

Rosacea

Systematic Review of Treatments

Source: van Zuuren EJ, Gupta AK, Grover MD, Graber M, Hollis S. Systematic review of rosacea treatments. J Am Acad Dermatol. 2007 Jan;56(1): 107–15

Conflicts of Interest: None identified to the journal citation

CLINICAL SUMMARY

EFFECTIVE

- Topical metronidazole and azelaic acid are effective for short-term use.
- There is some evidence that oral tetracycline may be effective for ocular rosacea.

UNKNOWN EFFECT

- There is insufficient RCT evidence to assess rilmenidine (for flushing), benzoyl peroxide/clindamycin (for limited pustules), or sulfacetamide/sulfur (for limited pustules).
- There is no RCT evidence available on clonidine (for flushing), tretinoin cream (for limited pustules), ampicillin (for extensive skin lesions), isotretinoin (for persistent rosacea), metronidazole (for ocular rosacea), or fusidic acid gel (for ocular rosacea).
- There is no RCT evidence available on any treatments for vascular symptoms or rhinophyma.

UNLIKELY EFFECTIVE

- Nothing to report.

POSSIBLY INNEFFECTIVE OR HARMFUL

- Nothing to report.

REVIEW INFORMATION

Participants	Adults, 19 years or older with moderate to severe rosacea
Interventions	Any type of rosacea treatment
Outcomes	Participant-assessed changes in rosacea severity and impact on quality of life
Study Types	Randomized controlled trials
Limitations	Quality of the studies was generally poor

ODDS RATIOS (OR)

Compares if the odds of an event is the same for two groups	
OR=1	The event is equally likely in both groups.
OR>1	The event is more likely in the exposed group.

CLINICAL CONDITION	TREATMENTS	# weeks follow-up in trial participants	# trials	OUTCOMES	ADVERSE EVENTS
Limited Number of Papules / Pustules	Meta-Analysis Topical metronidazole (0.75% and 1%) Participants: 68 (topical metronidazole), 32 (placebo)	8–9	2	●●○ Favours topical metronidazole OR: 5.96; 95% CI: 2.96–12.06	Mild: including pruritis, skin irritation, dry skin
		Topical azelaic acid (15% gel, 20% cream) Participants: 260 (azelaic cream), 149 (placebo)	9–12	3	●●○ Favours topical azelaic acid OR 2.45; 95% CI: 1.82–3.28
	Benzoyl peroxide 5% / clindamycin 1% gel	12	1	Significantly superior to placebo ($p = .0002$)	Site burning and itching
	Sodium sulfacetamide 10% / sulfur 5%	n/a	1	Significantly superior to placebo ($p < .001$)	Dryness, erythema, pruritis
	Topical permethrin v. Topical metronidazole	n/a	1	Inferior to topical metronidazole	Not addressed in study
	Topical azelaic acid v. Topical metronidazole	15	2	No statistical significant difference in efficacy between topical metronidazole and topical azelaic acid	Mild to moderate, mostly transient: burning, stinging, irritation
	Metronidazole plus sunscreen SPF 15	n/a	1	Poorly designed study favoured metronidazole plus sun-screen over placebo	Not addressed in study
More Extensive Skin Lesions	Tetracycline	4–6	3	Oral tetracycline is more effective than placebo by physician assessment (OR: 6.06; 95% CI: 2.96–12.42) but not by patient assessment	Not addressed in study
	Oral metronidazole v. Oral oxytetracycline	12	1	No statistically significant difference between the two therapies	Not addressed in study
	Oral tetracycline v. Topical metronidazole	8	2		
	Benzoyl peroxide 5% / erythromycin 3% gel and metronidazole	4	1		
	Clarithromycin and omeprazole	n/a	1	Impossible to draw conclusions from data	Not addressed in study
Flushing	Rilmenidine	n/a	1	Rilmenidine not significantly better than placebo	Not addressed in study
Eye Irritation (Ocular Rosacea)	Tetracycline (250 mg b.d. for 6 weeks)	6	1	Oral oxytetracycline may be more effective for ocular rosacea by physician assessment	Not addressed in study

