

Medication adherence among acne patients: a review

Robert Lott, MD,¹ Sarah L Taylor, MD, MPH,¹ Jenna L O'Neill, MD,¹ Daniel P Krowchuk, MD,^{1,4} & Steven R Feldman, MD PhD,^{1,2,3}

¹Department of Dermatology, Center for Dermatology Research, Wake Forest University School of Medicine, Winston-Salem, North Carolina, USA

²Department of Pathology, Center for Dermatology Research, Wake Forest University School of Medicine, Winston-Salem, North Carolina, USA

³Department of Public Health Sciences, Center for Dermatology Research, Wake Forest University School of Medicine, Winston-Salem, North Carolina, USA

⁴Department of Pediatrics, Center for Dermatology Research, Wake Forest University School of Medicine, Winston-Salem, North Carolina, USA

Summary

Background Acne is a chronic disease often requiring the use of medications for extended periods of time. In general, adherence decreases over time in patients with chronic diseases, and adherence to topical medications is poor compared to adherence to oral medications, placing individuals using topical medications at increased risk for nonadherence and treatment failure. Poor adherence may also be a common cause of treatment failure in teens with acne.

Purpose We reviewed the current literature on medication adherence in teenagers with acne to assess adherence levels and predictors of adherence. We hope to provide a foundation for further research into medication adherence in acne patients.

Methods A Medline search was conducted using the key words “acne” and “adherence” or “compliance.” Studies reporting adherence were included in the analysis.

Results A positive correlation was found between quality of life of patients with acne and medication adherence. Weaker predictors of adherence include increased age, female gender, and employment. The most commonly reported reason for nonadherence was inadequate time to use the treatment medication. Patients taking medications requiring less frequent dosing had better adherence, and medication adherence correlated with better health status among acne patients. A longer duration between office visits may be associated with decreased compliance.

Limitations Few studies investigating the prevalence and causes of nonadherence in acne patients were identified.

Conclusions Adherence to medications is difficult to measure and rates reported by patients often overestimate actual adherence. Patients cite lack of time as a common reason for nonadherence to topical medications.

Keywords: acne vulgaris, adherence, quality of life, medical therapy

Introduction

Acne vulgaris is a common skin condition affecting approximately 85% of people at some time in their lives.¹

Correspondence: Steven R. Feldman, Department of Dermatology, Wake Forest University School of Medicine, Medical Center Boulevard, Winston-Salem, NC 27157-1071, USA. E-mail: sfeldman@wfubmc.edu

Accepted for publication January 9, 2010

Acne is linked to poor quality of life and significant psychological problems.^{2,3} The psychological effects of acne on an individual may be varied and can include anger, sadness, frustration, and social avoidance. While acne is likely to eventually clear spontaneously, active disease and scarring may continue to persist for years, often well into adulthood.

The first-line treatment of milder forms of acne is topical medication with or without oral antibiotics.

Unfortunately, as is the case in many chronic diseases, acne treatment suffers due to poor medication adherence, a common cause of treatment failure. There are a number of reasons for poor adherence, including concerns about side effects, frustration with previous treatment failures, difficulty incorporating medication regimens into one's daily routine, and costs of treatment or lack of insurance. Failure of first-line drugs may result in costly visits and otherwise unnecessary exposure to higher doses of medications. Alternatively, should the patient become frustrated and cease treatment, psychological effects of untreated or undertreated acne will persist. Thus, further research into the causes of acne nonadherence and the development of interventions to improve acne adherence are important areas of research. The purpose of this article is to describe recent studies on rates and predictors of adherence to acne medications, and to serve as a basis for development of future research.

