

A Review of Patient Adherence to Topical Therapies for Treatment of Atopic Dermatitis

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PRACTICE POINTS

- When used correctly, topical treatments for atopic dermatitis (AD) generally are straightforward and efficacious, but poor adherence to treatment can prevent patients from achieving disease control.
- Patients tend to overestimate their adherence to topical treatment regimens for AD compared to actual adherence rates.
- Improved treatment adherence in this patient population may be achieved by allowing patients to choose their preferred topical vehicle and providing patient education about how to apply medications effectively; for pediatric patients, AD action plans also may be useful.

Atopic dermatitis (AD) is one of the most commonly diagnosed dermatologic conditions in the United States. Topical agents are the mainstay of treatment for AD, and when used correctly, these therapies generally are straightforward and efficacious. However, poor adherence to treatment can prevent patients from achieving disease control. This article provides a review of the literature on patient adherence to topical therapies for AD as well as a discussion of methods to improve patient adherence to treatment in the clinical setting.

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Atopic dermatitis (AD) is a chronic inflammatory skin disease that typically begins in early childhood (Figure). It is one of the most commonly diagnosed dermatologic conditions, affecting up to 25% of children and 2% to 3% of adults in the United States.^{1,2} The mainstays of treatment for AD are topical emollients and topical medications, of which corticosteroids are most commonly prescribed.³ Although treatments for AD generally are straightforward and efficacious when used correctly, poor adherence to treatment often prevents patients from achieving disease control.⁴ Patient adherence to therapy is a familiar challenge in dermatology, especially for diseases like AD that require long-term treatment with topical medications.^{4,5} In some instances, poor adherence may be misconstrued as poor response to treatment, which may lead to escalation to more powerful and potentially dangerous systemic medications.⁶ Ensuring good adherence to treatment leads to better outcomes and disease control, averts unnecessary treatment, prevents disease complications, improves quality of life, and decreases treatment cost.^{4,5} This article provides a review of the literature on patient adherence to topical therapies for AD as well as a discussion of methods to improve patient adherence to treatment in the clinical setting.



Atopic dermatitis on the bilateral popliteal fossae. Photograph printed with permission from the Graham Dermatopathology Archive, Wake Forest University School of Medicine, Winston-Salem, North Carolina.

Methods

A PubMed search of articles indexed for MEDLINE from January 2005 to May 2015 was conducted to identify studies that focused on treatment adherence in AD using the search terms *atopic dermatitis* and *medication adherence* and *atopic dermatitis* and *patient compliance*. After excluding duplicate results and those that were not in the English language, a final list of clinical trials that investigated patient adherence/compliance to topical medications for the treatment of AD was extracted for evaluation.

Results

Our review of the literature yielded 7 quantitative studies that evaluated adherence to topical medications in AD using electronic monitoring and/or self-reporting (Table).⁷⁻¹³ Participant demographics, disease severity, drug and vehicle used, duration of treatment, and number of follow-up visits varied. All studies used medication event monitoring system caps on medication jars to objectively track patient adherence by recording the date and time when the cap was removed. To assess disease response, the studies used such measures as the Investigator Global Assessment scale, Eczema Area and Severity Index score, or other visual analog scales.

In all of the studies, treatment proved effective and disease severity declined from baseline regardless of the rate of adherence, with benefit continuing after treatment had ended.⁷⁻¹³ Some results suggested that better adherence increased treatment efficacy and reduced disease severity.^{8,9} However, one 10-day trial found no difference in severity and efficacy among participants who applied the medication

at least once daily, missed applications some days, or applied the medication more than twice daily.¹³

Study participants typically overestimated their adherence to treatment compared to actual adherence rates, with most reporting near 100% adherence.^{7-9,11,12} Average measured adherence rates ranged from 32% to 93% (Table). Adherence rates typically were highest at the beginning of the study and decreased as the study continued.⁷⁻¹³ The study with the best average adherence rate of 93% had the shortest treatment period of 3 days,¹¹ and the study with the lowest average adherence rate of 32% had the longest treatment period of 8 weeks.⁷ The study with the lowest adherence rate was the only study wherein participants were blinded to their enrollment in the study, which would most closely mimic adherence rates in clinical practice.⁷ The participants in the other studies were not aware that their adherence was being monitored, but their behavior may have been influenced since they were aware of their enrollment in the study.

