

Outcomes comparison of long-acting injectable antipsychotic initiation in treatment-naïve veterans in the inpatient versus outpatient setting

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Abstract

Introduction: Long-acting injectable (LAI) antipsychotics have become an integral component in the treatment of schizophrenia and other psychotic disorders. Long-acting injectables may be initiated in either the inpatient or outpatient setting; however, there have been no studies to evaluate whether LAI treatment initiation setting impacts patient outcomes. This study sought to assess whether outcomes, specifically psychiatric hospitalization rates, time to hospitalization, and adherence with injections, differed between patients started on LAIs in the inpatient versus outpatient setting.

Methods: The electronic medical records of all veterans prescribed an LAI at the McGuire Veterans Affairs Medical Center from September 2009 through September 2014 were reviewed in this retrospective study. Veterans met inclusion criteria if they were prescribed an LAI during the study period and were excluded if they had received an LAI prior to September 2009 or if the LAI was started at an outside facility. Patients were separated into treatment groups according to initiation location. The primary outcomes included psychiatric hospitalization rates and time to hospitalization. The secondary outcome measured the proportion of LAI injections received.

Results: Fifty-five LAI treatment-naïve veterans were included in this study. No statistically significant differences were found in psychiatric hospitalization rates, time to hospitalization, or proportion of LAI injections received when comparing the inpatient and outpatient treatment initiation groups.

Discussion: Psychiatric hospitalization rates, time to hospitalization, and adherence to LAIs did not differ between the inpatient and outpatient treatment groups, suggesting that treatment initiation location does not have an effect on patient outcomes.

Keywords: long-acting injectable antipsychotics, antipsychotics, schizophrenia, psychotic disorders

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Introduction

Antipsychotic medications have become an integral component in the management of schizophrenia and

other psychotic disorders. However, numerous studies have estimated that approximately 40% to 50% of patients are nonadherent to prescribed oral antipsychotics with medication nonadherence identified as the most frequent cause for psychiatric hospitalization in patients with schizophrenia.¹⁻³ Additional consequences of non-adherence may include an increased risk of functional decline, symptom relapse, and treatment resistance, ultimately contributing to personal suffering and decreased quality of life.⁴⁻⁶ The use of long-acting injectable (LAI) antipsychotic formulations has become more prevalent with the intent that they will increase medica-



tion adherence compared to oral formulations and lead to improved patient outcomes.

Long-acting injectables are frequently used in this patient population, and primary literature is available to educate practitioners on appropriate use based on individual patient characteristics.^{7,8} However, there is limited literature available to guide providers in the decision of when to initiate LAIs in regards to the inpatient or outpatient treatment setting. There are several variables to consider when determining whether to initiate an LAI, which may include individual patient demographics, acuity of illness, and available resources at the facility where the patient is being treated. These variables have led to a disparity in practice with many facilities restricting LAI initiation to a particular setting. Currently, there are no studies that directly compare different LAI treatment initiation settings to determine whether restricting LAI use has a clinically relevant impact on patient outcomes.

The McGuire Veterans Affairs Medical Center (VAMC) is a 400-bed medical facility that provides both inpatient and outpatient mental health services. Providers at this facility are able to order LAIs in both the inpatient and outpatient treatment settings without restrictions on the timing of initiation. LAIs available for use at this facility during the study period included fluphenazine, haloperidol, risperidone, and paliperidone LAI formulations.

Given the limited available literature on this topic, it is essential that researchers collect more data to determine if LAI initiation setting impacts patient outcomes and use these results to guide clinical practice. The authors of this study sought to assess whether LAI treatment initiation setting had an effect on patient outcomes at this large medical facility with the hypothesis that outcomes would differ between the 2 groups. Veterans who received outpatient LAI injections were initiated on LAIs in either the inpatient or outpatient treatment setting, which allowed the investigators a unique opportunity to analyze and compare data from both settings within the same facility. Specific outcomes analyzed in this study include psychiatric hospitalization rates, time to hospitalization, and adherence to LAI administrations. The results of this study not only assess the current practice in place at this facility, but also add to the body of scientific literature available regarding the use of LAIs.

