e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2026; 18(4); 1931-1935

Original Research Article

When 'Safe' Doses Are Not: Acute Oromandibular Dystonia Following Very Low-Dose Quetiapine Augmentation in a Patient on Long-Term Escitalopram

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Received: 06-02-2026 / Revised: 16-03-2026 / Accepted: 10-04-2026

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Conflict of interest: Nil

Abstract

Background: Quetiapine is widely regarded as having low propensity for extrapyramidal symptoms (EPS) because of transient striatal dopamine D_2 receptor occupancy and rapid dissociation kinetics. However, acute dystonic reactions have been reported, occasionally at very low doses used off-label for insomnia and anxiety.

Case Presentation: A 32-year-old Indian male presented to the emergency department with abrupt onset of lateral tongue deviation, sustained jaw and facial muscle spasms, and dysarthria. Symptoms emerged on day 3 after initiation of quetiapine 25 mg at bedtime for insomnia and anxiety, while he remained on a stable one-year regimen of escitalopram 20 mg and clonazepam 0.5 mg daily. Neurological examination confirmed isolated oromandibular dystonia without oculogyric crisis, rigidity, autonomic instability, or altered sensorium. Serum electrolytes, including calcium, were within normal limits. Intravenous promethazine 50 mg produced complete symptom resolution within two hours. Quetiapine was discontinued; escitalopram was continued unchanged. The Naranjo Adverse Drug Reaction Probability Scale yielded a score of 7 (probable). At one-week follow-up, no recurrence or residual symptoms were noted.

Conclusion: Acute oromandibular dystonia may occur with very low-dose quetiapine even in patients stabilised on serotonergic co-medication. Young male sex, early treatment exposure, and concomitant selective serotonin reuptake inhibitor (SSRI) therapy are plausible modifiers of susceptibility. Prompt recognition and parenteral anticholinergic or antihistaminic therapy yield rapid resolution. Clinicians prescribing quetiapine off-label for sleep and anxiety should remain vigilant for EPS and report such reactions to pharmacovigilance systems.

Keywords: Quetiapine; Dystonia; Extrapyramidal Symptoms; Selective Serotonin Reuptake Inhibitors; Drug-Related Side Effects and Adverse Reactions.

DOI: 10.25258/ijcpr.18.2.319

Introduction

Acute dystonia is a drug-induced movement disorder characterised by sustained, involuntary muscle contractions that produce abnormal postures or repetitive movements, typically involving the face, jaw, tongue, neck, and upper limbs.[1] It usually occurs within hours to days after initiation or dose escalation of a dopamine receptor-blocking agent, with approximately half of cases presenting within 48 hours and the large majority within five days of drug exposure.[1] Although first-generation antipsychotics carry the highest risk, second-generation antipsychotics (SGAs) may also precipitate acute dystonic reactions, particularly during the early phase of treatment.[2] Quetiapine is frequently cited as the SGA with the lowest EPS liability, attributed to relatively low and transient striatal D_2 receptor occupancy and rapid dissociation from the D_2 receptor.[2] A recent systematic review

and dose-response meta-analysis of 110 fixed-dose studies confirmed that, unlike most antipsychotics, quetiapine shows a negligible dose–EPS relationship across its clinical dose range, with odds ratios that do not significantly differ from placebo.[3] Nevertheless, pharmacovigilance signals and isolated case reports indicate that EPS — including acute dystonia and akathisia — can still emerge, sometimes at the very low doses commonly used off-label for insomnia and anxiety.[4,5] Contemporary evidence also recognises that concomitant serotonergic therapy may shift the threshold for drug-induced movement disorders, as serotonergic modulation exerts a tonic inhibitory influence on nigrostriatal dopaminergic transmission.[6,7]

We describe an episode of acute oromandibular dystonia occurring three days after initiation of quetiapine 25 mg at bedtime in a 32-year-old male maintained on long-term escitalopram, and we situate this observation within the current literature on low-dose quetiapine-associated EPS.

Case Presentation

A 32-year-old Indian male presented to the emergency department with abrupt-onset persistent lateral deviation of the tongue, painful tightening of the jaw and facial muscles, and difficulty in articulation. Symptoms had developed suddenly several hours earlier and progressively intensified.

Three days prior to presentation, he had been started on quetiapine 25 mg at bedtime for insomnia and anxiety. He had been on a fixed-dose combination of escitalopram 20 mg and clonazepam 0.5 mg daily for approximately one year for a somatoform disorder. His past history was notable for nicotine dependence. There was no prior exposure to antipsychotics, antiemetics, or other dopamine-blocking agents, and no history of seizures, head injury, substance intoxication, or pre-existing neurological disease. Family history was unremarkable for movement disorders.

On examination, the patient was alert, oriented, and cooperative, with stable vital signs. Neurological evaluation revealed sustained involuntary contractions of the oromandibular musculature with lateral tongue deviation and dysarthria. Oculogyric crisis, limb dystonia, tremor, cogwheel rigidity, bradykinesia, altered sensorium, and autonomic instability were absent. There were no features to suggest a generalised seizure (no loss of awareness, generalised motor jerks, tongue bite, urinary incontinence, or post-ictal confusion) or anaphylaxis/angioedema (no urticaria, facial oedema, or stridor). Hyperthermia, lead-pipe rigidity, and fluctuation in consciousness — features that would raise suspicion of neuroleptic malignant syndrome — were also absent. Cranial nerve, motor, sensory, and cerebellar examinations were otherwise unremarkable.

