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REVIEW

To Follow or Not to Follow Dermatological Treatment – A Review of the Literature

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Creams, ointments and solutions applied to the skin surface by patients as part of a daily routine might be expected to provide a more variable dosage than do standard tablets. However, adherence to treatment in dermatology has been little studied. This article reviews recent publications in the field. These are dominated by questionnaire-based studies, which tend to over-estimate adherence. Reduced adherence to dermatological treatment is noted in 34–45% of patients. It is likely that the percentage of patients who practice truly optimal treatment in their daily life is even lower considering the variable practice of self-treatment. Self-reported psychiatric morbidity contributes to poor adherence to dermatological treatment, while a well-functioning doctor–patient interaction is a major determinant of good adherence, as is patient satisfaction. In conclusion, adherence to dermatological treatment is unsatisfactory and there is a need for intervention and change in clinical routines. The therapeutic and economic benefits may be considerable. The immediate challenge is to stimulate a change in patient behaviour and improve self-treatment at home. ***Key words: adherence; concordance; compliance; local therapy; cream; ointment; solution.***

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Adherence to treatment refers to the extent to which a patient's medicine-taking behaviour coincides with what has been decided in "concordance" with the provider. The term "adherence" is now gradually replacing the well-known term "compliance", since the latter represents a paternalistic view of the patient. A recent World Health Organization (WHO) report highlights adherence to drug treatment in chronic disease as one of the major issues limiting efficient healthcare delivery to the population (1) and leading to disease-related medical costs (2) due to improper cure, additional consultations and treatments and loss of income.

Reports of non-adherence are in the range 20–80%, with an estimated average of 50%. According to the WHO review, poor adherence is associated with long-term regimens, asymptomatic disease, regimen complexity (number of medications per day), unstable housing, mental illness, major life crises and alcoholism. Good adherence is associated with more severe symptoms or illness, knowledge about and belief in efficacy of treatment, adequate social support and trust in the clinician (1). When trying to understand adherence, both the patients' practical ability to take their medicine as instructed and their motivation to follow the treatment have to be considered (3). Unintentional non-adherence is linked to problems of ability, while deliberate non-adherence depends on motivation. The individual patient's own assessment of the perceived advantages and disadvantages of a certain treatment influences the motivation to adhere.

The magnitude of the problem of poor adherence to topical therapy in dermatology is little documented, albeit recognized in the clinic. Over the last decades, approximately 10 studies on adherence in dermatology have been published, contrasting with the total number of some 15,000 references about adherence in the medical literature as a whole. Although the number of studies is scarce, adherence to dermatological treatment is gaining increasing attention; the topic was addressed in a workshop organized by the European Academy of Dermatology and Venereology in 1998, and in the Dowling Oration given by Dr A. Y. Finlay in 2000 (4, 5). Chren recently addressed the problem in an editorial in the *Archives of Dermatology* (6).

The aim of this review is to summarize the findings from original studies assessing the level of adherence to dermatological therapy, identifying factors associated with adherence to dermatological treatment, and evaluating interventions aimed at improving adherence.

METHODS

The following databases were searched for articles on adherence to dermatological treatment published between 1966 and 2004: Amed, Cinahl, Embase, Eric, Psychinfo, Pubmed, and SCI/SSCI/Art&Hum (search terms: dermatology; skin disease;

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adherence; concordance; compliance; topical therapy). In total, 112 hits were traced. Only publications based on original data were included in this review.

LITERATURE COMPILATION

Impact of non-adherence on treatment outcomes

Only one paper studying how non-adherence to topical treatments impacts on treatment outcomes was found. A 10% decrease in adherence to topical treatment for psoriasis (salicylic acid plus topical tacrolimus) increases disease severity corresponding to 1 point on a 9-point disease severity scale, while decreased adherence to placebo treatment (salicylic acid plus tacrolimus' vehicle) does not (7).

Degree of adherence and factors associated with adherence to dermatological treatment

The rate of adherence to dermatological treatment varies between 55% and 66% depending on population and measurement method used (7–11), meaning that the treatment effect is jeopardized in 34–45% of patients. Adherence to topical treatment tends to be lower than for other dosage forms (12). The number and length of treatment gaps in topical therapy increase with increasing time on treatment and often occur at weekends (8).

Self-reported psychiatric morbidity (broadly defined) is a major determinant of poor adherence to dermatological treatment (10), while a well-functioning doctor–patient interaction, on the premises of the patient, is a major determinant of good adherence (13), as is patient satisfaction (10). Patient satisfaction correlates with the patient's rating of the doctor's concerns for their health, the quality of the doctor's explanation about their skin problem, and the quality of the doctor's answers to their questions (14).