Methods

The electronic medical records of all veterans prescribed an LAI at the McGuire VAMC from September 2009 through September 2014 were reviewed in this retrospective study. Veterans met inclusion criteria if they were prescribed an LAI during the study period. Patients were

excluded if they had received a LAI prior to September 2009, were started on an LAI at an outside facility, or were not continued on the LAI at discharge. Patients who transferred their outpatient care to a facility other than the McGuire VAMC were not included. Veterans were excluded if they were readmitted to the psychiatric unit before the first outpatient dose was due. One hundred fifty-eight patients were excluded from the study. The most common reason for exclusion was exposure to an LAI prior to study period. The 2 treatment groups were then analyzed based on LAI initiation location, either the inpatient or outpatient setting. The use of concomitant psychotropic medications was not restricted.

An institutional review board waiver was granted in November 2015, recognizing this study as a performance improvement project. Data was collected via chart review and included demographic information, primary psychiatric diagnosis, psychiatric hospitalization dates, and LAI administration history during the 1-year period following initiation. The primary outcomes were psychiatric hospitalization rates and the number of days from LAI initiation to documented psychiatric admission, which served as a measure of relapse. The secondary outcome was the proportion of outpatient LAI injections received, which used patient data obtained from administration notes documented in the chart and served as a measure of adherence. The proportion of injections received was determined by dividing the total number of outpatient injections received by all possible injection opportunities. The number of LAI injection opportunities was calculated based on the LAI prescribed frequency and whether a loading course was required. Veterans were then separated into 4 different adherence categories (100% adherence, 50%–99% adherence, 1%–49% adherence, and 0% adherence) based on proportion of LAI injections received.

Two exploratory outcomes were included in this study. The first exploratory outcome analyzed the rates of hospitalization separated by psychiatric diagnosis to determine whether patients with a particular psychiatric diagnosis were more likely to be admitted within the first year. The second exploratory outcome measured was the rate of hospitalization separated by LAI, which sought to determine whether a particular agent was associated with psychiatric admission.

The first primary outcome, which evaluated the difference in hospitalization rates between treatment groups (categorical data), was analyzed using chi-square test. The time in days to psychiatric hospitalization (continuous data) was then analyzed using the Student unpaired *t* test. The secondary outcome, which measured adherence to LAIs (categorical data), was evaluated using the Fisher exact test, which is more accurate than the chi-square test when comparing smaller sample sizes. Exploratory outcomes,

including rates of hospitalization differentiated by diagnosis and rates of hospitalization differentiated by LAI (categorical data), were also evaluated using the Fisher exact test. A significance level was established as $P < .05$. Sample size was not calculated for this study. The number of patients was limited to this single facility, and the treatment population included all veterans meeting criteria.

Results

Fifty-five LAI treatment-naïve veterans met inclusion criteria, which included 35 inpatient initiations and 20 outpatient initiations (Table). The average age at initiation was 51 years with 91% male patients and 49% of patients having a diagnosis of schizophrenia. The samples were compared by average age, sex, and psychiatric diagnosis with no statistically significant differences between these variables ($P > .05$).

The primary outcomes assessed psychiatric hospitalization rates and time to hospitalization within 1 year of LAI initiation. Of the 55 patients included in the study, 22 patients (40%) had a documented psychiatric hospital admission within 1 year following initiation. Thirteen patients (37%) in the inpatient LAI initiation group and 9 patients (45%) in the outpatient LAI initiation group had a psychiatric hospitalization within the 1-year follow-up period. There were no statistically significant differences between the 2 treatment groups with regards to hospitalization rates ($P = .28$). The average time to psychiatric admission following LAI initiation was 147 days in the inpatient group and 138 days in the outpatient group. There was no statistically significant difference in time to hospitalization between the treatment groups ($P = .42$).

The secondary outcome assessed adherence by identifying the proportion of outpatient LAI injections received out of total injection opportunities within 1 year following initiation. There were no statistically significant differences between the treatment groups with regards to adherence following initiation (100% adherence [$P = .51$], 50%–99% adherence [$P = .28$], 1%–49% adherence [$P = .46$], and 0% adherence [$P = .25$]).

