Interventions to increase adherence to acne treatment

Sara Moradi Tuchayi1
Tiffany M Alexander2
Anish Nadkarni1
Steven R Feldman1,3,4

1Center for Dermatology Research, Department of Dermatology, Wake Forest University School of Medicine, Winston-Salem, NC, 2Howard University College of Medicine, Washington, DC, 3Department of Public Health Sciences, Department of Pathology, Wake Forest University School of Medicine, Winston-Salem, NC, USA

Background: Adherence to acne medication is poor and is a major reason why treatment plans are ineffective. Recognizing solutions to nonadherence is critical.

Objective: The purpose of this study is to describe the hurdles associated with acne nonadherence and to provide mechanisms on how to ameliorate them.

Methods: PubMed database was searched. Of the 419 search results, 29 articles were reviewed to identify hurdles to adherence and corresponding solutions.

Results: Hurdles to primary nonadherence where the medication is not even started, include lack of knowledge, confusion about usage, weak physician–patient relationship, fear of adverse reactions, and cost. Secondary nonadherence hurdles where the medication is started but is not taken as directed include lack of results, complex regimens, side effects, busy lifestyle, forgetfulness, inconvenience, and psychiatric comorbidity. Solutions to these hurdles include treatment simplification, technology, and dynamic education.

Limitations: Adherence is affected by numerous factors, but available literature analyzing acne adherence and interventions to improve adherence to treatment is limited.

Conclusion: There are several hurdles in adhering to acne treatment. Recognition of these hurdles and finding appropriate solutions may be as important to treatment outcomes as choosing the right medication to prescribe.

Keywords: acne vulgaris, adherence, pathogenesis, treatment, quality of life, prevalence, physician–patient relationship, lifestyle, clinic visit, disease severity

Introduction

Acne vulgaris is a common chronic inflammatory disease that affects 45 million people in the USA.1 Acne negatively affects the quality of life—as measured by low self-esteem, increased social and emotional anxiety2,3—and imposes a considerable financial toll.4 Annually, US consumers spend $1.2 billion on acne medications,1 $233 per patient on prescribed acne treatments.4 The use of more than one medication due to multifactorial pathogenesis of the disease adds cost and complexity to the burden.

One of the factors negatively impacting acne treatment outcomes is poor adherence. Poor adherence is a problem in all medical disciplines, with the average adherence being only 50%–60%.5,6 Adherence to simple acne regimens is poor; adherence rates for complex regimens are worse. The purpose of this study is to describe the hurdles associated with adherence to acne treatment and to provide mechanisms on how to ameliorate them.

Methods

The PubMed literature database was searched with the goal of finding hurdles to acne treatment adherence. In PubMed, the search (“acne vulgaris” [all fields] OR...
“acne medication adherence” [all fields]) was performed in July 2015. Limitations consisted of the English language, humans, and publication dates of January 1, 1990 through July 1, 2015. In addition, the reference lists of these articles were searched. The titles, abstracts, and articles were analyzed and the following inclusion criteria were used:

Inclusion criteria:
1. Involvement of patients with acne
2. Studies examining acne treatments
3. Assessing adherence to acne treatments

The keyword search resulted in a total of 419 articles. Through an independent review, 29 articles were selected and used to generate a list of hurdles and interventions for acne medication nonadherence. The hurdles were identified as either primary or secondary medication nonadherence hurdles. Primary nonadherence was defined as “not obtaining or initiating a prescribed medication.” Secondary nonadherence refers to a “lack of sufficient treatment usage or early discontinuation of treatment.” Interventions identified within the articles were categorized as corresponding solutions to the aforementioned primary or secondary nonadherence hurdles.

Results
Hurdles to acne treatment adherence can be classified into primary and secondary. Primary adherence hurdles include lack of knowledge about acne condition, confusion about how to use treatment, weak physician–patient relationship, fear of side effects, and costs (Table 1). Secondary adherence hurdles include lack of efficacy, complicated regimens, adverse reactions, lifestyle factors, and psychiatric comorbidity. Solutions to address these hurdles lie in simplification, technology, and dynamic education (Table 2).

Findings of literature search with hurdles to acne treatment adherence and interventions are shown in Table 3.