Many variables affect treatment adherence in patients with AD. Average adherence rates were significantly higher ($P=.03$) in participants with greater disease severity.⁷ There is conflicting evidence regarding the role of medication vehicle in treatment adherence. While Wilson et al⁹ did not find any difference in adherence based on medication vehicle, Yentzer et al¹² found vehicle characteristics and medication side effects were among patients' top-ranked concerns about using topical medications. Sagrafsky et al¹⁰ compared treatment adherence between 2 groups of AD patients: one control group received a standard-of-care 4-week follow-up, and an active group received an additional 1-week follow-up. The mean adherence rate of the treatment group was 69% compared with 54% in the control group.¹⁰

Comment

Poor adherence to treatment is a pervasive problem in patients with AD. Our review of the literature confirmed that patients generally are not accurate historians of their medication usage, often reporting near-perfect treatment adherence even when actual adherence is poor. Rates of adherence from clinical trials are likely higher than those seen in clinical practice due in part to study incentives and differences between how patients in a study are treated compared to those in a physician's clinic; for example, research study participants often have additional follow-up visits compared to those being treated in the clinical population and by virtue of being enrolled in a study are aware that their behavior is being monitored, which can increase treatment adherence.⁷

The dogma suggesting that tachyphylaxis can occur with long-term use of topical corticosteroids

is not supported by clinical trials.¹⁴ Furthermore, in our review of the literature patient adherence was highest in the shortest study¹¹ and lowest in the longest study.⁷ Given that AD patients cannot benefit from a treatment if they do not use it, the supposed decrease in efficacy of topical corticosteroids over time may be because patients fail to use them consistently.

Our review of the literature was limited by the small body of research that exists on treatment adherence in AD patients, especially relating to topical medications, and did not reveal any studies evaluating systemic medications in AD. Of the studies we examined, sample sizes were small and treatment and follow-up periods were short. Our review only covered adherence to prescribed topical medications in

AD, chiefly corticosteroids; thus, we did not evaluate adherence to other therapies (eg, emollients) in this patient population.

The existing research also is limited by the relative paucity of data showing a correlation between improved adherence to topical treatment and improved disease outcomes, which may be due to the methodological limitations of the study designs that have been used; for instance, studies may use objective monitors to describe daily adherence to treatment, but disease severity typically is measured over longer periods of time, usually every few weeks or months. Short-term data may not be an accurate demonstration of how participants' actual treatment adherence impacts disease outcome, as the data does not account for more complex adherence factors; for example,

Studies Investigating Adherence to Topical Treatments in Pediatric Patients with Atopic Dermatitis

Reference (Year)	Study Design	Study Drug	Total No. of Participants	Treatment Duration, d	Disease Severity	Rate of Adherence, % ^a
Krejci-Manwaring et al ⁷ (2007)	Single center, open label, prospective	Triamcinolone ointment 0.1%	37	56	Mild to moderate	32
Conde et al ⁸ (2008)	Single center, open label, investigator blinded, prospective	Clocortolone pivalate cream 0.1%	10	28	Mild to moderate	70
Wilson et al ⁹ (2009)	Randomized, investigator blinded, prospective	Hydrocortisone 17-butyrate 0.1% (cream, lipocream, or ointment)	25 (cream, 9; lipocream, 9; ointment, 7)	14	Mild to moderate	70
Sagransky et al ¹⁰ (2010)	Randomized, controlled, open label, pilot	Tacrolimus ointment 0.03%	30 (active treatment, 15; control, 15)	28	Moderate to severe	69 (active treatment), 54 (control)
Yentzer et al ¹¹ (2010)	Open label, prospective	Fluocinonide cream 0.1%	20	3	Mild to severe	93
Yentzer et al ¹² (2010)	Open label, prospective	Desonide hydrogel 0.05%	41	28	Mild to moderate	50
Hix et al ¹³ (2013)	Single center, prospective, open label	Fluocinonide cream 0.1%	10	5	Mild to moderate	60 ^b

^aMean adherence rate unless otherwise noted.