Methods

A Medline search was performed using the keywords (acne AND (adherence OR compliance)) from the

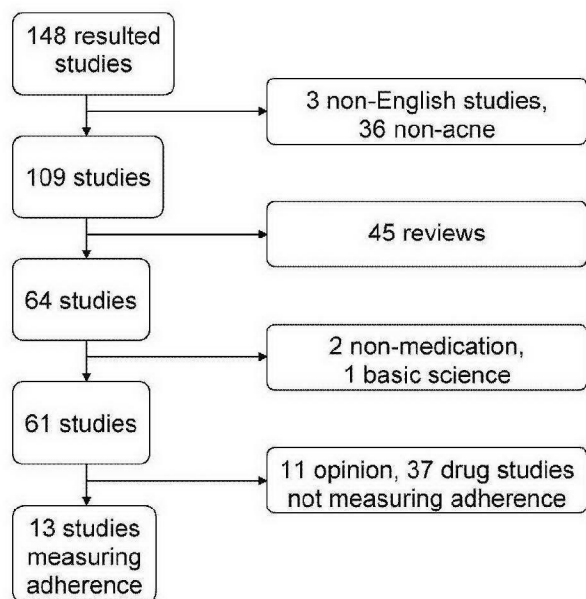


Figure 1 Acne adherence search results. Results of a Medline search using the keywords (acne AND (adherence OR compliance)) from the beginning of 1998 through September 1, 2008. Thirteen studies were reviewed that measured acne adherence, with results presented in Table 2.

beginning of 1998 through September 1, 2008. The search was limited to articles in English and to studies using humans. Studies were included if they reported medication adherence (Fig. 1). Of 148 studies initially identified, there were 63 English language studies excluding review articles. Of those, 13 studies were identified which measured adherence to acne treatments either subjectively or objectively. Four of these studies included only patients using topical medications without oral treatment or with stable long-term oral treatment. Five of these studies included patients initiating either topical or oral medications at the start of the study. No review articles were included in the results, but several were used as a source of background information. Figure 1 illustrates the literature search process.

Results

Six studies were identified that measured adherence by patient questionnaires, and two studies utilized patient diaries. The remaining five studies utilized various electronic methods to assess adherence, which are discussed below. These findings are summarized in Table 1. Tan *et al.*⁴ studied 287 teens with acne, of which 152 returned for follow-up at two months. Adherence was measured by a single question which asked subjects to rate as a percentage how often they used their medications as prescribed. Subjects reporting their medication usage as 100%, between 75% and 99%, and 74% and below were considered to have high, medium, and low adherence, respectively. Of the subjects returning for follow-up, 24% were rated as having high adherence, 49% were found to have medium adherence, and 26% were found to have low adherence. The most common reasons given for low adherence by subjects were side effects, forgetfulness, and lack of improvement. Sex, age, level of third party medication coverage, alcohol use, illicit drug use, tobacco use, and education level were not significantly associated with patient adherence. The authors concluded that adherence to topical acne therapy increases with impact on quality of life but decreases with increasing acne severity; seemingly contradictory statements since patients with more severe acne are likely to have a greater negative impact on quality of life. Additionally, those subjects who did not return for follow-up at study conclusion may have been less adherence than those who finished the study.

Eichenfield *et al.*⁵ performed an open-label, nonrandomized Phase 4 study to test the efficacy of tretinoin microsphere gel at 0.04% and 0.1% when used from a pump dispenser. The study population consisted of 544

Table 1 Summary of acne adherence study results.