Table 1 Hurdles to acne treatment adherence

<table>
<thead>
<tr>
<th>Primary nonadherence hurdles</th>
<th>Secondary nonadherence hurdles*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Little knowledge about severity of acne</td>
<td>Lack of acne improvement</td>
</tr>
<tr>
<td>Weak physician–patient relationship</td>
<td>Regimen too complex</td>
</tr>
<tr>
<td>Influence from media or other physicians</td>
<td>Adverse reaction</td>
</tr>
<tr>
<td>Already in possession of similar treatments</td>
<td>Difficulty delaying satisfaction</td>
</tr>
<tr>
<td>Fear of adverse reaction</td>
<td>Busy lifestyle</td>
</tr>
<tr>
<td>High QOL score</td>
<td>Forgetfulness</td>
</tr>
<tr>
<td>Confusion about how to use treatment</td>
<td>Inconvenient</td>
</tr>
<tr>
<td>Cost</td>
<td>Psychiatric comorbidity</td>
</tr>
</tbody>
</table>

Notes: *Some hurdles likely apply to both primary and secondary adherence.
Abbreviation: QOL, quality of life.

Discussion
Considering the huge burden of acne and low rates of adherence associated with acne medication, more attention to increasing adherence is needed. A variety of hurdles to adherence exist, stemming from both inside and outside the doctor’s office. Understanding these hurdles may help dermatologists in creating effective solutions for their patients.

Primary nonadherence is when a patient never even begins taking the medication. The existence of primary nonadherence highlights the need for a strong patient–physician relationship. In a weak relationship, a patient may be more likely to disagree with the dermatologist’s recommendations due to information obtained from nonmedical professionals, websites, television advertisements, commercials, and magazine articles. Other reasons also exist for primary nonadherence. Patients may be indifferent to filling their prescribed medication or begin using it due to a lack of motivation. They may already possess similar treatments or acne may not be bothersome enough for its treatment to be high on their list of priorities. There is also the possibility that the skin condition may improve before even obtaining their prescriptions, negating a need for primary adherence.

Secondary nonadherence is when the medication is not taken as prescribed. This type of nonadherence tends to be more prevalent in patients with chronic acne than in those with acute conditions. One common reason for secondary nonadherence in acne treatment would be side effects. Topical retinoids, which are a first-line therapy, can cause burning, irritation, and dryness. Topical and oral antibiotics used as monotherapy can lead to antibiotic resistance. Isotretinoin, which is used to treat moderate-to-severe acne has been known to be teratogenic and can contribute to cheilitis, dermatitis, arthralgia, increased liver enzymes, cholesterol levels, depression, and even attempted suicide. These large numbers of potential adverse events can scare patients from even starting the medication. They may also reduce patients’ use and if they occur, may cause patients to discontinue treatment altogether. Another reason for secondary nonadherence is poor efficacy. Many acne medication regimens take many weeks or months for improvement, leading patients into believing that the medication is not working, which leads to lower adherence. This may be especially true of the patient population suffering from acne, as difficulty “delaying satisfaction” is commonly seen in adolescents. Complex regimens may also lead to less adherence. One study has shown that going from a single treatment to multiple treatments leads to less adherence. Other patients may have confusion about treatment usage and...
be discouraged to use the medication.\textsuperscript{21} Lifestyle must also be considered when thinking about reasons for poor adherence. A patient with a busy lifestyle may simply forget to apply it, especially if other reasons for nonadherence exist.\textsuperscript{7} Additionally, tumultuous lifestyles or depressive emotional states may contribute to lower psychiatric comorbidities and decreased adherence.\textsuperscript{22}

Simplification serves as one solution to nonadherence, as it allows treatment to better fit into a patient’s lifestyle. Among patients who were prescribed one, two, or three acne treatments, primary adherence was significantly higher in the patients who were prescribed one medication.\textsuperscript{7} Simplifying the medication vehicle may increase adherence as well. Acne subjects preferred the pump over a tube for dispensing fixed-dose combination of adapalene 0.1%-benzoyl peroxide 2.5% gel because the pump made it easy to follow their doctor’s instructions and apply a consistent amount each time.\textsuperscript{21} Fixed-dose combinations such as a combination of retinoids and antimicrobials simplify the acne therapeutic regimen and increase adherence; this combination simultaneously combats the proliferation of follicular keratinization, \textit{Propionibacterium acnes} colonization, and release of inflammatory mediators.\textsuperscript{15} However, combination treatments have overcome all adherence obstacles, especially in maintaining good adherence over time. A pilot randomized controlled trial found that even after product demonstration and sampling of the fixed combination treatment of adapalene/benzoyl peroxide gel, medication adherence rates decreased from 86% after 1 week of treatment, to 36% in week 6 of treatment.\textsuperscript{23}

