A Trial of Compliance Therapy in Outpatients With Schizophrenia or Schizoaffective Disorder

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Objective: To evaluate the efficacy of compliance therapy when delivered to outpatients with schizophrenia or schizoaffective disorder.

Method: Thirty patients with schizophrenia or schizoaffective disorder (DSM-IV criteria) were recruited from urban psychiatric outpatient clinics in an open trial of compliance therapy. Compliance therapy is a cognitive/psychoeducational approach consisting of 4 to 6 sessions lasting 30 to 60 minutes each. The primary outcome was electronically measured antipsychotic medication adherence. Adherence data were analyzed for effects during an initial treatment period (month –1 to month +1) and a subsequent 5-month follow-up period. Secondary outcome measures included clinician and patient ratings of adherence, symptoms, insight, and attitudes to medication treatment. Data were collected from August 2001 to January 2004.

Results: Compliance therapy was not associated with improvements in antipsychotic medication adherence. Patient ratings of adherence improved during the month –1 to month +1 period, but not in the subsequent 5-month follow-up. A diagnosis of schizoaffective disorder was associated with poorer adherence than was a diagnosis of schizophrenia during the month –1 to month +1 period. A higher degree of insight at baseline (end of month –1) was associated with greater adherence in the 5-month follow-up period. Symptoms, insight, and attitudes to medication treatment did not change significantly during the study.

Conclusion: In this uncontrolled trial, outpatients with schizophrenia or schizoaffective disorder did not benefit from compliance therapy.

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Antipsychotic medication nonadherence is frequently encountered in persons with schizophrenia (i.e., approximately 50% of patients over 1 year).[1,2] Nonadherence is often associated with serious consequences including exacerbation of psychotic symptoms,[3] increased aggression toward self and others,[4] worse prognosis,[5,6] increased hospital and emergency room use,[7] and high societal costs.[8]

In 2 randomized controlled trials (one of 6 months'[9] and the other of 18 months'[10] duration) involving acutely hospitalized patients in England, the effect of compliance therapy, a brief, cognitively based psychosocial adherence intervention, was found to be superior to nonspecific counseling on measures of antipsychotic medication adherence, insight, attitudes toward taking medication, and risk of rehospitalization.[9–11] The first study[9] contained 47 inpatients suffering from DSM-III-R–defined schizophrenia; "severe affective disorders"; schizophreniform, schizoaffective, and delusional disorders; and psychotic disorder not otherwise classified. No mention was made of the relative representation for each disorder. The second study[10] enrolled 74 inpatients, 43 diagnosed with schizophrenia and the remaining with mood disorder with psychosis. However, when a third randomized controlled trial[12] of English inpatients was conducted, enrolling only patients with schizophrenia, compliance therapy did not appear to confer any advantages over nonspecific counseling in regard to adherence or any other clinical outcome. We chose to evaluate the efficacy of compliance therapy in outpatients with schizophrenia or schizoaffective disorder.

METHOD

The study consisted of a 3-month preintervention adherence assessment phase (designated as months –3, –2, and –1), baseline (occurring at the end of month –1), an intervention phase (occurring in month +1), and a 5-month follow-up period (months +2 through +6). Data were collected from August 2001 to January 2004.

Sample

Approval was obtained from the university institutional review board, and written informed consent was obtained from all subjects. Participants were outpatients

receiving care in 5 public mental health clinics of Dallas, Texas, a large urban setting. To be included, participants met DSM-IV criteria for schizophrenia or schizoaffective disorder as determined by treating physicians and confirmed by the study coordinator using a symptom checklist. Eligible patients had to be taking only 1 oral antipsychotic medication and had to have been hospitalized in a psychiatric inpatient unit or visited an emergency room for psychiatric purposes at least once in the 2 years prior to study entry. Patients who had received a depot antipsychotic medication within 1 treatment cycle, were using a pill box to organize their medication taking, were deaf, or had evidence of organic disturbance were excluded.

Assessments

Adherence assessments were collected monthly from month –3 to month +6. The Medication Event Monitoring System (MEMS),[13] a medication vial cap that electronically records the date and time of bottle opening, was used as the primary measure of antipsychotic medication use. Although patients were informed of the purpose and function of the MEMS cap prior to study participation, they had no access to MEMS results. Patients were determined to meet criteria for daily adherence, as assessed by the MEMS cap, if they opened their bottle the prescribed number of times per day, irrespective of the time of bottle opening. Those patients taking more than 1 dosage of a single antipsychotic were given 1 MEMS cap for each dosage. For these patients, adherence criteria were met only if they opened each bottle as prescribed per day. Adherence is reported as a percentage of the possible days that the bottles were opened as recommended.

Two secondary measures of adherence were completed with blinding to MEMS data. The first, a clinician rating of adherence used in previous trials of compliance therapy,[9,10] was administered by the clinical study coordinator who also provided the study intervention. The second was a patient self-administered instrument, the Medication Adherence Rating Scale.[14]

Clinical assessments included measures of symptoms (Positive and Negative Syndrome Scale [PANSS]),[15] insight (Schedule for the Assessment of Insight [SAI]),[16] and attitudes to medication treatment (Drug Attitude Inventory [DAI]).[17] These assessments were completed at baseline (end of month –1) and at the end of months +3 and +6.