Study author	Adherence assessment method	<i>n</i>	Adherence to treatment	Other results related to adherence
Tan <i>et al.</i> ⁴	Single question	287	24% rated as 100% adherent to therapy; 49% rated as 75%–99% adherent to therapy; 26% rated as <75% adherent to therapy.	152 of 287 subjects (53%) returned for follow-up; those who did not complete study may have lower adherence rates
Eichenfield <i>et al.</i> ⁵	Questionnaire	544	94.5%, 93.5%, 94.5% at weeks 3, 6, and 12, respectively, for patients using 0.04% tretinoin gel. 94.7%, 96.5%, 94.6% respectively for patients using 0.1% tretinoin gel	Nonadherent subjects could be removed from the study at investigator's discretion
Pawin <i>et al.</i> ⁶	Recall questionnaire	246	Topicals: 54% had good adherence; 46% had poor adherence. Combined oral and topicals: 81% had good adherence to one or both; 59% had poor adherence. Oral isotretinoin only: 96% had good adherence	Self-administered questionnaire was found to have a sensitivity of 0.47 and a specificity of 0.89 for detecting adherence
Jones-Caballero <i>et al.</i> ⁷	Single question	2221	57% reported medication adherence as "every day" and 38% as "almost every day"	Causes of nonadherence: most commonly "forgetting," "lack of time," and treatment being too boring
Rapp <i>et al.</i> ⁸	Single question	479	76% adherent "at least some of the time" (score of 3 or above on 5 point scale)	Sex, ethnicity, global health status, and acne severity are significant predictors of adherence; trait anger is not
Baker <i>et al.</i> ⁹	Questionnaire	2545	47% of subjects reported applying medication daily; 45% applied it almost daily	Phase 4, open-label study
Marazzi <i>et al.</i> ¹⁰	Patient diary cards	188	100% adherence reported in 55% of subjects using isotretinoin/erythromycin gel once daily versus 44% of subjects using benzoyl peroxide/erythromycin gel twice daily	Adherence improved with once daily treatment compared to twice daily therapy
Cunliffe <i>et al.</i> ¹¹	Patient diaries	246	Mean adherence rate among patients using clindamycin/zinc gel once daily, clindamycin/zinc gel twice daily, and dindamycin gel twice daily: 98%, 92%, and 92%, respectively	Efficacy and tolerability were equivalent among all treatment arms; once daily dosing may improve adherence
McEvoy <i>et al.</i> ¹²	No. of appointments kept during study period	144	28% kept all four appointments; 10% kept three appointments; 18% attended only the initial consultation appointment	Characteristics of subjects most likely to keep appointments: Caucasian, receiving isotretinoin, non-Medicaid insurance, reported their acne to be worse than their parent's acne
Zaghloul <i>et al.</i> ¹³	Pill counts, weighing of topical medications	403	Mean adherence reported as 64.7 ± 24%	Level of adherence has a direct linear relationship with a patient's quality of life
Cook-Bolden ¹⁴	Self-report and number of medication refills	1979	Adapalene only and add-on study arms adherence was 88.3% and 87% at 12 weeks, respectively. Objective adherence measured by prescription refills was 80.3% and 80.4%, respectively, at 12 weeks	Medication adherence decreases over time; patients may overestimate their own medication adherence
Balkrishnan <i>et al.</i> ¹⁵	Number of medication refills	~5 million	Average number of annual medication refills for acne per patient is 2.07	Patients refilling acne medications more often had better overall health status
Yentzer <i>et al.</i> ¹⁶	Electronic MEMS caps	11	82% adherent on day one; 45% at 6 weeks	Adherence to treatment decreases among adolescents as time since the last office visit increases

A total of 13 studies addressing acne adherence were selected for review. Studies are arranged by method of measuring adherence; methods ranged from single or multiquestion surveys to electronic monitoring systems. *n* = number of subjects, MEMS = Medication Event Monitoring System.

individuals with mild to moderate facial acne who were dissatisfied with their current acne treatment. The addition of the pump allowed a more precise amount of medication to be dispensed with each application. Additionally, subjects were allowed to use up to two other nonretinoid acne therapies concurrently. Compliance was assessed at weeks 3, 6, and 12 by subject responses to verbal questioning and grouped as: high compliance, 75–100% of doses taken; moderate compliance, 50–74% of doses taken; intermittent compliance, 25–49% of doses taken; and low compliance, less than 24% of doses taken. Noncompliant subjects could be removed from the study at the investigator's discretion. Compliance was measured as 94.5%, 93.5%, and 94.5% for individuals using the 0.04% gel at weeks 3, 6, and 12, respectively. For individuals using the 0.1% gel, 94.7%, 96.5%, and 94.6% of subjects were considered to be highly compliant at weeks 3, 6, and 12, respectively.