Initial investigations — including complete blood count, serum electrolytes, serum calcium, random blood glucose, and renal and hepatic function tests — were within normal limits, effectively excluding hypocalcaemic tetany and acute metabolic disturbances. Electrocardiography was unremarkable.

On the basis of the temporal association with quetiapine initiation, the characteristic phenomenology, and exclusion of alternative diagnoses, a clinical diagnosis of acute drug-induced oromandibular dystonia was made. The patient was treated with intravenous promethazine 50 mg, with complete resolution of dystonic symptoms within two hours. Quetiapine was discontinued; escitalopram and clonazepam were continued unchanged. The patient was observed in the emergency department and discharged with outpatient follow-up. At one-week follow-up, he reported no recurrence of dystonia, akathisia, or other EPS. The adverse drug reaction was reported to the institutional Adverse Drug Monitoring Centre (Report ID: IN-IPC-301204003).

Table 1: Timeline of clinical events

Day	Event
Day 0	Quetiapine 25 mg nocte initiated for insomnia and anxiety (stable regimen of escitalopram 20 mg + clonazepam 0.5 mg continued).
Day 3	Abrupt onset of oromandibular dystonia: tongue deviation, jaw and facial spasm, dysarthria. Emergency department presentation.
Day 3 (ED)	Clinical diagnosis of acute drug-induced dystonia. Serum electrolytes including calcium within normal limits. Intravenous promethazine 50 mg administered.
Day 3 (within 2 h)	Complete symptom resolution. Quetiapine discontinued.
Day 10	Follow-up: no recurrence. Escitalopram and clonazepam continued; patient clinically stable.

Causality Assessment (Naranjo Scale): Formal causality assessment using the Naranjo Adverse Drug Reaction Probability Scale yielded a total score of 7, classifying the reaction as probable.

Table 2: Naranjo Adverse Drug Reaction Probability Scale

Item	Response	Score
Previous conclusive reports of this reaction?	Yes	+1
Event appeared after suspected drug administered?	Yes	+2
Improved on discontinuation/antagonist?	Yes	+1
Reappeared on re-challenge?	Not done	0
Alternative causes reasonably excluded?	Yes	+2
Reappeared with placebo?	Not applicable	0
Drug level toxic?	Not measured	0
Dose-response relationship?	Not assessed	0
Similar reaction to same/similar drugs previously?	No	0
Objective evidence of reaction?	Clinical exam + rapid response	+1
Total score	Probable	7

The temporal association (onset within three days of initiation), clear dechallenge (rapid resolution after IV promethazine and drug discontinuation), absence of recurrence despite continuation of escitalopram, and exclusion of alternative pharmacological triggers collectively support quetiapine as the most likely precipitant. Re-challenge was not attempted on ethical grounds.

Discussion

Acute dystonia is thought to result from an acute imbalance between dopaminergic and cholinergic activity in the nigrostriatal pathway: D_2 receptor blockade reduces dopaminergic tone, producing relative cholinergic overactivity that manifests as sustained muscle contractions.1 The clinical presentation is typically abrupt and distressing, and parenteral anticholinergic agents (such as benztropine or trihexyphenidyl) or antihistamines with anticholinergic properties (promethazine, diphenhydramine) are rapidly effective.[1] In our patient, intravenous promethazine produced complete resolution within two hours, consistent with the expected pharmacological response.

Quetiapine is mechanistically distinct among SGAs in displaying only low and transient striatal D_2 occupancy, which underpins its favourable EPS profile.[2] The systematic review by Siafis and colleagues of 110 fixed-dose studies found that quetiapine, uniquely alongside sertindole, showed a negligible dose–EPS relationship across its entire clinical dose range, with odds ratios not significantly differing from placebo.[3] These population-level estimates, however, pertain largely to schizophrenia populations. A "low-risk" agent is not a "no-risk" agent: individual susceptibility, concomitant medications, and the early exposure window can all shift the threshold at which EPS emerge.[1,2]

