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Antipsychotic Adherence Intervention for Veterans over 40 with Schizophrenia: Results of a Pilot Study

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Abstract

This pilot study tested the feasibility, acceptability, and effect-sizes of a multimodal, individual intervention designed to optimize antipsychotic medication use in patients ≥ 40 years of age with schizophrenia or schizoaffective disorder.

Methods—We randomized 40 patients into two groups: usual care (UC) or a nine-session, manualized, antipsychotic adherence intervention (AAI). The AAI attempted to improve adherence by combining three psychosocial techniques: a) education, b) skills training, and c) alliance building. Sessions employed a semi-structured format to facilitate open communication. The primary outcome was antipsychotic adherence at study end. We obtained qualitative data regarding patient preferences for the duration and modality for receiving the adherence intervention.

Results—Compared to the UC group, a greater proportion of the AAI group was adherent post-intervention (65% vs. 55.6%; OR=1.49), a difference that was statistically not significant. The entire AAI group reported that they intended to take medications, and 75% were satisfied with the intervention.

Conclusions—The AAI was feasible and acceptable. Preliminary data on its effectiveness warrant a larger study. Qualitative data shows that patients prefer brief adherence interventions and accept telephone strategies.

Keywords

Adherence; compliance; antipsychotics; skills; education; alliance

Introduction

Medication nonadherence among patients with schizophrenia is common and costly. Within a year of hospital discharge for treatment of acute symptoms, 40–50% of patients deviate from their prescription regimen. (1–3) Nonadherent patients are three times more likely to relapse, (4) are 2.5 times more likely to be rehospitalized, (2) remain hospitalized twice as long, and experience deterioration in their and their caregivers' quality of life. (5–8) This “revolving door phenomenon” (9–11) adds \$2.3 billion a year to hospital costs, and of which \$700 million stem from medication nonadherence. (12;13)

Population of veterans over age 50 with psychosis has risen from 49.7% to 66.1% in 2004, yet, studies seldom have assessed the risks of nonadherence in this group. Older patients with schizophrenia are more susceptible to side effects of antipsychotic drugs, (14) have complex medication regimens for multiple chronic conditions, (15;16) experience greater difficulty comprehending and managing their medication, (17) discount psychiatric treatments, and have cognitive deficits that interfere with therapy. (18) Further, the effectiveness of adherence interventions in predominantly younger samples may not generalize to older persons. (19)

This pilot study tested the feasibility, assessed the acceptability, and estimated the effect size of a multimodal, individual strategy entitled the Antipsychotic Adherence Intervention (AAI) to optimize medication adherence in veterans ≥ 40 years with schizophrenia or schizoaffective disorder. The intervention was modeled on Functional Adaptation Skills Training (20) and a medication management module for schizophrenia. (21)

Methods

Intervention

We tested a nine-session, manualized AAI by combining three psychosocial techniques: a) learning to manage antipsychotic prescriptions; b) learning to communicate, organize and manage medications, and access the healthcare system; and c) building relationships with healthcare providers. These sessions involved repetition of information, role-playing, and practice in a semi-structured format to facilitate open communication. Face-to-face training occurred daily for sessions 1–3 and weekly for 4–6. Telephone training transpired monthly for sessions 7–9 to maintain a therapeutic alliance and encourage use of adherence strategies. Trainers provided support, reflective listening, open-ended questioning, confrontation avoidance, and shared problem-solving.

Usual Care

Inpatient usual care (UC) consisted of nursing care, group therapy, and 15 minutes of medication education at discharge. Outpatient UC included medications, supportive therapy, group therapy, and case management.

Participants

Participants were recruited from three inpatient units of the Central Arkansas Veterans Healthcare System (CAVHS). Inclusion criteria were: age ≥ 40 years, DSM IV (22) diagnosis of schizophrenia or schizoaffective disorder, prescription for a maintenance antipsychotic (oral or depot), and ability to consent to and participate in the study. Exclusion criteria were: dementia, lack of transportation to outpatient sessions, and no telephone. Eligible patients were randomized to receive AAI or UC based on a computer-generated schedule.

The University of Arkansas for Medical Sciences (UAMS) Institutional Review Board and the CAVHS Research and Development Committee approved the study. Each participant provided written informed consent.

Assessments

Raters blinded to group assignment conducted assessments at baseline on the inpatient unit and at four weeks and four months in the outpatient setting.

Measures

Demographics—Patients provided age, gender, ethnicity, education, marital status, living situation, usual medication supervision, physical health diagnoses, and alcohol or other substance use. Medical records indicated the psychiatric diagnosis.

Medication Adherence Assessment—Interviews with patients and caregivers were combined with pharmacy refill records into an overall assessment. Scoring details follow.

