International Journal of Medical Science and Health Research

Vol.10, No.03; 2026

ISSN: 2581-3366

Importance of Medication Reconciliation in Treatment of a Transgender Male Patient With Bipolar Disorder Undergoing Gender-affirming Hormone Therapy

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doi: 10.51505/ijmshr.2026.10307 URL: http://dx.doi.org/10.51505/ijmshr.2026.10307

Received: May 07, 2026 Accepted: May 20, 2026 Online Published: May 29, 2026

Abstract

Bipolar disorder is characterized by depressive and manic symptoms that occur in cycles, and higher prevalence rates have been reported in transgender populations. Female-to-male (FTM) and transmasculine people sometimes opt for gender-affirming hormone therapy (GAHT) via exogenous testosterone, a hormone responsible for body and brain masculinization. However, testosterone can exacerbate mental illness symptoms or trigger a depressive/manic episode, especially in the presence of mood disorder. A 38-year-old FTM man with stable bipolar disorder presented with symptoms of mania after increasing the dosage of his GAHT, which was not reported to his psychiatrist. Within a few days, the patient was hospitalized and required initiation of antipsychotic treatment and cessation of testosterone therapy. A lack of medical reconciliation and knowledge of GAHT interactions with neural circuitry led to an avoidable, significant consequence. While the neurobiological connections of testosterone GAHT, bipolar disorder, and transgenderism are still unclear, overlapping neuronal mechanisms could have

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ISSN: 2581-3366

warranted a severer consequence for the patient. This case highlights the importance of medication reconciliation and how clinicians should recognize potential implications of GAHT and mood disorder within the FTM/transmasculine population.

Keywords: medication reconciliation, bipolar disorder, gender-affirming hormone therapy, testosterone, transgender

1. Introduction

Bipolar disorders are chronic, severe psychopathologies associated with cycles of mania or hypomania, depression, mixed states, and functionally-impairing subsyndromal episodes (McIntyre et al., 2020). The average time between the onset of symptoms and the diagnosis of bipolar disorder is over seven years, and even a single manic or depressive episode is strongly related to cortical thinning in multiple regions of the brain (Scott et al., 2022; Förster et al., 2023). Common symptoms of depressive episodes include anhedonia, suicidal thoughts and behaviors, and loss of energy, while manic phases are characterized by rapid speech, racing thoughts, and possibly hallucinations and/or delusions (Bronkhorst & Motubatse, 2017). Globally, 37 million people experience the challenges and burdens of bipolar disorder, with 34 million of those individuals being adults ("Bipolar Disorder," 2025). Certain groups are predisposed to developing bipolar disorder, including the transgender and gender non-conforming populations (Hanna et al., 2019).

Around seven in every 1000 adults in the United States identify as transgender, and 34 of every 100 transgender people in the United States identify as female-to-male (FTM) (Williams Institute, 2025). Though legislative and cultural progress have been made to promote societal equity for these individuals, the overall zeitgeist of the past 25 years has either remained stagnant or regressed to that of decades prior (Kinney et al., 2022). The trans community has been burdened with harsh scrutiny, and hate crimes driven by transphobia occur more frequently now than ever before ("Alert Desk: GLAAD's Anti-LGBTQ Extremism Reporting Tracker," 2025). Intrinsic stressors related to transitioning also contribute to the externally acquired psychological trauma, which may lead to maladaptive coping mechanisms such as self-harm and suicidality (Adão et al., 2026, Lee et al., 2025). An estimated 50 percent of trans people will attempt suicide in their lifetime: a clear indicator of a public health crisis within this population (Kohnepoushi et al., 2023). Further, trans people are (unsurprisingly) at an alarmingly high risk for developing anxiety, depression, psychosis, bipolar disorder, and other mental health disorders (Hanna et al., 2019). Despite the enormous burdens and challenges that accompany medically and socially transitioning, gender-affirming hormone therapy (GAHT) has exhibited therapeutic effects for some trans individuals who receive such care (Kranz et al., 2020). GAHT may entail exogenous testosterone for people identifying as FTM or transmasculine.

Testosterone is an endogenous hormone involved in sexual development, vocal deepening, and anabolic changes. The hypothalamic-pituitary-gonadal axis is responsible for the management of testosterone levels in the human body (Nassar & Leslie, 2023). Though testosterone is typically

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ISSN: 2581-3366

associated with males, it is not exclusive to males alone: the hormone is also found in females, albeit at much lower levels (Nassar & Leslie, 2023). It influences emotional processing and plays a key role in neural mechanisms involved in aggression (Sher, 2023). Too little testosterone is related to depression and anxiety, but an excess is strongly linked to competitiveness, impulsivity, and aggression (Zitzmann, 2020). Thus, testosterone is a hormone that must be closely monitored by doctors and psychiatrists alike for the safety of their patients. Short-acting injections, topical gels/creams, and pills are most frequently used by hypogonadal men, but transgender men and transmasculine people have found exogenous testosterone therapy to achieve desirable aesthetic and physiological changes (Auerbach et al., 2021; Baker et al., 2021). However, these individuals, especially those with a history of mental illness, must use caution when undergoing masculinizing GAHT since testosterone can worsen psychopathological symptoms and possibly trigger psychosis (Alastanos & Mullen, 2017).