The use of technology has the potential to play a major role in increased adherence. In an experiment where two different groups of adolescent acne patients were given a topical agent for acne treatment, the group given an automated weekly emailed survey was seen to have higher adherence than the group given no survey.\textsuperscript{24} This type of technological intervention may be more useful than other types of technologies such as automated text messaging reminders, which have been shown not to significantly increase adherence.\textsuperscript{25} The email survey technique encourages patients to act as active participants in their own treatment as opposed to automated text messaging reminders, where they play a more passive role. Surveys rather than reminders may also simulate a doctor’s visit and enhance the “white coat compliance” effect, the phenomena where patients are more likely to listen when given direct instructions by a doctor.\textsuperscript{24} Survey-based technology also takes advantage of the long amounts of time adolescents spend on the computer and can be a cost-effective alternative to frequent follow-up visits in an attempt to increase adherence.

Education, specifically dynamic education, which consists of a more informative physician–patient interaction can also increase adherence. Acne patients with higher adherence

\begin{table}[h]
\centering
\begin{tabular}{|l|l|l|}
\hline
\textbf{Intervention type} & \textbf{Interventions to primary nonadherence hurdles} & \textbf{Interventions to secondary nonadherence hurdles} \\
\hline
\textbf{Simplification} & Consider postponing therapy if patient is content and has little psychological distress and nonscarring acne & Simplify regimen by using combination therapies and allowing patients to choose their vehicle \\
& & Ask patients to incorporate use of their medication into their daily activities \\
& & Ask patients to place their medications within daily eyesight \\
& & Automated text messaging \\
& & Follow-up phone calls \\
& & Follow-up with internet-based surveys \\
& & Recommend phone applications \\
\hline
\textbf{Technology} & Electronic transmission of prescription to pharmacy & Determine if the patient is using medication correctly. If not, educate the patient again. If therapy is truly ineffective and there is no improvement, abandon treatment and consider alternatives \\
& & Proactively deal with anticipated side effects \\
& & Use adjunctive medications, consider comedone extraction and drainage of cysts \\
& & Simplify the regimen by using combination medication, allow patients to choose their vehicle, and ask patients to incorporate use of medication into their daily activities \\
& & Consider psychiatric consultacy, psychotherapy, or setting up acne vulgaris support groups \\
\hline
\textbf{Dynamic education} & Verbally and visually educate the patient about their condition & & & \\
& Discuss treatment options with the other physicians & & & \\
& Debunk myths by proactively educating the patients about side effects & & & \\
& Instruct the patient by giving a demonstration & & & \\
& Use open-ended questions and avoid nonjudgmental and accusatory remarks & & & \\
& Understanding the pervasive nature of the media and its influence on patients. Debunk myths and educate patients about their condition and any anticipated side effects & & & \\
& Ask about previously prescribed treatments and satisfaction with them & & & \\
& Demonstrate medication use & & & \\
& Know which insurance covers what medications & & & \\
\hline
\end{tabular}
\caption{Interventions to acne treatment hurdles}
\end{table}
reported that education and interaction with the dermatologist positively affected their behavior, while patients who were dissatisfied with their dermatologist interaction reported feeling unsure as to why they needed continuous treatment, what the expected results were, or how to prevent acne.\textsuperscript{26} Education could also involve using a more direct manner to teach the patient how to use the medication. Electronic adherence monitors revealed that mean adherence rates over a 6-week period were 15% higher in the group given a physical demonstration of how to apply the medication versus the group given no demonstration.\textsuperscript{23} As the long length of some acne regimens directly play a role in nonadherence, physicians should highlight the fact that it takes some time for these regimens to show their effects. Reinforcement of this idea as part of the education process may lead to higher adherence. Acne medication adherence decreases over time; however, around the time of follow-up visits, medication adherence increases.\textsuperscript{23,24,27} Scheduling follow-up visits is a potent intervention to increase adherence.\textsuperscript{28} Several of the hurdles that prevent adherence to medication stem from patients’ concerns about things like adverse reactions to the medication, which can be further reinforced by media influences and their lack of knowledge about acne as a whole.\textsuperscript{9,17} Hurdles such as these can be addressed through dynamic education in combination with scheduling more follow-up visits. At follow-up visits, physicians can address concerns about side effects or usage and reassure patients on the importance of adherence if the patient feels as if there is