- a. Patients stated the number of prescribed doses they had taken during the previous week. They were classified as adherent if they took $\geq 80\%$ of the prescribed doses. Although a specific threshold at which partial adherence with antipsychotics becomes problematic remains unknown, taking 80% of prescribed medications is a traditional cut-off point for “good adherence” and seems reasonable for patients and their providers.(23;24)
- b. Caregivers identified the number of doses the patient took during the previous week. Patients were classified as adherent if they took $\geq 80\%$ of the doses.
- c. Pharmacy Refill Records(25): We reviewed the computerized pharmacy database, assumed that the patient took the medication as prescribed, and calculated the medication possession ratio (MPR). The MPR is calculated by dividing the number of pharmacy prescriptions filled by the number of pills needed to cover all noninstitutionalized days during a specified period. Any MPR score ≥ 0.80 was considered adherent. We calculated the MPR for the year before baseline and the four months after enrollment.
- d. Overall Assessment of Medication Adherence: Since each of the individual measures has limitations,(26) and no gold standard exists, we considered patients adherent only if all three measures indicated adherence at baseline and four months.

Participant Feedback—At the end of the study, a semi-structured interview with AAI participants determined if they had a better understanding of psychosis, symptoms, benefits of taking medications, medication side effects and their management, getting information about their medications, and communication skills. We also asked if they were better off and intended to take their medications. Additionally, we asked their preferences regarding duration of adherence intervention and mode of receiving information (paper material, DVD, or telephone).

For exploration, we administered the Quality of Well-Being Scale (QWB) (27), Positive And Negative Syndrome Scale (PANSS) (28), Calgary Depression Scale (CDS) (29), and Dementia Rating Scale (DRS) (30). To measure antipsychotic side-effects, we administered the Modified Simpson-Angus Extrapyramidal Scale (SAEPS) (31), Barnes Akathisia Scale (BAS) (32), and Abnormal Involuntary Movement Scale (AIMS) (33). To determine medication knowledge and patient attitudes, we used the 14-Point Questionnaire (14-Q),(34) Drug Attitude Inventory (DAI),(35) and Insight and Treatment Attitudes Questionnaire (ITAQ).

Statistical Analysis: We report descriptive statistics for all baseline measures. Data were examined for homogeneity of variance and normality of distribution. To identify any variable that might confound the comparisons of outcomes between the groups, we compared distributional characteristics of baseline measures between the groups with two-sample *t*-tests for approximately normal measures, median tests for non-normal and ordinal measures, and chi-square tests for categorical measures. We compared the groups on binary adherence measures (adhering or not) with logistic regression including group and baseline-adherence measures as independent variables. Data are included for all subjects completing at least one follow-up assessment (n=38). For dropouts, we carried forward outcomes from their last visit to the subsequent (missed) outcomes.

All analyses were conducted in SAS® Version 9.1. We report 95% confidence intervals when estimating differences or odds ratios.

Results

Recruitment and retention

We screened 157 potential participants. Of the 62 who were eligible, 40 participated. Reasons for ineligibility included inability to return to the clinic or no telephone (n=35) and lack of cognitive capacity (n=26). Two participants did not return for subsequent assessments. Average AAI attendance was 8.8 sessions out of 9. Completers (attended at least two sessions) and dropouts did not differ significantly on variables.

Baseline Sample characteristics

The mean (standard deviation) age was 51.3 (5.1) years. Most were male (95%), unmarried (85%), had schizophrenia (62.5%), managed their own medications (72.5%), and used alcohol or drugs (62.5%) in the 30 days before enrollment. The group had a mean 12.4 (1.5) years of education. A minority (32.5%) lived alone. Subjects were enrolled in the outpatient clinic (52.5%), an outreach program with monthly case management (30%), or intensive case management (12.5%). Table I compares the demographic and clinical characteristics of the UC (N=18) and AAI (N=22) groups.

At baseline, the percentage of the UC and AAI groups who were nonadherent based on the MPR was 50% and 45.5%, and “overall non-adherence” was 77.8% and 77.3%, respectively. The UC and AAI group baseline non-adherence rates reported by patients and caregivers were 55.6% and 59.1%, and 50% and 78.6%, respectively.

Participant Satisfaction and Feedback

In the exit interview by the Principal Investigator, the AAI group reported improved understanding of psychosis (47.1%), symptoms (64.7%), benefits of medications (88.2%), managing side effects (82.4%), taking medications properly (88.2%), obtaining information about medications (70.6%), tracking medications (64.7%), and communicating with providers (70.6%). All intended to take medications, and 76.5% were satisfied with the intervention.

Most (76.5%) preferred face-to-face sessions, but attendance was problematic for 41.2%. Telephone sessions were helpful to 70.6%.

Qualitative Data

A majority preferred to receive medication adherence information on paper instead of through slide shows or videotapes, preferred obtaining information in a briefer time frame than four months, and viewed telephone contact as helpful and caring.

The AAI group varied in knowledge about available treatments especially non-pharmacological interventions.

