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Stabilization of Schizoaffective Disorder after Transition from Olanzapine to Paliperidone: A Case Report

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Abstract Schizoaffective disorder may require antipsychotic modification when persistent psychotic symptoms coexist with treatment-related adverse effects. We report a 29-year-old woman with schizoaffective disorder who continued to experience prominent auditory hallucinations despite olanzapine 20 mg daily and had developed weight gain and prediabetes. A gradual transition to paliperidone was initiated because of persistent symptoms and metabolic concerns. During cross-titration, she experienced psychiatric destabilization requiring inpatient hospitalization. Following discharge, paliperidone was titrated to 12 mg daily while olanzapine was progressively reduced. Auditory hallucinations persisted but became less intense and less impairing, with concurrent improvement in anxiety, sleep, cognition, and functioning. Olanzapine was subsequently discontinued, and clinical improvement was maintained for approximately two months on paliperidone 12 mg monotherapy. At the most recent follow-up, paliperidone was reduced to 9 mg daily at the patient's request, although response to the lower dose was not yet available. This case highlights the complexity of antipsychotic transitions in schizoaffective disorder and the importance of individualized titration, close monitoring, and balancing symptom control with medication tolerability.

Keywords: *schizoaffective disorder, paliperidone, olanzapine, antipsychotic switching, auditory hallucinations, metabolic adverse effects*

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1. Introduction

Schizoaffective disorder is a chronic and potentially disabling psychotic disorder characterized by the coexistence of prominent mood symptoms and schizophrenia-spectrum features, including hallucinations, delusions, and disorganized thinking [1]. Pharmacologic management can be challenging because treatment must address both psychotic and affective symptoms while supporting long-term stability and functioning. Antipsychotic medications remain central to treatment, although the evidence base specifically focused on schizoaffective disorder is more limited than that for schizophrenia. Among available agents, paliperidone has comparatively strong disorder-specific evidence supporting its use [1,2].

Selection of an antipsychotic requires consideration not only of symptom control but also of adverse effects that may compromise long-term treatment. Second-generation antipsychotics differ substantially in their metabolic profiles, with olanzapine consistently associated with a relatively high risk of weight gain and metabolic dysregulation [3,4]. These effects can become clinically significant during prolonged treatment and may contribute to the decision to modify therapy, particularly when substantial psychiatric symptoms persist despite treatment. However, switching antipsychotics is not without risk, and potential benefits in tolerability must be balanced against the possibility of psychiatric worsening during the transition [5].

Paliperidone is a second-generation antipsychotic with evidence supporting its use for psychotic and affective symptoms in schizoaffective disorder [2,6]. This report describes a young woman with schizoaffective disorder who experienced persistent auditory hallucinations and metabolic complications during olanzapine treatment. Transition to paliperidone was complicated by psychiatric destabilization requiring hospitalization but was subsequently followed by progressive symptomatic improvement, successful discontinuation of olanzapine, and stabilization on paliperidone. The case illustrates the clinical challenges of balancing persistent psychotic symptoms, antipsychotic tolerability, and psychiatric stability during a medication transition.

2. Case Presentation

A 29-year-old woman with a history of schizoaffective disorder and anxiety presented to establish outpatient neuropsychiatric care because of worsening psychotic symptoms despite pharmacotherapy. Her psychiatric

history included two prior inpatient psychiatric hospitalizations, in 2022 and 2024, and intermittent outpatient treatment. She denied substance use. She was employed from home and reported strong support from her fiancé and parents.

Her predominant symptoms were persistent auditory hallucinations that had recently increased in intensity. She described the voices as loud, threatening, and paranoid, with intermittent command content involving harm to herself or others. Approximately two days before the initial evaluation, she had experienced suicidal-themed auditory content but denied current suicidal intent or plan. She also reported anxiety, impaired concentration, slowed cognitive processing, and frequent internal preoccupation. Poor sleep and psychosocial stress coincided with worsening symptoms. Despite the severity of her symptoms, she demonstrated insight, remained engaged in treatment, and maintained a safety plan that included seeking emergency or inpatient psychiatric care if symptoms or safety concerns worsened.