Phobia of topical corticosteroids may have a negative impact on treatment adherence. A quarter of patients with atopic eczema admit that they have been non-adherent to topical corticosteroid treatment because of concerns about skin thinning and systemic effects on growth and development (15).

Demographic variables (e.g. sex, age and educational level) and disease severity seem to play a variable, minor or no role for adherence to dermatological treatment. While these factors had no impact on adherence in a study of patients with a variety of dermatological conditions (10), studies of psoriatic patients show that non-adherers are significantly younger (8, 11) and male (8). Furthermore, psoriatic non-adherers have a younger age at onset of disease and a higher self-rated severity of the disease (11).

In a study of children with atopic eczema (13), self-efficacy, parents' co-operation, resentment against treatment, reluctance to bathe, late bedtimes, lack of social support, worry about eczema, feelings of victimization, and perceived severity, were factors associated with adherence. The strongest predictor of adherence to skin-care treatment was a good doctor–patient (mother) relationship, followed by the severity of the disease as perceived by the mother. Adherence was not influenced by concerns about costs.

Impact of topical treatment on patients' daily life

Application of topical drugs is cumbersome and time-consuming. Treatment itself causes problems for the patients, although problems caused by the disease itself are a major concern. The length of time taken to use the treatments each day may vary between 1 min and 3 h 25 min (mean 38 min) for psoriatic patients, and 26% of patients find the time taken to apply the treatment too long (11). Between 8% (16) and 13% (17) of psoriatic patients find the unpleasantness of treatment the worst aspect of their psoriasis. However, 84% of patients perceive the consequences of the disease on their social life as an even worse aspect (17). Cosmetic factors, symptoms and embarrassment are perceived as the worst aspects in 33%, 25% and17% of the patients, respectively. Lifestyle is affected in 67% of patients (16).

Interventions to improve adherence

Provision of instructions by the prescribing doctor on how to apply the topical drug, how much and how often, is highly variable and often imprecise (18). For example, according to one study less than 5% of parents of children with atopic eczema had received, or recalled receiving, any information about the causes of eczema or how to apply topical treatments (19). Furthermore, 25% of the children were not treated with an emollient, while 25% were inappropriately treated with potent corticosteroids. The eczema was poorly controlled in all children.

A number of interventions have been tested in order to improve the quality of treatment of dermatological conditions. Interventions consisting of in-depth treatment instructions, intensified follow-up and advice about liberal application of the topical treatment may result in marked improvement in cases that were responding poorly to the same active agent before the intervention (18).

In a study of patients with acne, intensified treatment instructions using education materials (a booklet and a videotape) resulted in a 66% improvement in adherence, as assessed by the treating doctors, and a 38% decrease in patient calls (20). A randomized controlled study confirms that patient knowledge about topical treatment (with corticosteroids) increases if either written or oral

information is provided by the doctor, while a combination of both is most effective (21).

So-called "eczema schools" may also contribute to improved treatment. Following explanation and demonstration of topical therapies by a specialist nurse there was an 89% reduction in the severity of childhood atopic eczema, the main change being an eight-fold increase in the use of emollients (19). Randomized controlled studies confirm that eczema schools run by nurses have a positive impact on the therapeutic effect in children with atopic dermatitis (22), although the effect on their quality of life is marginal (23). A parental training program delivered by a multidisciplinary team (paediatricians, psychologists and nutritionists) also improved adherence, patient satisfaction and treatment costs, but had no effect on disease severity or quality of life (24).

Methodological considerations

Most of the studies included in this review have used questionnaires where the patients respond to issues that are pre-defined by the researcher. Only one study used anonymous questionnaires.

Self-reported adherence estimates may be biased due to social desirability, giving an over-estimate of medicine use. In their answer to a questionnaire, dermatology patients do not report the quality of their application of the topical treatment. The dose variability relates to the imprecise spread of the product on the skin surface. Non-adherent patients, who do not even collect the medicine from the pharmacy, are unlikely to respond to a questionnaire and are thereby not included in these studies. Taking all these practical aspects into consideration, non-adherence is likely to be more frequent than these studies suggest.

DISCUSSION

According to the review, application of a topical drug is cumbersome and instructions from the prescribing doctor on how to apply the treatment, how much and how often, are highly variable. Manual application of a topical treatment to the skin by patients, being a trivial routine, would be expected to provide a highly variable dosage. Provision of detailed instructions on how to apply a topical treatment correctly is normally outside the scope of a dermatology consultation. The dose variability related to topical application of cream, ointment or solution is often neglected. Topical drugs can be applied under visual control to the anterior aspect of the body and extremities and to the face, representing about 50% of the integument, while application to the posterior aspect and the scalp cannot be made with the same precision. Creams and solutions have to be spread rapidly, as evaporation of emulsion water or alcoholic solvent occurs within only 3–5 min, leading to increased viscosity and reduction in the ability of the formulation to be spread (24–26). The "fingertip unit", which was developed to standardize local application, does not appeal to the average patient and has not become popular; it only defines how much to apply (27).