^bMedian adherence rate.

participants who achieve good disease control using topical corticosteroids for an 8-week study period may actually demonstrate poor treatment adherence overall, as topical corticosteroids have good short-term efficacy and the patient may have stopped using the product after the first few weeks of the treatment period. In contrast, poorly adherent patients may never use the medication well enough to achieve improvement and may continue low-level use throughout the study period. Therefore, studies that measure disease severity at more regular intervals are required to show the true effect of treatment adherence on disease outcomes.

Since AD mainly affects children, family issues can pose special challenges to attaining good treatment adherence.^{15,16} The physician–patient (or parent) relationship and the family’s perception of the patient’s disease severity are strong predictors of adherence to topical treatment.¹⁶ Potential barriers to adherence in the pediatric population are caregivers with negative beliefs about treatment, the time-consuming nature of applying topical therapies, or a child who is uncooperative.^{15,17} In the treatment of infants, critical factors are caregiver availability and beliefs and fears about medications and their side effects, while in the teenage population, the desire to “fit in” and oppositional behavior can lead to poor adherence to treatment.¹⁷ Regardless of age, other barriers to treatment adherence are forgetfulness, belief that the drug is not working, and the messiness of treatment.¹⁷

Educational tools (eg, action plans, instructions about how to apply topical medications correctly) may be underutilized in patients with AD. If consistently implemented, these tools could have a positive impact on adherence to medication in patients with AD. For example, written action plans pioneered in the asthma community have shown to improve quality of life and reduce disease severity and may offer the same benefits for AD patients due to the similarities of the diseases.¹⁸ Since AD patients and their caregivers often are not well versed in how to apply topical medications correctly, efforts to educate patients could potentially increase adherence to treatment. In one study, AD patients began to use medications more effectively after applying a fluorescent cream to reveal affected areas they had missed, and clinicians were able to provide additional instruction based on the findings.¹⁹

Adherence to topical treatments among AD patients is a multifactorial issue. Regimens often are complex and inconvenient due to the need for multiple medications, the topical nature of the products, and the need for frequent application. To optimize prescription treatments, patients also must be diligent with preventive measures such as application of

topical emollients and use of bathing techniques (eg, bleach baths). A way to overcome treatment complexity and increase adherence may be to provide a written action plan and involve the patient and caregiver in the plan’s development. If a drug formulation is not aesthetically acceptable to the patient (eg, the greasiness of an ointment), allowing the patient to choose the medication vehicle may increase satisfaction and use.¹² Fear of steroid side effects also is common among patients and caregivers and could be overcome with education about the product.²⁰

Conclusion

Treatment adherence can have a dramatic effect on diseases outcomes and can be particularly challenging in AD due to the use of topical medications with complex treatment regimens. Additionally, a large majority of patients with AD are children, from infants to teenagers, adding another layer of treatment challenges. Further research is needed to more definitively develop effective methods for enhancing treatment adherence in this patient population. Although enormous amounts of money are being spent to develop improved treatments for AD, we may be able to achieve far more benefit at a much lower cost by figuring out how to get patients to adhere to the treatments that are already available.

