoin, are associated with improvements in rosacea. Lower-quality evidence is available for topical metronidazole, oral tetracycline, laser and light-based therapy, and topical cyclosporine for ocular rosacea. Most treatments are not associated with higher adverse event rates than placebo.

Rosacea is a chronic facial skin disease affecting 10% of the population. Eye involvement may occur in up to 60% of those with the condition.¹ This JAMA Clinical Evidence Synopsis summarizes a Cochrane review¹ on interventions for rosacea.

Summary of Findings

Topical brimonidine was associated with 2 grades of improvement (scale, 0-4) of facial erythema among 114 of 227 participants (50%) compared with 54 of 276 participants (20%) with vehicle (excipient) alone (risk ratio [RR], 2.11 [95% CI, 1.60-2.78]; 2 studies; high-quality evidence) (Figure). Azelaic acid was associated with marked to excellent improvement in 383 of 607 participants (63%) compared with 241 of 572 participants (42%) taking placebo (RR, 1.46 [95% CI, 1.30-1.63]; 4 studies; high-quality evidence). Topical ivermectin was associated with good to excellent im-

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provement of rosacea in 615 of 910 participants (68%) vs 169 of 461 participants (37%) taking vehicle alone (RR, 1.84 [95% CI, 1.62-2.09]; 2 studies; high-quality evidence) as well as quality of life improvement. Topical ivermectin was associated with greater improvements in rosacea (409 of 478 participants [86%]) than topical metronidazole (362 of 484 participants [75%]) (RR, 1.14 [95% CI, 1.07-1.22]; 1 study; high-quality evidence). Oral doxycycline (40 mg) compared with placebo was associated with 2 grades of improvement (scale, 0-4) among 90 of 269 participants (33%) vs 55 of 268 (21%) (RR, 1.63 [95% CI, 1.22-2.18]; 2 studies; high-quality evidence). Oral isotretinoin (0.3 mg/kg) was associated with good to excellent improvement in 102 of 129 participants (79%) compared with 85 of 132 (64%) taking daily doxycycline (50-100 mg) (RR, 1.23 [95% CI, 1.05-1.43]; 1 study; high-quality evidence).

Topical metronidazole compared with placebo was associated with improved rosacea among 94 of 195 participants (48%) vs 40 of 139 participants (29%) (RR, 1.98 [95% CI, 1.29 to 3.02]; 3 studies; moderate-quality evidence). Oral tetracycline (250 mg) twice daily was associated with improved rosacea among 45 of 56 participants (80%) compared with 23 of 51 participants (45%) taking placebo (RR, 1.78 [95% CI, 1.28 to 2.48]; 2 studies; moderate-quality evidence). Pulsed dye laser and intense pulsed light therapy (1 study, 40 participants) were each associated with erythema and telangiectasia improvement, but without difference between treatments (moderate-quality evidence). Pulsed dye laser was associated with greater improvements of erythema and telangiectasia compared with yttrium-aluminum-garnet laser (mean difference, -16.33% [95% CI, -34.6% to -1.94%]; 1 study, 14 participants; low-quality evidence). For ocular rosacea, topical cyclosporine was associated with improvement of Schirmer score (mean difference, 4.1 mm [95% CI, 1.66 to 6.54]) and quality of life (1 study, 37 participants; low-quality evidence). Adverse effects were mild and transient with no difference between active and placebo groups.

