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BRIEF REPORT

Recovery-Oriented Outcomes Associated with Long-Acting Injectable Antipsychotics in an Urban Safety-Net Population

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Abstract
This study examined whether transitioning patients from oral antipsychotics (POs) to long-acting injectable antipsychotics (LAIs) helps patients achieve recovery-oriented goals. Data was extracted from San Francisco County's electronic medical record system for this retrospective pre-post observational study. Patients reflect a safety-net population treated in community-based mental health settings during 2015. The San Francisco Adult Strengths and Needs Assessment (SF ANSA), a measure of psychosocial functioning, was used to assess within-subject change when treated with POs versus LAIs. In our study sample (N = 77), LAI SF ANSA scores showed significant improvements in criminal behaviors (p = .017), medication adherence (p = .008), and spirituality (p = .028), and a non-significant trend for residential stability (p = .073). This is the first study to evaluate improvements in key psychosocial areas after treatment with LAIs. This work suggests that LAIs can be another tool for providers to help patients work towards their recovery-oriented goals.

Keywords Long-acting injectable antipsychotic medications · Recovery · Psychosis · Schizophrenia · Depot medications

Introduction

Schizophrenia spectrum disorders are chronic, debilitating illnesses that require long-term treatment. Pharmacotherapy is a key tenant of treatment, though non-adherence to medication is relatively common and can lead to worsening of symptoms and psychosocial functioning (Lindenmayer et al. 2009). Long-acting injectable antipsychotics (LAIs), when compared to oral antipsychotics (POs), have been shown to improve adherence in people with chronic psychotic illnesses (Marcus et al. 2015). Patients on LAIs often experience lower rates of re-hospitalization and show improved functioning, quality of life, and satisfaction (Kaplan et al. 2013). Though promising, some LAI studies report mixed results. Some randomized controlled trials (RCTs) show no advantage to LAIs (Rosenheck et al. 2011), though this is likely due to the structure of RCTs increasing adherence to POs and obscuring the main advantage of LAIs (Kane et al. 2013). Taken together, the literature points towards the need for further studies on the effectiveness of LAIs.

Because of LAI's promise for improving clinical outcomes in real-world conditions, there is a growing research emphasis on their use in the public mental health sector. In homeless patients with schizophrenia, LAIs and psychosocial interventions led to improvements in both adherence to treatment and overall functioning including housing instability (Sajatovic et al. 2017). In a study of homeless patients on antipsychotics, LAIs were a key predictor of long-term treatment adherence and were associated with decreased hospitalization (Rezansoff et al. 2016). LAIs have been effective in the incarcerated population (Miyamoto et al. 2017), as well as those with co-occurring substance use disorders (Lynn Starr et al. 2017). As providers of mental health services in safety-net settings, the authors recognize the need for treatment options that address these complexities.

To our knowledge, prior research has not specifically addressed the role of LAIs in achieving recovery-oriented goals. In safety-net settings where many patients with chronic psychotic illness are treated with LAIs and services are recovery-oriented, it is especially valuable to know

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whether psychosocial outcomes improve with this treatment (Thomas et al. 2017). This exploratory, observational study aims to bring attention to this knowledge gap by examining changes in psychosocial functioning associated with LAI treatment within a community mental health population with high rates of trauma, homelessness, incarceration, and poverty.

Methods

Study Design

We conducted an exploratory, retrospective, pre-post observational study using longitudinal data extracted from AVATAR, the electronic health record system used by San Francisco County for documentation and billing of specialty mental health services.

Study Setting

Treatment settings for this patient population included inpatient psychiatric wards, outpatient mental health clinics, and county jails.

Study Sample

Our sample was drawn from the San Francisco County public mental health system, which serves predominantly Medicaid or uninsured patients with high prevalence of trauma, homelessness, and substance use. We defined our initial cohort as any patient served in the public mental health system in 2015 having an LAI prescription for at least twelve months with no gaps lasting longer than ninety days (n = 316). Inclusion criteria were: (1) had a baseline San Francisco Adult Needs and Strength Assessment (SF ANSA) score while on oral antipsychotic medications for at least four weeks prior to initiating a LAI antipsychotic medication; (2) had a subsequent SF ANSA score at least 6 months after starting LAI antipsychotic medications. These timeframes ensured that SF ANSA scores were collected long enough after initiation to ensure therapeutic dosing of medication. Notably, patients had variable lengths of time on medication (oral medication ranged 4 weeks–2 years; LAI medication ranged from 6 months to 4 years). These additional criteria reduced our sample size to n = 77.