Pawin *et al.*⁶ created a tool designed to assess adherence to topical and oral medication usage in an outpatient office setting. They measured adherence by providing a self-administered questionnaire to 246 subjects returning for follow-up for acne treatment to determine their recall of the treatment prescribed. A subject who correctly named his or her treatment and answered the questions in a way that suggested use of medications as directed by a dermatologist was considered to have good adherence. If the subject was unable to describe his or her drug regimen or answered questions in a way that suggested he or she had not been using them as directed, the patient was considered to be poorly adherent. Of subjects using only topical medications, 54% had good adherence and 46% had poor adherence. Among those using a combination of oral and topical medications, 81% were considered to have good adherence to either the topical or oral aspect of their medication regimen while 59% were considered poorly adherent to one or both aspects of their treatment regimens. Ninety-six percent of subjects using only oral isotretinoin for their acne were considered to have good adherence to therapy.

Jones-Caballero *et al.*⁷ reported an analysis of a previously published observational, prospective, multicenter study of one oral and one topical acne medication used twice daily. There were 2221 subjects who participated in two office visits, one at the beginning and one at the end of the 12-week study. Adherence was measured subjectively by asking subjects to rate adherence as daily, almost daily, sometimes, or rarely. Daily or almost daily use was considered adherence and sometimes or rarely was considered nonadherence; overall 96.2% of subjects reported daily or almost daily use.

Adherent subjects were slightly older and had less severe acne than nonadherent subjects at the end of the study. Despite having objectively more severe acne than adherent males and females and nonadherent females, these subjects viewed their acne as less severe, and believed it had less impact on their emotional state and functioning. Nonadherent women were affected emotionally and functionally much more than adherent women. Nonadherent women felt their acne improved to a lesser extent than women who were adherent or mostly adherent. Sixty-five percent of patients listed "forgetting" as their main reason for nonadherence to treatment. Other reasons cited included "lack of time," being bored, and less commonly medication side effects. Males, younger patients, and unemployed patients had poorer adherence overall.

Rapp *et al.*⁸ assessed anger, global quality of life, skin-related quality of life, satisfaction, and adherence in 479 subjects with acne. Trait anger was measured with six items describing angry mood; subjects were asked to rate how often they experienced each mood, and the average rating was calculated to determine a mean trait anger score. Adherence was measured using a single question which asked the patient how often she had been adherent in the last week. Poor adherence was associated with male gender, nonwhite ethnicity, and poor overall health. More severe acne was also related to poorer adherence. A subject's level of anger was not significantly related to adherence although there was a trend towards poorer adherence among individuals with high trait anger.

Baker *et al.*⁹ reported a Phase IV multicenter non-comparative study with 2545 subjects participating in a 12-week open-label trial examining the efficacy and tolerability of once daily application of adapalene gel 0.1%. Adherence was assessed at the end of the study by a questionnaire. Overall 92% of the subjects reported themselves as always or almost always adherent, with the remainder of subjects reporting their medication adherence as sometimes or seldom.

A 12-week multicenter study of 188 patients with acne conducted by Marrazi *et al.*¹⁰ found that those applying isotretinoin/erythromycin gels once a day had a better compliance rate than patients applying benzoyl peroxide/erythromycin gel twice a day. Subjects in each group were given verbal and written instructions on how to apply the study medication, including storage of the benzoyl peroxide/erythromycin medication in a refrigerator (but not the isotretinoin/erythromycin product). Subjects returned for follow-up visits 2, 4, 8, and 12 weeks into the study. There was no statistically significant difference in the efficacy of the two

medications at 12 weeks as rated by subjects and by the investigators. Adherence to the study regimen was measured by patient diary cards filled out daily by participating subjects. Between 8 and 12 weeks, 55% of patients using isotretinoin/erythromycin gel and 44% of patients using benzoyl peroxide/erythromycin gel were 100% compliant, while 2% of patients using isotretinoin/erythromycin gel and 13% of patients using benzoyl peroxide/erythromycin gel were less than 50% compliant.