Here, we present reports of increased aggression, irritability, and mood swings in the case of a 38-year-old transgender man ("Mr. M") with a history of bipolar disorder undergoing testosterone GAHT.

2. Case Presentation

We present a thirty-eight-year-old FTM patient with prior diagnosis of Bipolar I Disorder and two previous hospitalizations, who had been stable for six years on Valproate 1000 mg, Latuda 120 mg, and Buspar 30 mg. He started on Jantezo 158 mg (two tablets) after top surgery.

Prior to coming out as trans, Mr. M was diagnosed with bipolar disorder when he was twenty-one years old. Overall, his condition was well-controlled and regularly monitored. In the four years following his initial manic episode warranting his diagnosis, he experienced two depressive episodes and one other manic episode. Throughout the first years of his diagnosis, strict adherence to his antipsychotics was followed as well as routine cognitive behavioral therapy. At the age of thirty-two, the patient started socially and medically transitioning to male. Mr. M was started on testosterone cypionate 50 mg QW for 4 weeks followed by a switch to testosterone undecanoate 158 mg BID, which was achieving the hormonal and physical changes Mr. M expected from treatment. He has remained on this dose of testosterone undecanoate since then.

In accordance with Mr. M's testosterone therapy, he and his treatment team closely tracked any possible manic symptoms and strictly adhered to his prescription of lurasidone 120 mg QD. Mr. M did not exhibit any symptoms for the first few weeks of his treatment. However, by the end of the first month, the patient started experiencing symptoms of anxiety (i.e., rumination, perseverative thinking, nervousness) and difficulty sleeping. His medical team decided to temporarily stop GAHT and add 25 mg of quetiapine QD to his regimen, which resolved his symptoms in four days. He restarted his GAHT afterwards.

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From then on, Mr. M showed no signs of bipolar disorder. Approximately a year ago, bloodwork confirmed his plasma testosterone levels were lower than the targeted range. He was prescribed testosterone transdermal gel, four pumps of 1.62% QD, which was augmented to his testosterone undecanoate. He tolerated the change very well until one week ago, when his dose of oral testosterone (Jatenzo) was increased to 237 mg (two tablets). Unknown to the psychiatrist about these recent changes, the patient reported increasing agitation, aggression, and decreased inhibition (e.g., spending sprees, risky behavior) within 72 hours of the dose change. The patient was presenting with symptoms of hypomania and sleep disturbances. The treatment team decided to temporarily stop GAHT, increase his Valproate to 1500 mg, lower Buspirone to 15 mg, and continued Lurasidone 120 mg. His symptoms improved greatly with the adjusted medication regimen, and his GAHT was restarted after two weeks. The patient was not a danger to himself or others and was managed as an outpatient. This case highlights the need for medication reconciliation in the treatment of a transgender patient with multispecialty providers

3. Discussion

Testosterone can increase vulnerability to or trigger psychiatric and/or manic symptoms, notably among individuals who already have been diagnosed with a psychiatric illness like bipolar disorder (Pfaff et al., 2022; Zubiarre-Elorza et al., 2021; Duradiakova et al., 2011). The biological activity of testosterone overlaps with the neural circuitry of bipolar disorder since hormonal levels heavily contribute to brain areas controlling mood lability, aggression, and impulsivity (Pfaff et al., 2022; Gouveia et al., 2019; Juruena et al., 2020). That said, supraphysiological testosterone may contribute to the heightened risk of mania, so testosterone levels should be closely monitored in FTM people with bipolar disorder undergoing GAHT (Yang et al., 2022; Mehta & Beer, 2010).

Medication reconciliation is a practice of crafting an accurate, comprehensive list of a patient's current medications by corroborating such medications with medical records and medication orders. It is critical to formulate, adjust, and switch treatment regimens, primarily for patients who have multiple medications and/or medical diagnoses. Errors, even slight ones, can result in adverse events that warrant hospital admission, acute psychiatric evaluation, and possibly death (Bock, 2018). Medication discrepancies have been reported to be as common as in 90 percent of patients in outpatient facilities, with 57 percent being linked to prescription medications and 38 percent possibly moderately/severely harming patients (Albano et al., 2017).