Outcome Measures

For each patient, we extracted age, sex, race/ethnicity, psychiatric diagnosis, and various LAI prescription information (name of medication, months on LAI, date initiated).

All of our main outcomes were drawn from the SF ANSA (Community Behavioral Health Services 2010), a 27-item version of the evidenced-based, clinically-validated tool used to measure psychosocial functioning in the realms of housing stability, employment, and relationships in addition to other areas (Lyons and Anderson 1999). This tool has been shown to have good reliability ($\alpha = .75–.90$) and clinical validity as used in the community as guide for clinical placement and classification (Olson and Allen 2015).

There are two categories of items: "needs" and "strengths." For each SF ANSA "needs" item, clinicians rate the level of need on a scale of 0 ("No need for action") to 3 ("Need for immediate/intensive action"). "Strengths" items are used by clinicians to identify strengths around which they can build a treatment plan and are scored on a scale of 0 ("Significant strength present") to 3 ("Strength not present") (Lyons and Anderson 1999). We did not include "Behavioral Health Needs" items, as scores on these items may have been inflated by staff to ensure that patients continue to meet criteria for mental health services. We also threw out the "exploitation" item, as the regular and long SF ANSA manuals contained conflicting definitions of exploitation. To facilitate a better understanding of our results, below we further explain relevant SF ANSA items.

"Criminal behavior" refers to any criminal activity including status offenses, sexual offenses, and drug sales and related activity. The rating system differentiates between non-violent crimes (i.e. shoplifting, rated a 2) and violent crimes (i.e. assault, rated a 3) (Lyons and Anderson 1999). "Spirituality" is based on the individual's involvement in spiritual or religious beliefs and activities (Lyons and Anderson 1999). An individual with strong religious/spiritual beliefs or a high level involvement in a religious community would be rated a 0, while someone with no religious/spiritual activity would be rated a 3 (Lyons and Anderson 1999). "Medication adherence" is related to both non/psychotropic medications and focuses on the level of the individual's willingness and participation in taking prescribed medications (Lyons and Anderson 1999). At the most extreme (rating of 3), this would refer to someone who "refused to take prescribed psychotropic medications" or "has abused his or her medications" (Lyons and Anderson 1999). "Housing stability" encompasses current and likely future housing circumstances for the individual, which can range from stable housing (rated a 0) to homeless or living in transitional housing (rated a 3) (Lyons and Anderson 1999).

We chose to look at individual SF ANSA items instead of composite SF ANSA domains because the individual items are reliable. To our knowledge, the various domains of the SF ANSA have not been psychometrically validated. Furthermore, analyzing individual items allowed us to focus on our original, exploratory hypothesis regarding concrete recovery outcomes rather than abstract domains. We

also evaluated total SF ANSA scores, but only a subset of patients had complete SF ANSA data for both time points.

Data Analysis

We utilized Stata software (version 15.1) for data analysis. Demographic information was characterized using descriptive statistics and compared to the patients that did not meet all inclusion criteria using Pearson's Chi square tests where applicable. We compared the difference between SF ANSA items when patients were on PO versus LAI using the two-tailed Wilcoxon signed rank test. For the subset of patients who were not missing data any items, we summed the item scores to get a total SF ANSA score and analyzed these scores using the two-tailed paired *t* test.

Ethical Considerations

The authors declare no conflicts of interest and certify responsibility for this manuscript. We received verification from UCSF's Internal Review Board (IRB) that this study is classified as a quality improvement project and does not require IRB oversight per federal regulations documented in 45 CFR 46.102(d). The project was also approved by San Francisco Department of Public Health's Quality Management Department.

Results

In our sample of 77 participants, the average age was 46, with 34% identifying as female and a diverse racial/ethnic composition of 31% Asian, 29% African American, 18% white, 17% Latino, and 5% other/unknown. The average length of prescription, which we considered as a proxy for adherence, for LAIs in our sample was 2.21 years. The most frequent diagnosis was schizophrenia (57%) and the most common LAI agent was paliperidone 1-month formulation (52%). Compared to patients excluded from analyses, our study sample had similar age (excluded mean = 52, sample mean = 46) and gender ($\chi^2 = .04$, p = .852) distributions, but more Latino patients and fewer Asian/Pacific Islander patients ($\chi^2 = 15.99$, p = .003).