Mental status examination showed a well-groomed and cooperative patient with an anxious and dysphoric mood and a subdued, congruent affect. Thought process was linear and goal directed, although responses were somewhat slowed. Auditory hallucinations and internal preoccupation were prominent by history, without reported visual hallucinations. She denied current suicidal or homicidal intent or plan. Insight and judgment were preserved. No abnormal involuntary movements were observed, and her Abnormal Involuntary Movement Scale score was 0.

At presentation, her medications included olanzapine 20 mg daily, administered as 5 mg in the morning, 5 mg later in the day, and 10 mg at bedtime, hydroxyzine 25 mg twice daily as needed, and metformin 850 mg daily. Previous haloperidol treatment had caused drooling and muscle spasms. Escitalopram and trazodone had previously been discontinued. Despite olanzapine treatment, clinically significant auditory hallucinations persisted. She had also experienced weight gain and developed prediabetes, for which metformin had been prescribed.

At the initial psychiatric evaluation in late May 2026, paliperidone 3 mg nightly was initiated while the 10 mg bedtime dose of olanzapine was discontinued; olanzapine 5 mg in the morning and 5 mg later in the day was temporarily continued during cross-titration. She was advised to seek emergency psychiatric evaluation if hallucinations, suicidal thoughts, or other safety concerns worsened.

The following day, the patient experienced worsening anxiety, tachycardia, and psychiatric destabilization requiring inpatient psychiatric hospitalization. By early June 2026, she had been discharged on paliperidone 9 mg each morning and olanzapine 5 mg nightly, with metformin 850 mg daily continued. Collateral information from her boyfriend indicated that auditory hallucinations persisted but were less severe than before hospitalization. Anxiety and insomnia remained prominent initially, and hydroxyzine 25 mg nightly as needed was used with reported benefit. Mild daytime drowsiness and slowed responses were observed, but no acute safety concerns were reported.

At a subsequent collateral telephone follow-up, her boyfriend subjectively rated her anxiety at approximately 3/10 and reported improvement in mood and engagement in daily activities. Auditory hallucinations remained fairly constant, with their intensity subjectively estimated at approximately 5/10 and worsening with psychosocial stress. These values represented informal collateral estimates rather than validated symptom-scale scores. No suicidal ideation had been reported since hospitalization, and no homicidal ideation or other acute safety concerns were identified. Sleep had improved to approximately eight to nine hours nightly, and medication adherence was reported as good. Metformin was continued, and hydroxyzine remained available as needed for anxiety and insomnia. Because hallucinations remained clinically significant, olanzapine was reduced to 2.5 mg nightly and paliperidone was increased to 12 mg daily.

At outpatient follow-up in July 2026, while taking paliperidone 12 mg daily and olanzapine 2.5 mg nightly, the patient reported substantial improvement in psychotic symptoms. Auditory hallucinations persisted but were less intense and less impairing. She described improved cognition, awareness, and ability to cope with the voices, although intermittent internal preoccupation continued to affect occupational and interpersonal functioning. Anxiety had improved, sleep had stabilized at approximately eight hours nightly, and she reported no recent self-harm thoughts or behaviors. She requested discontinuation of olanzapine to minimize polypharmacy, and olanzapine was subsequently discontinued in July 2026.

At telephone follow-up in September 2026, after approximately two months off olanzapine while maintained on paliperidone 12 mg daily, the patient reported that she was doing significantly better overall. She described stable mood and functioning, confirmed medication adherence, and reported no acute psychiatric or safety concerns. She also reported approximately two months of amenorrhea; however, similar menstrual irregularity had previously occurred during olanzapine treatment, and a medication-specific cause could not be established. Follow-up with her primary care physician was planned. Follow-up glycemic laboratory data, including hemoglobin A1c, were not available to determine whether prediabetes improved or persisted after olanzapine discontinuation. Given her sustained improvement, she requested reduction of paliperidone from 12 mg to 9 mg daily. Paliperidone 9 mg daily was initiated at the most recent follow-up, with instructions to return to 12 mg if symptoms worsened or additional symptom control became necessary. Clinical response to the lower dose was not yet available.