REFERENCES

1. Eichenfield LF, Tom WL, Chamlin SL, et al. Guidelines of care for the management of atopic dermatitis: section 1. diagnosis and assessment of atopic dermatitis. *J Am Acad Dermatol*. 2014;70:338-351.
2. Landis ET, Davis SA, Taheri A, et al. Top dermatologic diagnoses by age. *Dermatol Online J*. 2014;20:22368.
3. Eichenfield LF, Tom WL, Berger TG, et al. Guidelines of care for the management of atopic dermatitis: section 2. management and treatment of atopic dermatitis with topical therapies. *J Am Acad Dermatol*. 2014;71:116-132.
4. Lee IA, Maibach HI. Pharmionics in dermatology: a review of topical medication adherence. *Am J Clin Dermatol*. 2006;7:231-236.
5. Tan X, Feldman SR, Chang J, et al. Topical drug delivery systems in dermatology: a review of patient adherence issues. *Expert Opin Drug Deliv*. 2012;9:1263-1271.
6. Sidbury R, Davis DM, Cohen DE, et al. Guidelines of care for the management of atopic dermatitis: section 3. Management and treatment with phototherapy and systemic agents. *J Am Acad Dermatol*. 2014;71:327-349.
7. Krejci-Manwaring J, Tusa MG, Carroll C, et al. Stealth monitoring of adherence to topical medication: adherence is very poor in children with atopic dermatitis. *J Am Acad Dermatol*. 2007;56:211-216.
8. Conde JF, Kaur M, Fleischer AB Jr, et al. Adherence to clocortolone pivalate cream 0.1% in a pediatric population with atopic dermatitis. *Cutis*. 2008;81:435-441.

9. Wilson R, Camacho F, Clark AR, et al. Adherence to topical hydrocortisone 17-butyrate 0.1% in different vehicles in adults with atopic dermatitis. *J Am Acad Dermatol*. 2009;60:166-168.
10. Sagrafsky MJ, Yentzer BA, Williams LL, et al. A randomized controlled pilot study of the effects of an extra office visit on adherence and outcomes in atopic dermatitis. *Arch Dermatol*. 2010;146:1428-1430.
11. Yentzer BA, Ade RA, Fountain JM, et al. Improvement in treatment adherence with a 3-day course of fluocinonide cream 0.1% for atopic dermatitis. *Cutis*. 2010;86:208-213.
12. Yentzer BA, Camacho FT, Young T, et al. Good adherence and early efficacy using desonide hydrogel for atopic dermatitis: results from a program addressing patient compliance. *J Drugs Dermatol*. 2010;9:324-329.
13. Hix E, Gustafson CJ, O'Neill JL, et al. Adherence to a five day treatment course of topical fluocinonide 0.1% cream in atopic dermatitis. *Dermatol Online J*. 2013;19:20029.
14. Taheri A, Cantrell J, Feldman SR. Tachyphylaxis to topical glucocorticoids; what is the evidence? *Dermatol Online J*. 2013;19:18954.
15. Santer M, Burgess H, Yardley L, et al. Managing childhood eczema: qualitative study exploring carers' experiences of barriers and facilitators to treatment adherence. *J Adv Nurs*. 2013;69:2493-2501.
16. Ohya Y, Williams H, Steptoe A, et al. Psychosocial factors and adherence to treatment advice in childhood atopic dermatitis. *J Invest Dermatol*. 2001;117:852-857.
17. Ou HT, Feldman SR, Balkrishnan R. Understanding and improving treatment adherence in pediatric patients. *Semin Cutan Med Surg*. 2010;29:137-140.
18. Chisolm SS, Taylor SL, Balkrishnan R, et al. Written action plans: potential for improving outcomes in children with atopic dermatitis. *J Am Acad Dermatol*. 2008;59:677-683.
19. Ulf E, Maroti M, Serup J. Fluorescent cream used as an educational intervention to improve the effectiveness of self-application by patients with atopic dermatitis. *J Dermatolog Treat*. 2013;24:268-271.
20. Aubert-Wastiaux H, Moret L, Le Rhun A, et al. Topical corticosteroid phobia in atopic dermatitis: a study of its nature, origins and frequency. *Br J Dermatol*. 2011;165:808-814.