Intervention

During the 3-week period immediately following their baseline assessment, patients were treated openly with compliance therapy, which combines aspects of motivational interviewing[18] with cognitive and psychoeducational approaches that target psychotic symptoms, especially when these symptoms impinge on adherence.[9] Compliance therapy, guided by the manual of Kemp et al.,[19] was delivered in 4 to 6 individual sessions, each lasting 30 to 60 minutes, conducted by a licensed mental health counselor with more than 20 years of clinical experience treating patients with psychotic disorders in a public health setting. Sessions focused on the patient's (1) illness and treatment history, (2) beliefs and understanding of the illness, and (3) ambivalence toward treatments and stigma.

Prior to initiating the study, the principal investigator (M.J.B.) and the study counselor reviewed the compliance therapy manual[19] and accompanying videotape materials[20] developed by the originator of this intervention, then utilized this information in detailed discussions and role playing of multiple sessions to gain agreement on the treatment approaches to be used in the trial. The principal investigator was not an expert in the delivery of motivational interviewing or cognitive therapy. Additional training of the counselor prior to initiating the study included a detailed review of a 6-tape videotape series of motivational interviewing techniques.[21] Quality control of the treatment intervention included frequent detailed review (usually weekly during the first few months of the study, then at least monthly) of the content of the sessions through verbal report of the counselor to the principal investigator. Such sessions were used to establish and maintain an approach that consistently adhered to the elements of compliance therapy.

Statistics

To detect a 20% improvement in adherence with 80% power ($\alpha = .05$, 2-tailed), the study required a sample size of 30 patients.[22] Analyses of primary and secondary outcomes were conducted using a declining effects hierarchical linear model (HLM). Patient characteristics including age, gender, type of disorder, and baseline PANSS, SAI, and DAI scores were added one at a time as covariates in the HLM to test for influence on electronically measured adherence.

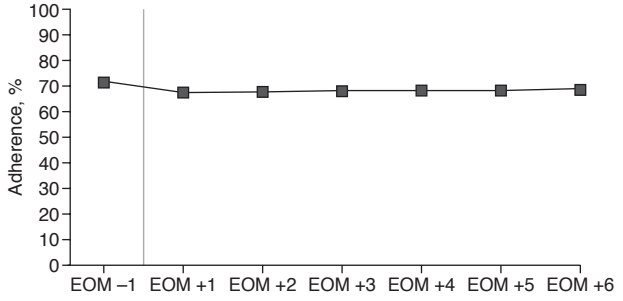
RESULTS

Of 30 study participants (20 men and 10 women), 21 met criteria for schizophrenia and 9 met schizoaffective disorder criteria. Subjects completed the 3-month preintervention electronic adherence assessment phase (N = 30), baseline (N = 30), the intervention phase (N = 29), and the 5-month follow-up period (N = 19). The mean ± SD age of the patients was 39.2 ± 8.3 years. Patients were mildly to moderately ill at baseline, as evidenced by mean ± SD total PANSS scores of 71.6 ± 17.8 (range, 38–105).

Outcome Measures

Electronically measured adherence declined from month –3 (mean ± SD = 82% ± 21%) to month –1 (mean ± SD = 72% ± 28%). To eliminate potential effects of early study participation on electronically measured adherence

Figure 1. MEMS Scores by Month in Patients With Schizophrenia or Schizoaffective Disorder Receiving Compliance Therapy[a]



[a]Bold dots connected by solid line indicate fitted curve of HLM. Vertical line indicates baseline.
Abbreviations: EOM = end of month, HLM = hierarchical linear model, MEMS = Medication Event Monitoring System.

(e.g., initial use of electronic caps, motivation to please staff during initial meetings), month –3 and month –2 electronically measured adherence data were not used.

The primary study outcome of electronically measured adherence declined 4% from baseline (month –1) to month +1 and then increased by 0.19% per month thereafter. Neither the initial decline ($p = .12$) nor the subsequent increase ($p = .83$) was significant. The data for the fitted curve are shown in Figure 1.

Of baseline patient characteristics, a diagnosis of schizoaffective disorder was the only factor with a significant effect on electronic adherence in the initial treatment period (month –1 to month +1), during which it was associated with a larger decrease in adherence (HLM, $p = .03$). Insight was the only baseline characteristic affecting adherence during the follow-up period (month +2 through month +6), with greater insight at baseline being associated with a greater increase in adherence (HLM, $p < .01$).

Clinician ratings of adherence did not change significantly during the study. The clinician-rated adherence decreased by 1.6% from baseline to end of month +1 ($p = .36$), then decreased by 0.3% per month during the rest of the study ($p = .61$).

Patient ratings of adherence did change significantly between the baseline and end of month +1 evaluation, but not during the follow-up period. The patient ratings increased by 8.9% from baseline to end of month +1 ($p = .04$), then decreased by 1.4% per month during the rest of the study ($p = .07$).