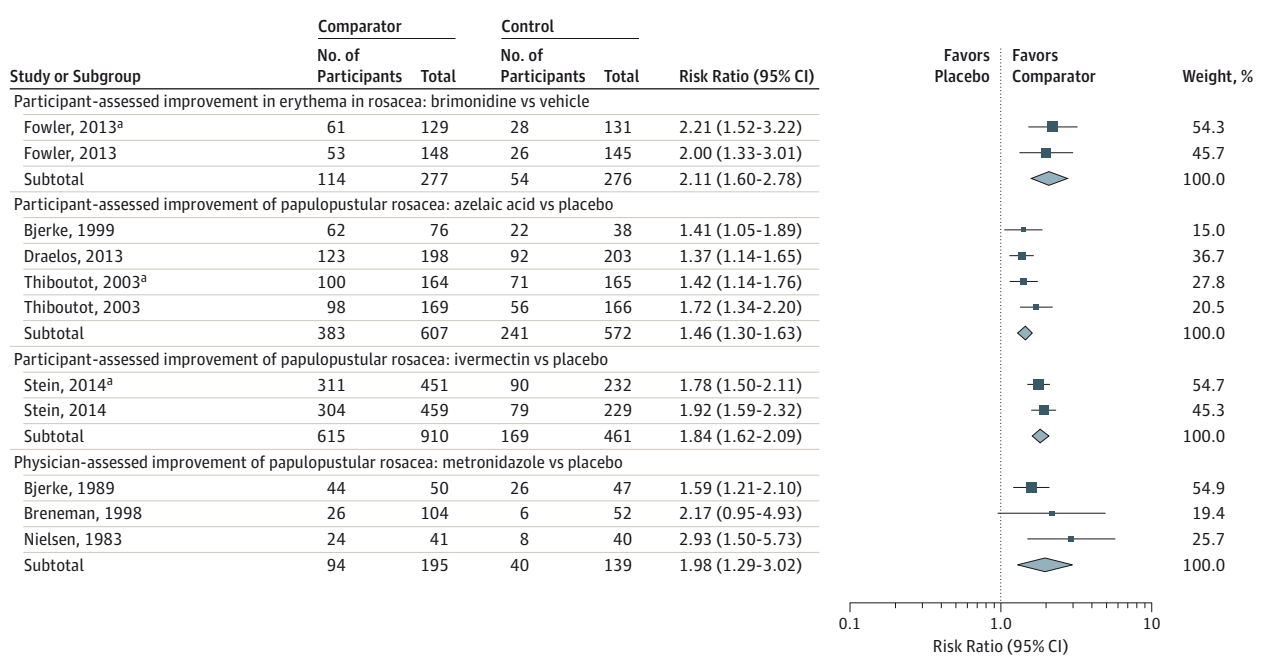
Discussion

Brimonidine was associated with reduced erythema compared with vehicle. Laser- and light-based therapies were associated with reductions in erythema and telangiectasia compared with baseline. Topical metronidazole, azelaic acid, and ivermectin compared with placebo were associated with improvements mainly for papulopustular rosacea (eAppendix in the Supplement). Oral tetracycline and

Evidence Profile

No. of randomized clinical trials: 106
 Study years: Conducted, 1966-2013; published, 1966-2014 (last search date, July 2014)
 No. of participants: 13 631
 Men: 31% Women: 69%
 Race/Ethnicity: Unavailable
 Age, mean (range): 48.6 years (25-73)
 Settings: Hospitals and medical centers
 Countries: Europe (32 studies), United States and Canada (62 studies), Latin America (2 studies), Asia (8 studies), Africa (2 studies)
 Comparisons: Treatments compared with placebo or alternative active treatment: topical treatments (41 comparisons), oral antibiotics (9 comparisons), combinations of these treatments (6 comparisons), other systemic treatments (5 comparisons), laser-based or light-based therapies (6 comparisons)
 Primary outcomes: Health-related quality of life, participant-reported improvement (\geq marked improvement) using Likert scales, and adverse events
 Secondary outcome: Clinician-assessed improvement

Figure. Comparisons of Topical Brimonidine, Azelaic Acid, Ivermectin, and Metronidazole vs Placebo for Treating Rosacea



Source: Data were adapted with permission from Wiley.¹ The size of the data markers indicates the weight of the study. The point estimate is an overall estimate of effect, summarizing the effect size (risk ratio) from

each individual study, with the diamond representing the pooled point estimate of effect.

^a Fowler, Stein, and Thiboutot report on 2 studies.

doxycycline (40 mg) were associated with improvements in papulopustular rosacea compared with placebo and isotretinoin was associated with improvement in papulopustular rosacea compared with doxycycline. For ocular rosacea, topical cyclosporine was associated with some benefits compared with placebo. We updated our search in August 2015 and identified 5 additional studies. None changed our reported conclusions.

Limitations

Mainly due to lack of blinding and attrition, 57 of 106 studies were designated at unclear risk and 37 of 106 studies were at high risk of bias. Quality of life was assessed in 11 studies and participant-reported improvements in 52 studies.

Comparison of Findings With Current Guidelines

Guidelines of the American Acne and Rosacea Society and German Society of Dermatology describe azelaic acid and metronidazole as first-line treatments. This recommendation is partly consistent with our findings because ivermectin and brimonidine were only recently approved by the US Food and Drug Administration. Oral tetracyclines, specifically doxycycline (40 mg), were regarded as second-line treatments. Both guidelines acknowledge the efficacy of isotretinoin and laser-based or light-based therapies.²⁻⁵

Areas in Need of Future Study

Further studies evaluating ocular rosacea treatments are needed. Future studies should emphasize participant-reported outcomes.¹

ARTICLE INFORMATION

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Submissions: We encourage authors to submit papers for consideration as a JAMA Clinical Evidence Synopsis. Please contact Dr McDermott at mdm608@northwestern.edu.

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