

Comparison of Different Compliance Behaviors in a Clinical Trial

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Demographics, regimen complexity, patient attitude, disease severity, and psychology determine a patient's adherence (ie, compliance) behavior. In a study of 30 patients with moderate to severe hand dermatitis, we found 2 extremes of adherence behavior: overusage and underusage. We compared these 2 patients to one patient who engaged in near-ideal usage of medication.

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Medication nonadherence is a common medical problem. Whether it is intentional or unintentional, nonadherence can lead to unnecessary treatments, costs, and side effects. We performed a pilot study on 30 patients with moderate to severe hand dermatitis. They were given a 3-week prednisone taper (week 1, 30 mg/d; week 2, 20 mg/d; week 3, 10 mg/d) and simultaneous (concomitant) topical tacrolimus ointment 0.1% or vehicle to apply twice daily for 12 weeks. Adherence to oral and topical medication was monitored by self-report, pill counts, medication weights (for topical therapy), and a Medication Event

Monitoring System[®] (MEMS). Although patients were informed that their compliance was going to be monitored, they were not informed that their behavior was going to be electronically monitored. The MEMS cap monitors adherence by time stamping. Whenever a patient removes the cap from the bottle, a microchip embedded within the cap records the date and time of the opening and stores the information in its memory. The information is then downloaded onto PowerView software when the patient returns to the physician's office for follow-up and can be displayed in various graphic formats.

Adherence rates were calculated from the MEMS caps in 2 ways: (1) "percent doses" of prescribed doses taken (ie, the number of cap openings divided by the number of prescribed doses within a specific time period) and (2) "percent days" (ie, the number of days that the correct number of cap openings were recorded divided by the number of days within the specific time period). Upon completion of the study, we found 2 extremes of adherence behavior: overusage and underusage. We compared these 2 patients to one patient who engaged in near-ideal usage of medication.

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Case Reports

Patient 1 (Underusage of Medication)—A 70-year-old Chinese woman presented with moderate hand dermatitis. Her medical history included hypertension, hypercholesterolemia, and type II diabetes. The patient had limited understanding of the English language and her husband, another study participant, was her translator. Of note, her husband, a physician and a diabetic, enrolled in the study 2 months earlier and experienced hyperglycemia while on prednisone. He subsequently received a reduced dose of prednisone.

At baseline, the patient received one bottle containing a 3-week tapering course of prednisone tablets (10-mg tablets) and one bottle containing

60 g of ointment; both were fitted with MEMS caps. At week 1, the patient reported that her husband had instructed her to take a reduced dose of prednisone (10 mg/d for week 1 and 5 mg/d for weeks 2 and 3) as a precaution. She recorded this information in her medication log. The dosage was subsequently approved by the investigating physician. The patient used approximately 20 g of ointment and her disease improved to mild. Between visits at weeks 4, 8, and 12, she used approximately 60 g of ointment, but her condition reverted to moderate severity. Pill counts were performed at week 4, at which time her bottle was empty.

Her mean adherence rate as measured by the MEMS cap for prednisone for percent doses and percent days was 9% and 5%, respectively. For topical therapy, her mean adherence rate for percent doses and percent days was 23% and 6%, respectively. The patient log indicated that her adherence to prednisone and ointment was 100%. The patient had opened the cap on her prednisone bottle only once in the 3 weeks, presumably at which time she dumped the medication. Upon completion of the study, she denied using any sort of pill organizing system and insisted she took the pills from the bottle each day. For 168 possible doses of ointment (twice daily for 12 weeks), the patient had opened the bottle only 39 times.

Patient 2 (Overusage of Medication)—A 54-year-old black woman presented with moderately severe hand dermatitis. She was a hairdresser but was unable to work because of her condition. She had no other history of hand dermatitis. The investigator noted that she was a nervous individual and admitted to compulsive behavior (excessive hand washing). She was extremely concerned about her personal hygiene, despite reassurance that hand dermatitis was not caused by “bugs.”

At baseline, she was given one bottle containing a 3-week tapering course of prednisone tablets (10-mg tablets) and one bottle containing 60 g of ointment. Both bottles were fitted with MEMS caps. At week 1, she had used approximately 20 g of ointment and had moderate improvement of her disease. She also stated she frequently washed her hands and used alcohol-based hand sanitizer because she felt her hands were dirty. Thirty grams of ointment was added to her bottle (bottle weight 81.1g).

At week 4, she returned the empty pill and ointment bottles. The patient stated she had run out of ointment 7 days before her appointment. Her hand dermatitis was moderately severe. Her bottle was refilled with 90 g of ointment. At week 8, she again returned an empty ointment bottle and her hands had mild disease. She was then given another

90 g of ointment. At week 12, her bottle was empty once again and her condition had reverted to moderately severe. The patient then discontinued the study but returned her medication bottles and log book.

Her mean adherence rate as measured by the MEMS cap for prednisone for percent doses and percent days was 114% and 86%, respectively. For topical therapy, her mean adherence rate for percent doses and percent days was 246% and 8%, respectively. By patient log, her adherence to prednisone and ointment was 100% and 79%, respectively; however, she had stopped recording her usage after 4 weeks. The extremely high adherence rate for percent doses (246%) resulted from frequent cap openings. The patient had opened the ointment bottle as many as 8 to 14 times daily. The extremely low adherence rate for percent days (8%) resulted from the rare occasions when the bottle was opened only twice daily, as prescribed.

Patient 3 (Near-Ideal Usage of Medication)—A 48-year-old white woman presented with moderate hand dermatitis. She had a college education, held a professional job, and learned of the study from a newspaper advertisement. Her medical history included seasonal allergies and depression. She was polite and reserved, always on time, and brought her study supplies to every scheduled visit. The patient was given the same amount of prednisone and ointment at baseline as the other patients. Her disease severity improved to mild at week 1, flared to moderate at week 4, and improved again to mild by week 12. She had used approximately 20 g of ointment at week 1 and 40 g at weeks 4, 8, and 12.

Her mean adherence rate as measured by the MEMS cap for prednisone for percent doses and percent days was 95% and 95%, respectively. For topical therapy, her mean adherence rate for percent doses and percent days was 96% and 45%, respectively. By patient log, her adherence to prednisone and ointment was 100%.

Comment

There are many factors that are considered when determining patient adherence. All 3 subjects were women and all had been randomized to receive topical tacrolimus, not the vehicle. In the first case, the patient was older, had a language barrier, was worried about side effects, and took multiple other medications. The second patient was anxious and unconvinced of the noninfectious etiology of her disease. After repeated attempts to wash away the “bugs,” she apparently reapplied the ointment. The third patient was well-educated and could be described as one who follows the rules.

Demographics, regimen complexity, patient attitude, disease severity, and psychology all are reported as risks for adherence.¹⁻⁵ Although a certain amount of nonadherence is expected, extreme behaviors are found even in clinical trials and might be related to intrinsic personality traits. These individual portraits of patient adherence, detectable only through electronic monitoring, undoubtedly affect clinical study outcomes. Patient compliance is a critical factor in disease amelioration, yet remains a challenge when researchers and physicians attempt to quantify it.

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