In the case of Mr. M, his worsening bipolar disorder symptoms could easily be linked to a lapse in medication reconciliation. His pill form of testosterone GAHT was nearly doubled, and he began using topical testosterone gel—neither of which were reported to his psychiatrist. Thus, when his parents endorsed heightened aggression, irritability, and mood swings with greater amplitude, his antipsychotic regimen was adjusted as if his GAHT remained constant. Unbeknownst to the psychiatrist, his testosterone levels were skyrocketing at the same time. This is incredibly dangerous because testosterone is involved in a milieu of brain mechanisms critical to mental and physical homeostasis.

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More research is required to fully understand the neurobiological pathways relating testosterone, bipolar disorder, transgender individuals, along with the precise balance between achieving desirable effects without causing harm in these patients. Mr. M's heightened testosterone levels likely contributed to the rapid onset of his irritability, aggression, and mood lability related to bipolar disorder. As a result of the spike in testosterone levels, it is possible that Mr. M experienced serotonin depletion in the brain regions involved in emotional regulation. His history of bipolar disorder predisposed him to manic symptoms, so the unregulated supraphysiological testosterone levels may have created a "perfect storm." Luckily, he was stabilized within one week, but gray matter is irreversibly lost with every manic episode (Abé et al., 2023; Nasrallah, 2023).

Mr. M's case is a testament to the importance of medication reconciliation and communication among clinicians. Medical professionals treating patients undergoing testosterone GAHT, chiefly those susceptible to mania, should consider developing or maintaining excellent medication reconciliation habits through consistent monitoring of the patient's pharmaceutical treatments, medical conditions, and chief complaints. Exceptionally important is communication between members of a patient's care team that are not within the same clinic, as was the case for Mr. M. Therefore, slight lapses in updating medication reconciliation can result in consequences much greater than Mr. M's. His case exemplifies the need for research on testosterone neurobiology in the presence of bipolar disorder while also promoting the necessity of accurate medication reconciliation.

Given the severe risks of uncoordinated GAHT and psychiatric medication management, we propose the following guidelines for clinicians in monitoring and treating FTM/transmasculine patients with bipolar or mood disorders:

1. **Enforce mandatory cross-specialty communication**. Any change in GAHT dosage, formulation, or route of administration should be immediately communicated to the patient's providers. A shared medication list accessible to all specialties is strongly advised.
2. **Consistent testosterone monitoring from baseline onwards**. Obtain plasma testosterone levels at the baseline appointment, within four to six weeks of dosage change, and (at minimum) every three months thereafter. Supraphysiological exposure can be avoided when levels are maintained within physiological range.
3. **Surveillance of mood symptoms.** Administer a mood monitoring survey or scale (e.g., PHQ-9) at each visit. Keep the threshold for contacting the psychiatric provider low should scores change meaningfully.
4. **Psychoeducation of patients**. Patients should be explicitly counseled that GAHT dose changes, formulation switches, and/or additional exogenous testosterone supplementation must be reported to all providers before or immediately after implementation.
5. **Care agreements in coordination with multiple providers**. Practices seeing patients who are transgender with comorbid psychopathologies should consider formal care coordination agreements or shared electronic health record access between endocrinology, primary care, and psychiatry to reduce gaps in reconciliation.

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4. Conclusion

Bipolar disorder is a chronic psychiatric condition that requires medication adherence concurrent with metabolic, physical, and psychological stability in order to achieve long-term control and avoid significant adverse effects of the disorder itself and/or the pharmaceutical interventions. Complex processes such as gender transition, which often warrants profound social, physical, psychological, and metabolic transformations, can still be achieved in patients with bipolar disorder. However, strict medication reconciliation is essential to maintain adequate control of psychiatric symptoms and hormonal levels so the patient can safely reach their aesthetic and physiological goals.

The role of medication reconciliation is critical in scenarios akin to the presented case. Exogenous testosterone, known for its potential to induce mania, must be used with caution and closely monitored. Research on the connections among testosterone therapy, transgenderism, bipolar disorder, and neurobiological interactions are strongly recommended. In the meantime, clinicians are advised to maintain precise medication reconciliation to avoid adverse effects and cultivate the wellbeing of their patients.

Acknowledgments

The authors would like to thank Mr. M for allowing us to discuss his case for the betterment of medication reconciliation among transgender individuals.

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ISSN: 2581-3366

administration, supervision, writing – review & editing. *Arushi Chandra Parikh:* Writing – review & editing. *Parinda Parikh:* Conceptualization, investigation, supervision, writing – review & editing.

Disclosure of interest: The authors declare that they have no conflict of interest.
Consent: Consent to publish anonymous case details was obtained from the patient whose case was reviewed. No institutional approval was required.

Data availability statement: Data sharing is not applicable to this article as no new data were created or analyzed in this case report.