Topical antimicrobial acne treatment tolerability: A meaningful factor in treatment adherence?

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Adherence to dermatologic treatment is estimated to range from 55% to 66%[1] but is as low as 45% for daily application of topical antimicrobial acne treatments.[2] Poor adherence may be the most important factor in acne treatment failure.[3] Dogma suggests that irritation and poor tolerability reduce patients' adherence to treatment. Is there evidence to support this dogma?

We identified 35 studies that evaluated the tolerability of topical antimicrobials in acne treatment.[4-38] Of those, 13 (37%) made the claim that better tolerability improves treatment adherence (Table I).[10-12,14,15,26,27,29,31,33,36-38] Three made this claim without citing any sources.[10,31,38] One found an association between tolerability and adherence.[37] The remaining studies cited sources that provided no data to substantiate the claim.

We found 1 controlled trial in which subjects using a 2.5% benzoyl peroxide/adapalene product reported more missed doses as a result of irritation and adverse events than with a less irritating 5% benzoyl peroxide/clindamycin product with hydrating excipients.[37] However, when the number of discontinuations caused by tolerability was assessed across the remaining 34 studies of topical antibiotics for acne, there was no significant correlation between poorer tolerability and discontinuations (with the exception of a subanalysis on peeling that yielded a *negative* correlation).

We did not find strong evidence to support the dogma of an association between tolerability and adherence in the treatment of acne. Irritation may remind patients to use medication; some of the best adherence to topical treatment was seen in a study of 5-fluorouracil for actinic keratosis, with a mean adherence rate of 86%.[39] Although patients with actinic keratoses are different from patients with acne (more likely to be more mature, older, and possibly more motivated to spare themselves surgery or other treatments), the good adherence in this population shows that a high degree of irritation does not mean that adherence will be poor. The effects of tolerability on adherence are not necessarily predictable, and care must be taken to avoid the propagation of unsubstantiated dogma in the scientific literature.

Please visit http://www.jaad.org for the reference list.

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Table I. Tracing the evidence in support of claims that tolerability of acne treatments affects adherence

Study claim*†	Total No. of citations to support the claim‡	Was the claim substantiated by supporting citations?
Well-tolerated acne treatments may improve adherence[14]	2[1,40]	Unsubstantiated: 1 citation provided data, but was on a study for corticosteroid use in eczema.[40] The adherence data were patient self-reported.
Well-tolerated acne treatments may improve adherence[26]	4[41-44]	Unsubstantiated: the study was unable to provide data on adherence.[26] The citations provided no data on a tolerability-adherence association in acne treatment.
Well-tolerated acne treatments may improve adherence[27]	3[45-47]	Unsubstantiated: the citations provided no data on a tolerability-adherence association in acne treatment.
Well-tolerated acne treatments improve adherence[38]	No citations	Unsubstantiated
Well-tolerated acne treatments may improve adherence[15]	4[1,40,48,49]	Unsubstantiated: the citations provided no data on a tolerability-adherence association in acne treatment.
Well-tolerated acne treatments improve adherence[12]	2[3,50]	Unsubstantiated: the citations provided no data on a tolerability-adherence association in acne treatment.
Well-tolerated acne treatments may improve adherence[31]	No citations	Unsubstantiated: no adherence data were provided to support a tolerability-adherence association.
Well-tolerated acne treatments may improve adherence[37]	3[41,44,51]	Data showed that more missed doses occurred with the less tolerable medication due to its decreased tolerability. The more tolerable medication also had an earlier onset of improvement which may have encouraged continued use.
Well-tolerated acne treatments may improve adherence[10]	No citations	Unsubstantiated: no adherence data were provided to support the affect of a tolerability-adherence association.
Clinical trials have shown that patients are more likely to comply with well-tolerated treatments[36]	1[52]	Unsubstantiated: the citation provided no data on a tolerability-adherence association in acne treatment, and made no claim of a tolerability-adherence association.
Tolerability of acne treatment influences adherence to therapy[29]	1[53]	Unsubstantiated: the citation provides no data for tolerability-adherence association.
Poor tolerability of acne treatment leads to poor adherence[33]	6[53-58]	Unsubstantiated: although tolerability was the same between male and female genders, responses to treatment significantly favored females at all time points.[33] The citations provided no data on a tolerability-adherence association in acne treatment.
Poor tolerability of acne treatment leads to poor adherence[11]	4[59-62]	Unsubstantiated: in addition to an absence of evidence linking adherence and tolerability, 1 of the studies cited was not for acne, it was for use of moisturizer to reduce retinoid dermatitis used for facial peels after facial photodamage.

*The claim is a summarization of the original author's original claim in the article.

†Please visit http://www.jaad.org for references cited in this table.

‡Although this column represents the total number of citations, some citations included in that number were second-level, third-level, or even fourth-level citations, as we attempted to track back to the original source (evidence) for the claim.

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