Cunliffe *et al.*¹¹ reported on the adherence among 246 subjects in a Phase III clinical trial assessing a new clindamycin/zinc product for the treatment of mild to moderate acne. Study subjects received topical clindamycin/zinc gel daily, clindamycin/zinc gel twice daily, or clindamycin lotion twice daily for 16 weeks. Adherence was recorded by patient diaries. Mean reported adherence rates were 98%, 92%, and 92%, respectively, for the three treatment groups.

Other methods used to measure medication adherence include appointment records, pharmacy refill records, and electronic adherence monitoring systems. McEvoy *et al.*¹² used appointment keeping as a measure of adherence to treatment. Pre- and posttreatment questionnaires assessing subjects' beliefs about acne treatment and adherence behaviors also were administered. A total of 144 patients participated in the study, and 97 returned the post-study questionnaire. Subjects were scheduled for a follow-up visit with a nurse 1 week after the initial visit; all other appointments were scheduled with a doctor every 4–6 weeks after the initial visit for a total of one nurse visit and four doctor visits. Eighteen percent of subjects did not return for any follow-up appointments, 13% returned only for the nurse visit, and 28% kept all four doctor appointments. The remainder of the subjects kept two or three visits, or dropped out of treatment and then returned later in the study. Subjects who were most likely to keep appointments were Caucasian, subjects with insurance other than Medicaid, women whose acne did not worsen with menses, and individuals who believed their acne to be worse than their parents' acne. Of the 65 subjects who did not keep all the appointments and returned poststudy questionnaires, 24 reported that they had kept all appointments. Age, sex, or acne severity did not correlate with individual likelihood of keeping follow-up appointments. Reasons given for failure to follow-up included not enough time to keep appointments, improvement of acne, financial reasons, and giving up because of no observed improvement.

Zaghoul *et al.*¹³ measured acne patient compliance in 403 subjects on oral isotretinoin or conventional

acne therapy via medication weight for topical medications and pill count for oral medications. The effects on adherence of patient's age, sex, isotretinoin vs. other medication use, and quality of life measured by the Dermatology Life Quality Index (DLQI) on adherence were assessed. The majority of subjects involved in this study were taking isotretinoin during the study; 19% used topical and oral medications other than isotretinoin. Nonadherent subjects were more likely to be young, single, male, unemployed, and to have personally paid for their medications. A distinct and significant negative correlation was found between medication adherence and quality of life. Adherence among subjects using topical and oral medications other than isotretinoin was 35.2% while adherence among isotretinoin subjects was 71.4%. The main reasons for missing treatment were frustration, forgetfulness, and being too busy. Medication adherence was assessed during an interview in which each subject was asked to assess how much medication he or she had used during the study.

The MORE (Measuring Acne Outcomes in a Real-World Experience) trial¹⁴ examined the efficacy, tolerability, patient satisfaction, and adherence of 1979 acne patients in two treatment arms: those using only adapalene 0.1% gel for their acne treatment, and those adding adapalene 0.1% gel to their current acne treatment regimen. Among the adapalene only and add-on study arms, self-reported medication adherence was 94.6% and 94.2%, respectively, at 6 weeks and 88.3% and 87%, respectively, at 12 weeks. Objective measurement of adherence based on number of prescriptions filled was 94% of the adapalene only and 92.8% of the add-on groups at 6 weeks and 80.3% and 80.4%, respectively, at 12 weeks.

A cross-sectional study by Balkrishnan *et al.*¹⁵ that examined the charts of 5.6 million acne patients reported a positive correlation between patient medication adherence, measured by pharmacy refills of acne medications, and better health status.

Yentzer *et al.*¹⁶ in a small study of 11 teenagers returning for follow-up, found after 6 weeks of therapy with once daily benzoyl peroxide a drop in adherence from 82% on the first day of treatment to 45% on the final day of the study. This study measured the adherence of study subjects without their knowledge until the end of the study and so attempted to replicate the conditions found in a nonresearch setting. Adherence was measured via the Medication Event Monitoring System (MEMS[®], AARDEX Corp., Fremont, CA, USA), which records the date and time when the cap on the medication tube is removed.

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts



Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research



With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips



Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS

Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS

Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS

Sync your system to PACER to automate legal marketing.