Several demographic and pharmacological factors plausibly contributed to our patient's susceptibility despite a very low dose (25 mg/day). First, young age and male sex are well-established demographic risk factors for acute drug-induced dystonia.[1] Second, the first week of antipsychotic exposure is the classical high-risk window for acute dystonic reactions.[1] Third, and perhaps most importantly, concomitant SSRI therapy may have lowered the dystonia threshold. SSRIs are themselves recognised, though uncommon, causes of drug-induced EPS; the proposed mechanism involves serotonergically-mediated inhibition of nigrostriatal dopaminergic transmission, functionally resembling partial dopamine blockade.[6,7] Our patient had tolerated escitalopram 20 mg daily for approximately one year without any movement disorder, but the introduction of quetiapine — even at sub-therapeutic antipsychotic dosing — appears to have added a second dopaminergic insult that exceeded his individual threshold. The temporal sequence, dechallenge response, and absence of recurrence after quetiapine withdrawal despite continued escitalopram strongly support quetiapine as the primary trigger, with the SSRI acting as a probable sensitising co-factor. The off-label use of quetiapine at doses of 12.5–50 mg/day for insomnia and anxiety is widespread in clinical practice, despite limited efficacy evidence at these doses and often under-appreciated safety signals. Gazzellone and colleagues reported acute dystonia and akathisia in an 18-year-old psychotropic-naïve man after only three doses of quetiapine 25 mg twice daily, with rapid resolution following benztropine and drug discontinuation.[4] Dutta and colleagues described akathisia emerging at quetiapine doses of 25–37.5 mg/day in two patients with underlying neurological illness (autoimmune encephalitis and possible CNS vasculitis), with causality supported by Naranjo scoring and improvement after discontinuation.[5] Our case extends this spectrum in two respects: the phenomenology is isolated oromandibular dystonia rather than akathisia or generalised dystonia, and the clinical context is a medically stable individual without neurological disease but with long-standing SSRI exposure. Taken together, these reports argue against the perception that low-dose quetiapine is uniformly EPS-sparing and emphasise that individual vulnerability factors can shift the dose–risk curve.

From a differential diagnostic standpoint, it was essential in this case to systematically exclude

conditions that mimic acute dystonia: neuroleptic malignant syndrome (excluded by absence of hyperthermia, rigidity, and autonomic dysregulation), hypocalcaemic tetany (excluded biochemically), partial seizure with post-ictal facial dyskinesia (no witnessed seizure activity, preserved consciousness throughout, and rapid response to anticholinergic therapy), and anaphylaxis or angioedema (no mucocutaneous or airway involvement). The rapid and complete response to intravenous promethazine further reinforced the diagnosis.[8]

Clinically, three management principles are reinforced by this case:

(i) prompt recognition of acute dystonia, including systematic exclusion of mimics; (ii) immediate parenteral anticholinergic or antihistaminic therapy, which is both diagnostic and therapeutic; and (iii) avoidance of re-exposure to the offending agent, with cautious selection of alternatives if antipsychotic therapy is subsequently indicated.

Pharmacovigilance reporting is particularly valuable for low-dose off-label prescribing, where EPS may otherwise remain under-recognised and under-reported.[5]

Table 3: Selected reports of EPS with low-dose quetiapine

Study (Year)	Dose	Onset	Phenomenology	Concomitant medication / context	Outcome
Gazzellone et al. (2022)[4]	25 mg BID	After 3 doses	Acute dystonia (arms/hands) + akathisia	Psychotropic-naïve; psychotic depression	Resolved with benztropine; quetiapine stopped
Dutta et al. (2024)[5]	25–37.5 mg/day	Day 5 (index case)	Akathisia	Autoimmune encephalitis / possible CNS vasculitis	Improved after discontinuation; Naranjo probable
Present case (2026)	25 mg nocte	Day 3	Oromandibular dystonia	Long-term escitalopram 20 mg + clonazepam 0.5 mg	Resolved with IV promethazine; quetiapine stopped; no recurrence at 1 week

EPS: extrapyramidal symptoms; BID: twice daily; CNS: central nervous system; IV: intravenous.

Conclusion

Acute oromandibular dystonia can occur with very low-dose quetiapine, including at the 25 mg/day level commonly used off-label for insomnia and anxiety. Young male sex, the early treatment window, and long-standing serotonergic co-medication may each lower the threshold for this reaction, even in otherwise medically stable individuals. Clinicians prescribing low-dose quetiapine for non-psychotic indications should counsel patients about early movement-disorder symptoms, recognise and systematically exclude mimics of acute dystonia at presentation, and treat promptly with parenteral anticholinergic or antihistaminic therapy. Active pharmacovigilance reporting of such reactions is essential to strengthen the evidence base on the safety of off-label low-dose quetiapine prescribing.

Declarations

Patient consent: Written informed consent was obtained from the patient for publication of this case report. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Ethical approval: Not applicable. Institutional ethics committee approval is not required for a single anonymised case report at our institution; however, the case was duly reported to the institutional Adverse Drug Monitoring Centre (Report ID: IN-IPC-301204003).

Conflict of interest: None declared.

Funding: This case report received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Author contributions: A managed the case, collected clinical details, and drafted the manuscript. SR supervised the clinical management, reviewed, and critically edited the manuscript. SPC, MBK, and GSG contributed to clinical care, literature review, and manuscript revision. All authors read and approved the final manuscript.

Data availability: Not applicable; no primary dataset was generated for this single-case report. Anonymised clinical records are maintained at the Department of Psychiatry, Shri B. M. Patil Medical College, and may be made available on reasonable request, subject to institutional policy.

Acknowledgements: The authors thank the patient for permitting publication of his clinical details, and the staff of the emergency department and Adverse Drug Monitoring Centre at Shri B. M. Patil Medical

College, Hospital and Research Centre for their assistance in clinical management and reporting.

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