Adherence Outcomes

Using patient report, caregiver report, and MPR at four months as separate adherence outcome measures, the proportion (conditioned on baseline adherence) of adherence to AAI compared to UC were 83.33% vs. 85%, 85% vs. 81.25%, and 85% vs. 66.67%, respectively. For the composite adherence measure, the proportion for AAI vs. UC was 65% vs. 55.56% (See Table II). We did not control for baseline adherence while computing composite adherence as only one participant was adherent at baseline.

Effect Size Estimation: Using an $MPR \geq 0.8$ as an indicator of acceptable adherence, about 33% of the subjects in the UC group were adherent, both at baseline (13/40) and at 4-month follow-up (6/18). Assuming an OR of 2 (or 2.5 or 3) is clinically important to detect when comparing an intervention group to a UC group *and* assuming the true OR is at least 2 (or 2.5 or 3), a future study would need 107 (or 61 or 42) subjects in each group to have at least 0.80 probability of verifying the effectiveness of AAI at the .05 level of significance.

Discussion

The primary finding demonstrates that older veterans with schizophrenia can participate in and accept the AAI. The AAI group reported intent to take medications, and the majority was satisfied with intervention. The odds of a subject being adherent, as measured by caregiver report and MPR, were greater for the AAI than the UC group, although these were not statistically significant. Nonetheless, the study provides estimates for planning a larger study to demonstrate effectiveness.

The study provides qualitative information about veteran preferences on such interventions. Future application of the intervention should include delivery of the intervention to provide skills and education over a shorter period of time followed by sustained, brief telephone and face-to-face contact to ensure skills maintenance.

Manualized interventions have been advocated with the argument that all patients could benefit from learning medication adherence skills because of high nonadherence rates. Moreover, they provide uniform information to patients. Based on the qualitative feedback, we would argue for shorter and more targeted manualized interventions. We found that some patients had good information and skills in managing their illness and medications while others lacked basic information. One notable challenge was how to sufficiently individualize the manualized intervention. We attempted to individualize the intervention by spending less time on known material and more time on unfamiliar content or training. We suggest that the manual should allow participants to choose the modules that seem most relevant to target their needs. For example, a person with cognitive deficits may need more family/environmental support to organize the pill box; whereas, someone with sexual side effects may need education and problem solving. Incorporation of motivational interviewing (36;37) and shared decision-making (when clinicians directly elicit patient treatment preferences), (38;39) may enhance effectiveness of the intervention. Adherence to interventions may increase by targeting comorbid substance dependence where appropriate.(40;41) Essentially, the manual should allow for using specific techniques and content to target specific skill deficits.

The study's limitations follow: a) small sample size without sufficient power to detect small-to-moderate differences; b) inpatient recruitment and outpatient follow-up (inpatient admission in itself is a powerful intervention that possibly prevented us from detecting the difference

between AAI and UC; d) an insufficient observation period to detect adherence changes; and e) veterans only sample limiting generalizability of the findings.

Overall, we found that veterans ≥ 40 years of age with schizophrenia were eager to learn strategies to manage their medications. They showed modest improvement in the adherence outcome measures. These preliminary findings provide estimates of effect sizes for larger, randomized controlled studies. We hope this study will stimulate further research on medication adherence interventions for older patients in schizophrenia.

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Table I

Table I a. Baseline Clinical Variables: AAI and UC Groups		
Variables	AAI Group n = 22 Mean (SD)	UC Group n = 18 Mean (SD)
Age (years)	50.77 (5.56)	52.0 (4.58)
Age of Onset (years)	24.95 (9.41)	21.72 (7.32)
Education (years)	12.5(1.26)	12.33 (1.85)
Current Drug Abuse	54.55%	66.67%
Past Drug Abuse	86.36%	94.44%
Current Alcohol Abuse	27.27%	33.33%
Past Alcohol Abuse	68.18%	50%

Table I b. Baseline Clinical Variables		
Variables	AAI Group n = 22 Mean (SD)	UC Group n = 18 Mean (SD)
DRS Total	130.90 (7.48)	135.33 (6.87)
PANSS Total	72.59 (18.56)	71.38(15.41)
PANSS Negative	18.7(5.23)	18.50 (3.39)
PANSS Positive	17.86 (5.17)	18.72 (6.79)
PANSS General	36.00 (9.70)	34.16 (7.68)
Calgary Depression Score	8.37(5.73)	5.54(4.96)
Quality of Well Being Score	0.56(.088)	0.510(.0493)
Q14 Score	9.77(2.18)	11.05(1.58)
DAI Score	4.63(3.17)	6.55(3.20)

Table II

Effect of Intervention on Adherence (Percentages and Odds Ratios) - Adjusted for Baseline Adherence (except *)

	Percentage adherent in AAI vs. UC groups	OR	95% CI
Patient Report	83.3 vs. 85	0.97	0.15 – 6.18
Caregiver Report	85 vs. 81.25	1.24	0.16 – 9.40
MPR-120	85 vs. 66.67	2.64	0.53 – 13.09
Composite Adherence*	65 vs. 55.56	1.49	.40 – 5.49