There may also be uncertainty about the optimal dose and the degree of imprecise local application, which is associated with inferior therapeutic effect. Dose titration studies are now mandatory in drug approvals for substantiation of the product claim and an authorized product recommendation. The acceptable unevenness of application probably varies between active agents and formulations and for between individuals, indications and body sites. In dose-titration studies typically a 2–4 times difference in concentration of the active agent for a topical drug will be associated with a measurable difference in efficacy in clinical trials. This would, since self-application is likely to be highly variable, indicate that treatment failure due to improper dose is common and often a direct result of inferior application practice.

There remains much uncertainty about recommended standards for the use of local corticosteroids. The issue is difficult to resolve because of the many confounding factors affecting the clinical endpoint, i.e. improvement or cure of disease. These factors include inter-individual and regional variation in drug penetration into the skin, and disease severity as a spontaneously moving target. The patient's attitude, including phobia of corticosteroids, with under-treatment due to unrealistic fear of skin thinning, rebound dermatitis mimicking disease and, finally, so-called tachyphylaxis, i.e. a desensitization to the effect of the active substance, also affect the treatment results (15, 28, 29). Declining effectiveness of a treatment due to tachyphylaxis or inferior adherence cannot be separated in clinical practice. Furthermore, there may be a ten-fold difference in skin penetration of a corticosteroid depending on body site (30). The corticosteroids exemplify that one optimal dose of a topical treatment is not always identified or realistic. The relationship between a variably applied dose due to poor adherence and poor efficacy may consequently be equally difficult to identify. The prescribing doctor can operate only on rational grounds by using a consistent treatment recommendation over a certain period, and monitor the individual response under the assumption that the patient applies the medication as agreed.

Adherence in dermatology may be measured in different ways: by self-report (questionnaires or diaries in which daily use of medications is recorded), or by using an "objective" method, such as measuring serum concentrations of the drug, counting/weighing remaining medicine, electronic monitoring, or measuring disease improvement (31, 32). Topical medication adherence

has been found to be overestimated when based on patient reports, while electronic monitoring allows for a higher detection rate of missed doses (32). All these methods have their strengths and weaknesses, and may disclose important aspects of the problem under the defined study conditions. However, the patients' perceptions, motivation and knowledge about the problem are difficult to depict. There is clearly a need for in-depth qualitative methods. Methods such as focus group interviews have been developed by other academic disciplines to outline complex problems. The qualitative approach may, due to the explorative character of the method, be a better and more productive instrument in the understanding of motives behind patient adherence in dermatology than the traditional quantitative study design with pre-defined study criteria.

Different strategies have been used to increase adherence to long-term treatment in general. Most interventions that have proved to be effective are complex and include combinations of more convenient care, information, reminders, self-monitoring, reinforcement, counselling, family therapy and other forms of additional supervision or attention by a healthcare provider (physician, nurse, pharmacist, etc.). However, the effects of these interventions are generally weak, and further innovations to assist patients to follow medication are warranted (33). In a study of patients with acne, it was concluded that patients learn better from other patients than from doctors. The following suggestions were made: do not overload patients with data – the average patient can absorb about three take-home messages; evaluate the patient's learning and allow the patient to ask questions; provide information at the appropriate reading/hearing/thinking level for the patient; and finally, provide information for home reference (20).

Fortunately, several factors that impact on adherence to dermatological treatment according to this review are amenable to change. Increased effort may be put into detecting and attending to psychiatric morbidity in dermatological patients and in improving the patient–provider relationship and patient satisfaction. Eliciting patient perceptions is important, since a patient may balance the advantage of the treatment against perceived disadvantages, e.g. the inconvenience of the treatment and fear of corticosteroids, in deciding whether they intend to follow the treatment. A qualitative study of dermatology patients and their providers confirms the importance of enhanced communication skills among the providers, but also the need for individualized patient education and continuous treatment support (34). Dermatologists, dermatology nurses and pharmacists must co-ordinate their efforts in order to form an effective treatment support network for the patients (35). Thus, the focus should be not only on treatment initiation, but also on close monitoring of the patient's self-treatment with due attention to psycho-social factors. In securing the quality of care in these aspects, a more holistic approach to patients and their self-treatment at home is likely to improve adherence to dermatological treatment.

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