Symptoms, insight, and attitudes to medication taking did not change significantly during the study. PANSS ratings increased by 0.8% from baseline to month +3 ($p = .59$), then decreased 0.4% from month +3 to month +6 ($p = .33$). Insight as determined by the SAI was also unchanged, increasing 6.8% from baseline to month +3 ($p = .18$), then decreasing by 3.2% from month +3 to month +6 ($p = .39$). Finally, attitudes toward medication taking as assessed by the DAI were unchanged. An increase of 15.2% from baseline to month +3 ($p = .15$), then a decrease of 0.5% from month +3 to month +6 ($p = .81$), were noted.

DISCUSSION

The present uncontrolled study found no benefit from compliance therapy in electronically measured and clinician-rated adherence for outpatients with schizophrenia and schizoaffective disorder. Symptoms, insight, and attitudes to medication treatment did not change. Patients' own ratings of adherence were improved during the initial month of treatment, but not during the 5-month follow-up period.

A diagnosis of schizoaffective disorder was associated with poorer adherence during the initial treatment period than a diagnosis of schizophrenia. This finding is consistent with reports that affective features are predictive of poor adherence among patients with psychotic disorders.[23] A higher degree of insight was associated with greater adherence during the follow-up period—a consistent finding in previous reports.[23]

These generally negative findings are in contrast to the positive findings of the initial studies of compliance therapy, which were delivered to psychotic inpatients with mixed diagnoses.[9,10] The negative results of the present study do, however, extend findings of a recently published randomized, rater-blinded trial[12] of compliance therapy delivered to inpatients with schizophrenia, in which a similar lack of improvement in adherence and clinical outcomes was noted.

Several important design elements of the present study may have contributed to differences seen in this and initial studies of compliance therapy. First, our study and a second negative study of compliance therapy[12] included only patients with psychotic disorders, whereas earlier studies included patients with both affective and psychotic disorders.[9,10] Thus, it is possible that patients with affective disorders experience greater benefit with compliance therapy than those with psychotic disorders. Second, the current study used electronic monitoring as the primary adherence outcome. Compared with clinician ratings, which were used in early studies of compliance therapy, electronic measurement may provide greater sophistication in assessing adherence of patients in general medical populations[13] and schizophrenia.[24]

Limitations of the Study

Several factors may affect the applicability of the study findings. First, the study did not utilize a control group; therefore, it is possible that compliance therapy prevented additional decline of adherence that would have otherwise occurred. Consistent with this possibility is the relatively high adherence observed during the postintervention

period, in which the mean group adherence ranged from 69% to 74%. Additionally, a minority of patients (40%) fell below a monthly adherence threshold of < 50% during the same postintervention period. Thus, a definitive evaluation of compliance therapy in outpatients with schizophrenia should include a randomized control group and the use of an objective measure of adherence such as electronic monitoring or urine antipsychotic levels.

Although the study analysis did control for several possible confounding factors of adherence and response to compliance therapy, including age, gender, type of disorder, and baseline PANSS, SAI, and DAI scores, it did not include some additional factors potentially predictive of adherence (e.g., dose frequency, medication side effects). As additional studies of the correlates of electronically determined adherence are reported, the inclusion of these variables into future analyses should provide a refined evaluation of adherence interventions.

Additionally, the study patients were not representative of the entire population of patients with schizophrenia and schizoaffective disorder, as they were outpatients of a single, urban, public treatment program in the United States. Furthermore, participation was restricted to those with a history of psychiatric hospitalization in the 2 years prior to study entry. The rates of antipsychotic adherence observed in our study were, however, similar to those of the only other published trial of MEMS-determined adherence in outpatients with schizophrenia and schizoaffective disorder.[25]

Use of MEMS technology is another potential limitation of the study. Although the advantages of MEMS over other adherence assessment methods have made it the reference standard for adherence monitoring in research involving general medical conditions,[13] it cannot verify whether patients actually ingest medication at times of bottle opening. Thus, error in overestimating true adherence could occur with MEMS. However, because MEMS effectively identifies periods when the medication vial is not opened, an underestimation of adherence is extremely unlikely.

Although MEMS cap use was associated with greater adherence during the initial month of the preintervention adherence assessment phase (mean adherence = 82% during month –3), a potential beneficial effect of the cap on adherence was unlikely to have either improved adherence or prevented further deterioration in adherence during the intervention phase of the study. MEMS-determined adherence had stabilized during the 2 months prior to the delivery of compliance therapy (mean adherence = 73% and 72% during months –2 and –1, respectively). MEMS-determined adherence then remained essentially unchanged through the remainder of the trial, with monthly group mean adherence rates ranging from 69% to 74%. The relatively high levels of adherence observed during the initial 3 months of the trial may also have contributed toward a "ceiling" effect, in which the potential benefits of compliance therapy were limited by the high degree of initial adherence observed in some patients.

CONCLUSION

Our findings in this uncontrolled trial, along with a negative finding of compliance therapy among inpatients with schizophrenia,[12] suggest that this intervention may not benefit patients with psychotic disorders.

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