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ORIGINAL ARTICLE

Initiating long-acting injectable antipsychotics during acute admission for patients with schizophrenia — A 3-year follow-up☆

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Background/Purpose: The debate on whether long-acting injectable antipsychotic (LAIA) medication is superior to oral medication, in preventing rehospitalization of patients with schizophrenia, remains inconclusive. We compared rehospitalization rates over 3 years following discharge from an acute admission, in which patients either began using LAIAs regularly for the first time, or continued to use oral antipsychotics.
Methods: A retrospective observational study of 92 inpatients with schizophrenia from a university-based medical center during 2004–2008. The primary outcome measure is the rehospitalization rates between groups, as estimated by Kaplan-Meier survival analysis.
Results: Eighteen of 47 (38.3%) LAIA patients, and 16 of 45 (35.6%) oral medication patients were rehospitalized (average time to rehospitalization, 378 ± 262 vs. 378 ± 340 days; $p = 0.997$). The estimated cumulative rates of rehospitalization were similar between groups. The overall odds comparing the LAIA to the oral medication group were 1.085 ± 0.373 (95%

Conflicts of interest: The authors have no conflicts of interest relevant to this article.

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confidence interval: 0.553—2.13, $p = 0.813$). Compared to the oral medication group, the LAIA group had fewer coded with sufficient previous treatment response (32% vs. 69%, $p < 0.001$), more poorly compliant (91% vs. 56%, $p < 0.001$), and a slightly longer length of stay at index admission (32.7 ± 11.3vs. 27.6 ± 12.1, $p = 0.04$).

Conclusion: Initiating LAIAs during admission for an acute psychotic episode, to a group of patients with an inadequate previous treatment response and poorer compliance, might keep their rehospitalization rates to the level of their oral antipsychotic medication treated counterparts.

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Introduction

In the treatment of schizophrenia, adherence to a prescribed medication regimen continues to be a problem, as is often seen when treating other chronic disorders pharmacologically.[1,2] Despite a relatively good initial treatment response for the first episode of psychosis, the discontinuation rate is generally high,[3,4] with both patients and their key caregivers being inclined to discontinue medication when symptoms improved. However, the risk of relapse was around four to five times higher in those who discontinued treatment.[5] A recent randomized control trial showed that among patients who remitted from their first episode of psychosis, relapse occurred in 79% of those who were treated with placebo for 1 year.[6] Another observational study revealed an astonishingly high relapse rate after discontinuing long-acting injectable antipsychotic treatment for remitted first episode schizophrenia.[7] In another two first-episode studies, resuming medication upon the first signs of relapse (a targeted maintenance or intermittent treatment strategy) still doubled the risk of relapse compared to continuous antipsychotic treatment.[8,9]

It seems obvious that maintenance of antipsychotic therapy should be the mainstay of relapse prevention for patients with schizophrenia, but many factors affect medication adherence, such as cognitive impairment, substance use, depressive symptoms, adverse effects, inconvenient medication regimen, feelings of being stigmatized, and prejudiced attitude and beliefs in an illness model.[2,10] A patient's attitude to medication compliance is more likely to improve, once their acute symptoms have subsided,[11] but sometimes a satisfactory response will not be obtained until medications have been used regularly for an extended period. Long-acting injectable antipsychotic (LAIA) agents were developed to ensure the continuation of treatment, with the aim of improving the patient's outcomes, in both acute and outpatient management.[12—14] LAIAs have been demonstrated to help patients in achieving remission[15,16]; hence, we were able to reshape the patient's attitudes toward treatment in a remitted state by initiating LAIAs in an acute state.[17]

However, the apparent advantage of this formulation was not translated into a wide application of LAIAs, a fact often related to the psychiatrist's negative attitudes toward conventional depot antipsychotics,[18,19] despite the patient's positive attitude.[20] Thus, the traditional depots of antipsychotics are generally reserved for chronic noncompliant patients.[21] Besides, the advantage of LAIAs over oral antipsychotics has not yet been shown to be conclusive. Haddad et al's review of the first-generation depot studies seemed to suggest favorable outcomes over oral antipsychotics, but the authors also pointed out this finding being subject to criticism over methodological issues.[22] A recent meta-analysis demonstrated an apparent advantage of LAIAs in reducing relapse rates, but not in preventing rehospitalization.[23] However, a large-scale randomized trial revealed no significant difference in hospitalization rates between patients using LAIAs and oral medications.[24]

In this study, we aimed to explore whether introducing regular use of LAIAs for patients with schizophrenia, the first time in their course of illness during admission for an acute episode, could substantially lower the risk of rehospitalization in the following 3 years, as compared to that of continued administration of oral antipsychotics at index admission.

Methods

This is a retrospective observational study conducted by reviewing patients' medical records. The study protocol has been approved by the Institutional Review Board of the study hospital.

Study samples

The researchers examined registration records regarding the diagnosis of all inpatients admitted to the psychiatric acute ward of a university-based medical center, between 2004 and 2008. The LAIAs group was defined by patients with an ICD-9-CM diagnosis of schizophrenia or schizoaffective disorder, who had not previously received more than three consecutive doses of LAIAs, in whom regular LAIA treatment was initiated during index admission for the first time in the course of their illness. These patients might have received only one or two injections during admission, while continuing LAIA therapy during outpatient visits immediately after discharge.

For comparison, an age- and sex-matched inpatient admitted in the same month as the index case, was identified using the following criteria: patients who also have not previously received more than three consecutive LAIA doses, and who continued to receive oral antipsychotic medications throughout index admission. If we failed to find an appropriate patient for comparison in that month, we tried to find one in the adjacent 2 months, so that we could find comparable numbers of patients treated under similar

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