<table>
<thead>
<tr>
<th>Table 3 Summary of findings of literature search with hurdles to acne treatment adherence and interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Study</strong></td>
</tr>
<tr>
<td>---------------------------------------------------------------</td>
</tr>
<tr>
<td>Anderson et al \textsuperscript{7} (2015)</td>
</tr>
<tr>
<td>Rueda \textsuperscript{10} (2014)</td>
</tr>
<tr>
<td>Tan et al \textsuperscript{13} (2012)</td>
</tr>
<tr>
<td>Gorelick et al \textsuperscript{14} (2015)</td>
</tr>
<tr>
<td>Gollnick \textsuperscript{13} (2015)</td>
</tr>
<tr>
<td>Charakida et al \textsuperscript{17} (2004)</td>
</tr>
<tr>
<td>Renzi et al \textsuperscript{22} (2002)</td>
</tr>
<tr>
<td>Sandoval et al \textsuperscript{23} (2014)</td>
</tr>
<tr>
<td>Yentzer et al \textsuperscript{24} (2011)</td>
</tr>
<tr>
<td>Boker et al \textsuperscript{25} (2012)</td>
</tr>
<tr>
<td>Miyachi et al \textsuperscript{26} (2011)</td>
</tr>
<tr>
<td>Feldman et al \textsuperscript{27} (2007)</td>
</tr>
<tr>
<td>Yentzer et al \textsuperscript{28} (2011)</td>
</tr>
</tbody>
</table>

For personal use only.
a lack of progress. When frequent follow-up visits are not feasible, using substitutive technology methods that mimic the effects of visits should be considered.

Research on pathophysiologic pathways in acne may lead to new treatment modalities, but numerous acne treatments and various guidelines will be ineffective if they are not used by patients.29 A variety of interventions have been introduced that may help to improve acne treatment adherence, especially with recent technology achievements; however, establishment of novel solutions to increasing adherence is still needed.

### Conclusion

- Acne medication adherence is poor and a major reason for treatment failure.
- This article examines the hurdles to adherence and solutions to these hurdles.
- Understanding hurdles to adherence and identifying the most effective solutions may help physicians to achieve better treatment outcomes.

### Acknowledgment

Center for Dermatology Research was supported in part by an unrestricted educational grant from Galderma Laboratories, L.P.

### Disclosure

Dr Feldman is a speaker for Janssen and Taro. He is a consultant and speaker for Galderma, Stiefel/GlaxoSmithKline, Abbott Labs, Leo Pharma Inc. Dr Feldman has received grants from Galderma, Janssen, Abbott Labs, Amgen, Stiefel/GlaxoSmithKline, Celgene, and Anacor. He is a consultant for Amgen, Baxter, Caremark, Gerson Lehrman Group, Guidepoint Global, Hanall Pharmaceutical Co Ltd, Kikaku, Lilly, Merck & Co Inc, Merz Pharmaceuticals, Mylan, Novartis Pharmaceuticals, Pfizer Inc, Quirient, Sun- care Research, and Xenopoint. He is on an advisory board for Pfizer Inc. Dr Feldman is the founder and holds stock in Causa Research and holds stock and is majority owner in Medical Quality Enhancement Corporation. He receives Royalties from UpToDate and Xlibris. Sara Moradi Tuchayi, Tiffany Alexander, and Anish Nadkarni have no conflicts of interest to disclose.

### References


21. Rueda MJ. Acne subject preference for pump over tube for dispensing fixed-dose combination adapalene 0.1%-benzoyl peroxide 2.5% gel. *Dermatol Ther (Heidel).* 2014;4(1):61–70.