The first exploratory outcome assessed whether patients with a particular psychiatric diagnosis were more likely to be hospitalized within 1 year. There were no statistically significant differences in psychiatric hospitalization rates when separated by most frequent diagnoses: schizophrenia ($n = 27$, 48% hospitalized, $P = .17$), schizoaffective disorder ($n = 17$, 35% hospitalized, $P = .43$), and bipolar disorder ($n = 8$, 25% hospitalized, $P = .29$). The second exploratory outcome assessed whether patients on a

TABLE: Baseline demographics of study population

	Inpatient (n = 35)	Outpatient (n = 20)	P Value
Age at initiation, y	50	52	.34
Sex, No. (%)			
Male	33 (94)	17 (85)	.34
Psychiatric diagnosis, No. (%)			
Schizophrenia	17 (49)	10 (50)	.57
Schizoaffective	11 (31)	6 (30)	.58
Bipolar disorder	5 (14)	3 (15)	.62
Dementia	1 (3)	0 (0)	.64
Depression with psychosis	1 (3)	1 (5)	.59

specific LAI were more likely to be hospitalized. Similarly, there were no statistically significant differences in psychiatric hospitalization rates when separated by LAI: paliperidone ($n = 25$, 40% hospitalized, $P = .61$); risperidone ($n = 19$, 42% hospitalized, $P = .52$); haloperidol ($n = 9$, 33% hospitalized, $P = .48$), and fluphenazine ($n = 2$, 50% hospitalized, $P = .64$).

Discussion

This study sought to determine whether patient outcomes differed based on LAI treatment initiation setting. Results from the primary outcomes indicate that there were no statistically significant differences in either psychiatric hospitalization rates or time to hospitalization when comparing veterans initiated on LAIs in the inpatient and outpatient settings. This suggests that patients had similar primary outcomes with regards to psychiatric hospitalization. Similarly, results from the secondary outcome indicate that there were no statistically significant differences in adherence based on inpatient or outpatient LAI initiation. This demonstrates that treatment initiation setting did not have an effect on the likelihood of patients obtaining prescribed outpatient LAI injections. Ultimately, these results suggest that patients who were initiated on a LAI in either the inpatient or outpatient setting had no statistically significant or clinically significant differences with regards to risk of psychiatric hospitalization or adherence with outpatient LAI injections.

The results from the exploratory outcomes show no significant differences in hospitalization rates when separating the patient population by psychiatric diagnosis or LAI used. The rates of psychiatric hospitalization were comparable between patients with a particular diagnosis or those who were prescribed a specific LAI.

The limitations of this study include the small sample size ($n = 55$) and retrospective design. As this was a single-site

study and evaluators were unable to recruit additional participants, a power calculation to determine sample size was not prospectively performed. Although no significant differences were found, it is possible that a difference would not be detected if the study were not adequately powered. Patients may have had a psychiatric hospitalization or received an LAI outside of the Veterans Affairs health care system, and thus, this data was not captured. Due to the retrospective nature of this study, evaluators were unable to apply standardized assessment tools to evaluate severity of psychiatric illness, which may have varied between treatment settings. Additionally, evaluators could not control for varying LAI dosing strategies, and the administration of a loading dose with paliperidone may have affected results by increasing the total number of injection opportunities with this agent. Other variables that were not controlled for in this study include differing lengths of hospitalization, psychiatric comorbidities, and concomitant psychotropic use both during and prior to the study period. The exclusion of patients who did not receive their first scheduled outpatient LAI dose due to rehospitalization may have influenced results and shown an advantage in adherence with the inpatient group. Finally, the differences in adherence definitions between this and other studies may limit the ability to compare results to existing literature.

Objectives for future research might include assessing whether severity of illness at time of LAI initiation varies based on treatment initiation location, thus impacting outcomes and whether nonadherence in either setting correlates to increased psychiatric hospitalization rates.

Conclusion

Overall, the results of this study suggest that outcomes of psychiatric hospitalization and adherence with LAI injections were comparable in patients initiated on an LAI in

the inpatient and outpatient treatment settings at the McGuire VAMC. Although this study was developed as a performance improvement project to assess the current practice at this facility, the findings of this study may be used to enhance the current body of pharmacy practice literature.

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