NO RANDOMIZED CONTROLLED TRIALS AVAILABLE FOR EVALUATION

CLINICAL CONDITION	TREATMENTS
Limited Number of Papules / Pustules	Tretinoin
More Extensive Skin Lesions	Ampicillin
Flushing	Clonidine
Vascular Rosacea	Pulse dye laser, intense pulsed light
Severe or Persistent Rosacea	Isotretinoin
Eye Irritation (Ocular Rosacea)	Metronidazole; Fusidic acid gel
Rhinophyma	Isotretinoin (low-dose); Laser therapy; Surgical Interventions

STRENGTH OF RESEARCH EVIDENCE

Ratings are based on the overall quantity and quality of clinical evidence.	
●●● STRONG	Results consistent from high quality studies. Conclusions unlikely to change with further research.
●●○ MODERATE	Current research supports findings, however conclusions could change with further research.
●○○ WEAK	Limited studies available for drawing conclusions, or existing studies have significant limitations.

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SYSTEMATIC REVIEW ABSTRACT

Purpose

To assess the evidence for the efficacy and safety of rosacea therapies.

Methods

- Medline, EMBASE, the Cochrane Library, BIOSIS, and the Science Citation Index were systematically searched.
- Study selection, assessment of methodologic quality, data extraction, and analysis were carried out by two independent researchers.

Results

- 29 studies met the inclusion criteria.
- Topical metronidazole is more effective than placebo (odds ratio 5.96, 95% confidence interval 2.95–12.06).
- Azelaic acid is more effective than placebo (odds ratio 2.45, 95% confidence interval 1.82–3.28).
- Firm conclusions could not be drawn about other pharmacological and non-pharmacological therapies.

APPLYING THE EVIDENCE

Example

- A 35-year old woman had developed moderate swelling, erythma and papules of the central part of her face for 8 weeks.
- She had been applying various topical cosmetic products sold for acne with no change in her condition.
- One of her hobbies is hiking and she noticed sun exposure aggravated her skin condition, also resulting in burning and stinging sensations.

Treatment

- The patient consulted her family physician who prescribed topical treatment with metronidazole 1% and oral treatment with metronidazole 500 mg twice daily for two weeks.

Outcome & Follow-up

- After an initial worsening during the first 3 days the skin condition improved.
- The topical treatment was continued twice daily for 4 weeks and then reduced to once daily for an additional 4 weeks. As well, sun screen was applied whenever outdoors.



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The case study used in Applying the Evidence is adapted from: rosacea.dermis.net/content/e05quizcase/index_eng.html. Used with permission.

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EXPERT INTERPRETATION

- Topical metronidazole cream (0.75% and 1%) and azelaic acid cream (15 and 20%) are effective and safe for short term use (8–12 weeks).
- Oral oxytetracycline (250mg oxytetracycline dihydrate [Clinimycin] one capsule twice daily) may be effective for ocular rosacea.
- Oral tetracycline is more effective than placebo for physician assessment but not for patient outcomes.
- There is no evidence for use of other agents including dapsone, erythromycin, topical tretinoin, benzoyl peroxide, diet or sun protection.
- The quality of reported studies is poor with lack of blinding, allocation concealment, and intention to treat analysis.



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Conflict of Interest: None identified

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Interventions	Any type of rosacea treatment
Outcomes	Participant-assessed changes in rosacea severity and impact on quality of life
Study Types	Randomized controlled trials
Synopsis	29 RCTs were included, 8 were classified as high quality Topical metronidazole is more effective than placebo (OR 5.96; 95% confidence interval 2.95–12.06) Topical azelaic acid is more effective than placebo (OR 2.45; 95% confidence interval 1.82–3.28) Firm conclusions could not be drawn about other therapies

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		12	1	No statistically significant difference between the two therapies	Not addressed in study
		8	2		
		4	1		
		n/a	1	Impossible to draw conclusions from data	Not addressed in study
Flushing	Rilmenidine	n/a	1	Rilmenidine not significantly better than placebo	Not addressed in study
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