REVIEW

Assessment of rosacea severity: A review of evaluation methods used in clinical trials

Dennis Hopkinson, BA,[a] Sara Moradi Tuchayi, MD, MPH,[a] Hossein Alinia, MD,[a] and Steven R. Feldman, MD, PhD[a,b,c]
Winston-Salem, North Carolina

Background: Novel rosacea treatments are needed. Assessment methodologies for clinical trials of rosacea treatments are not standardized and are relatively inadequate. To determine the efficacy of new treatments, a valid and reliable assessment methodology is needed.

Objective: We sought to determine the assessment methodologies used in clinical trials for rosacea treatments, to demonstrate the need for a valid and reliable assessment tool, and to describe the relevant properties of such a tool.

Methods: PubMed and MEDLINE were searched for clinical trials of rosacea treatments since January 1, 1985.

Results: In all, 32 clinical trials met inclusion criteria. Assessment methodologies were highly variable, and standardized assessment methodologies were used in only 3 studies. The various manifestations of rosacea were assessed inconsistently.

Limitations: Eighteen articles could not be included as a result of lack of access to the full text.

Conclusions: The diverse methodologies make the assessment of novel treatments and comparison of treatments difficult. A valid and reliable assessment tool is needed to properly assess novel treatments to improve the management of rosacea. (J Am Acad Dermatol http://dx.doi.org/10.1016/j.jaad.2015.02.1121.)

Key words: erythema; ocular rosacea; papules and pustules; phymatous rosacea; rosacea; scale self-assessment; severity; telangiectasias; treatment.

Rosacea can present with erythema, telangiectasia, papules and pustules, phymatous change, and ocular lesions. The National Rosacea Society describes 4 subtypes: erythematotelangiectatic rosacea, papulopustular rosacea, phymatous rosacea, and ocular rosacea.[1] The etiology and pathophysiology of rosacea remain to be elucidated. Thus, current treatments are focused on the presenting physical symptoms and results are often unsatisfactory. Novel treatments for rosacea need to be developed.

The varied manifestations of the disease make it difficult to assess the efficacy of rosacea treatments. Despite these complexities, valid and reliable assessment tools are needed.[2-5] An effective assessment tool would allow for valid formal assessment to accurately determine efficacy of medications and surgical techniques. Such a standardized

From the Center for Dermatology Research, Department of Dermatology,[a] Department of Pathology,[b] and Department of Public Health Sciences,[c] Wake Forest University School of Medicine.

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Table II is available at http://www.jaad.org.

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Reprint requests: Hossein Alinia, MD, Department of Dermatology, Wake Forest University School of Medicine, 4618 Country Club Rd, Winston-Salem, NC 27104. E-mail: hos_alinia@yahoo.com.

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assessment tool could also simplify comparison of treatments. Moreover, a formal assessment methodology could aid in physician communication and allow a physician to track a patient's response to treatment and a patient's general progress over time. The aim of this study is to assess the rosacea assessment methods used in clinical trials, to assess the need for a valid assessment tool, and to establish what properties such a tool may consist of.

CAPSULE SUMMARY

- There is no valid and reliable methodology to assess the efficacy of novel rosacea treatments.
- This literature review demonstrates that assessment methodologies used in clinical trials are varied and often of substandard quality.
- A valid assessment methodology is needed to properly assess novel treatments to improve the management of rosacea.

METHODS

The literature was searched with the aim of retrieving methods used for assessing rosacea severity in clinical trials. Two literature databases were used: PubMed was searched, as was MEDLINE through the EbscoHost platform. In PubMed, we queried ("rosacea" [Medical Subject Headings terms] OR "rosacea" [all fields]) AND ("clinical trial" [publication type] OR "clinical trials as topic" [Medical Subject Headings terms] OR "clinical trial" [all fields]). In MEDLINE, "rosacea" AND "clinical" AND "trial" was searched in all text. In both instances, the search was performed in April 2014, and limitations consisted of the English language, human beings (as there is a marine animal of genus *Rosacea*), and publication dates of January 1, 1985, through January 31, 2014.

The titles, abstracts, and articles were then assessed with the following inclusion and exclusion criteria:

Inclusion criteria:

(i) Original research
(ii) The disease rosacea as defined by the National Rosacea Society types
(iii) Any method of performing a clinical trial (eg, double-blind randomized controlled trial, open label randomized clinical trial)

Exclusion criteria:

(i) Assessment of only rhinophyma or ocular rosacea
(ii) Clinical trials of treatments for "rosacea-like eruptions" or "rosacea-like redness"
(iii) Studies that focused on pathophysiological changes during treatment
(iv) Studies that primarily assessed cost-effectiveness
(v) Articles that are not available electronically
(vi) Duplicate articles

This resulted in a total of 32 articles (Fig 1).

RESULTS

A specific sign or symptom of rosacea was assessed in all 32 studies, with the exception of 1 study that relied solely on a clinician global assessment (Tables I and II). Erythema was the most frequently assessed sign, followed by papules and pustules, and then telangiectasia. The primary modality of assessment used in all 32 studies was visual inspection by a clinician who then rated the degree of severity of the aspect being assessed. A 4-point scale was the most frequently used scale. Advanced techniques (spectrophotometer, computer analysis of digital photographs) and global severity assessment were used in several studies.

Erythema was most frequently assessed using a 4-point scale. In terms of advanced technology to assess the degree of erythema, a spectrophotometer was used more frequently than computer analysis of a digital photograph. Studies that assessed erythema did not distinguish between background erythema (primarily a manifestation of vascular reactivity) and perilesional erythema (a manifestation of the inflammatory response).

To measure papules and pustules, lesion counts by the clinician were the primary mode of assessment, and in all studies that assessed papules and pustules the lesions were counted on the entire face. In 3 studies the counts were then grouped into quartiles to make a 4-point scale. In 6 studies, papules and pustules were not counted, but assessed on a scale.

The method for assessing the severity of telangiectasia was varied. Four-point scales were used in most studies that assessed the severity of telangiectasia. Four of these studies that used the 4-point scale used a clearly defined method of assessment that encompasses the size of the vessels and the percentage of the face that is covered by vessels.* In addition, 2 of the 4-point scales began

*In this method of assessing the severity of telangiectasias, 0 = absent; 1 = mild (fine vessels covering <10% of the face); 2 = moderate (several fine vessels and/or a few large vessels covering between 10%–30% of the face); and 3 = severe (many fine vessels and large vessels covering >30% of the face).