3. Discussion

This case illustrates the challenge of modifying antipsychotic therapy when persistent psychotic symptoms coexist with treatment-related adverse effects. Despite olanzapine 20 mg daily, the patient continued to experience prominent auditory hallucinations while also developing weight gain and prediabetes requiring metformin. Olanzapine has substantial metabolic liability, and switching antipsychotics may be considered when

inadequate symptom control and tolerability concerns occur together [3,4,5]. However, potential benefits must be balanced against the risk of psychiatric worsening during the transition. Metformin was continued after olanzapine discontinuation, but follow-up glycemic laboratory data were unavailable to assess metabolic recovery. A glucagon-like peptide-1 receptor agonist was not initiated during the reported course; if weight or glycemic abnormalities persist, additional metabolic therapy could be considered after reassessment.

The pharmacologic differences between olanzapine and paliperidone were relevant to treatment selection. Both agents antagonize dopamine D2 and serotonin 5-HT2A receptors, but olanzapine has broader activity at histamine H1, serotonin 5-HT2C, and muscarinic receptors, whereas paliperidone acts predominantly through D2 and 5-HT2A antagonism and has minimal muscarinic affinity [7]. This more selective receptor pattern provided a pharmacologically distinct alternative in a patient with persistent psychosis and substantial metabolic burden during olanzapine treatment. Paliperidone is not metabolically neutral and carries other risks, including hyperprolactinemia and extrapyramidal symptoms [6]; therefore, the transition represented a change in the balance of efficacy and tolerability rather than selection of an inherently superior antipsychotic.

The hospitalization during cross-titration highlights the vulnerability associated with antipsychotic transitions. Cross-titration is commonly used, although evidence establishing an optimal switching strategy remains limited [8,9]. In this patient, psychiatric destabilization occurred the day after paliperidone was initiated and required hospitalization. Because active psychosis, sleep disruption, and psychosocial stress were already present, the deterioration cannot be attributed solely to medication switching. Following hospitalization, paliperidone was increased from 9 mg to 12 mg daily while olanzapine was progressively reduced. Paliperidone has direct evidence supporting its use in schizoaffective disorder, including controlled treatment with oral doses of 3 to 12 mg daily [2,6,10]. Auditory hallucinations subsequently became less intense and less impairing, while anxiety, sleep, cognition, and overall functioning improved sufficiently to permit complete discontinuation of olanzapine.

The subsequent course allowed simplification to paliperidone monotherapy. After olanzapine was discontinued, the patient remained clinically improved for approximately two months while receiving paliperidone 12 mg daily. At the most recent follow-up, she requested reduction to 9 mg daily; however, clinical response to the lower dose was not yet available. Meaningful improvement had occurred despite residual auditory hallucinations, indicating that clinically important recovery may occur without complete symptomatic remission. Amenorrhea was also reported during follow-up, although similar menstrual irregularity had occurred during previous olanzapine treatment. Because prolactin measurements and a completed endocrine evaluation were unavailable, a medication-specific cause could not be established despite the known prolactin-elevating potential of paliperidone [11].

Several limitations should be considered. Symptom changes were assessed during routine clinical care and partly through collateral history rather than validated longitudinal rating scales. Detailed records from the intervening hospitalization, serial metabolic measurements, follow-up glycemic laboratory data after olanzapine discontinuation, and prolactin concentrations were unavailable. Follow-up after the most recent reduction of paliperidone to 9 mg daily was also not yet available. Hospitalization, improved sleep, psychosocial support, and the fluctuating course of schizoaffective disorder may have contributed to improvement. Nevertheless, this case demonstrates sustained clinical stabilization on paliperidone 12 mg monotherapy after a clinically difficult transition from olanzapine and successful discontinuation of the prior antipsychotic.

4. Conclusion

This case demonstrates successful stabilization of schizoaffective disorder after transition from olanzapine to paliperidone in the setting of persistent psychotic symptoms and metabolic treatment burden. Although the transition was complicated by psychiatric destabilization requiring hospitalization, subsequent paliperidone titration was associated with reduced hallucination severity and improvement in anxiety, sleep, cognition, and functioning, permitting complete discontinuation of olanzapine. Clinical improvement was maintained for approximately two months on paliperidone 12 mg monotherapy. At the most recent follow-up, a reduction to 9 mg daily was initiated, but response to the lower dose was not yet available. This case underscores the importance of individualized titration and close monitoring when balancing symptom control, tolerability, and psychiatric stability during antipsychotic transitions.

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