We observed significant improvements on psychosocial outcomes including criminal behaviors ($z = 2.39$, p = .017) and spirituality ($z = 2.20$, p = .028). Consistent with the literature, patients showed significant improvement in medication adherence ($z = 2.64$, p = .008). We observed a non-significant trend towards improved housing stability ($z = 1.79$, p = .073). All other SF ANSA items, including physical/medical health, family functioning, living skills, social functioning, employment, danger to self and others, grave disability, self-injurious behavior, cultural stress, substance use and severity, recovery stage, optimism, community connection, and recovery involvement, did not change significantly ($z \leq |1.64|$, p ≥ .100). The patients with no missing data (n = 10) showed a significant decrease in their total SF ANSA scores (*paired t* (9) = 3.30, p = .009), suggesting improvement in overall function on LAIs.

Discussion

We found that people who were transitioned from PO to LAI antipsychotic medications had statistically significant improvements in medication adherence, criminal behaviors, and spirituality but no other recovery-oriented goals. The association with housing stability was suggestive but not statistically significant. This exploratory study is novel in connecting the use of LAI medications to outcomes of recovery.

We have not seen any other studies showing a reduction in criminal behaviors when comparing oral versus LAI antipsychotic medications, a compelling benefit for this vulnerable patient population. To the authors' knowledge, improvements in the area of spirituality is also novel, though it has been thought of as a coping mechanism (Cohen et al. 2016). Our findings regarding adherence are important, but not surprising, given that LAIs are frequently used for people with adherence challenges (Marcus et al. 2015). The non-significant trend towards improved housing stability warrants further study given the strong linkage between housing stability and mental health (Gulcur et al. 2003). Taken together, these results suggest that rather than focusing solely on symptom-based outcomes, clinicians should actively measure improvements in recovery goals.

Our sample was likely representative of the general population of people taking LAIs. When compared to all the patients who did not meet all inclusion criteria, our sample was similar in terms of age and gender, with some minor differences in race/ethnicity for which we have no clear explanation. There are limitations associated with this study's design, sample, and analysis. First, this is an uncontrolled and un-randomized study which introduces sample and treatment biases. Our inclusion criteria (no LAI treatment gaps longer than 90 days) may have inadvertently selected a more adherent sample than the general population. Furthermore, most of the excluded patients were removed due to incomplete documentation which may have included acutely ill patients who were unable to tolerate discussions about their psychosocial goals. In addition to variability in types of antipsychotic medications used, it was common for the length of time taking the antipsychotic to vary significantly, which might influence outcomes. Our analysis assumes that the pharmacy records reflect patient adherence on both types of medication, but it is likely more accurate for LAIs than POs, which may skew our results in favor of LAIs because

we assume that the psychosocial improvements observed are due to the nature of LAIs when it may be the result of non-adherence to POs. Lastly, analysis of many SF ANSA items introduces the issue of multiple comparisons, though the benefits of looking at concrete items and the observational nature of this study must be weighed against this limitation.

Conclusion

In this unique, exploratory study of an urban, safety-net community mental health sample, patients on LAIs showed significant improvements in key psychosocial realms, including criminal behaviors, medication adherence, and spirituality, as well as a non-significant but suggestive trend towards greater housing stability. Community mental health providers need tools that can aid patients in achievement of recovery-oriented goals, and this study suggests that LAIs may be one such tool. Future research should focus on conducting rigorous effectiveness trials of LAIs to further characterize their effects on psychosocial functioning.

Compliance with Ethical Standards

Conflict of interest Dr. Mangurian received salary support from NIH Grants (K23MH093689, R01MH112420, and R03DK101857). Dr. Barnes was supported by the UCSF Mental Health Biostatistics Core. Dr. Wozniak is an employee of Behavioral Health Services at the San Francisco Department of Public Health. Drs. Thomas and Dilley are employees of UCSF, Department of Psychiatry. Dr. Yoshimatsu, Ms. Elser, and Ms. Ballinger were supported by the UCSF-San Francisco General Hospital Public Psychiatry Fellowship. All authors report no financial relationships with commercial interests.

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