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ANTIPSYCHOTIC-INDUCED HYPERPROLACTINEMIA: BALANCING PSYCHIATRIC STABILITY AND ENDOCRINE SAFETY

M. BOUBEKRI [1,*], Y. EL MARRAKI [2], S. BAHETTA [1], H. NAFIAA [1] and M. SABIR [1]

[1] The Department of Psychiatry at the Faculty of Medicine and Pharmacy in Rabat.
[2] Endocrinology, Diabetes and Metabolism, Avicenne Military Hospital, Marrakech, Morocco.
* Corresponding Author

ORCID Details
M. BOUBEKRI: https://orcid.org/0009-0001-0154-8946
Y. EL MARRAKI: https://orcid.org/0009-0002-5312-4114

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ABSTRACT

Antipsychotic-induced hyperprolactinemia presents a recurring clinical dilemma: an effective psychiatric treatment may produce distressing reproductive or sexual symptoms and raise concerns about prolonged endocrine disturbance. This narrative review examines assessment and management from a psychiatric perspective, drawing on a defined collection of clinical studies, evidence syntheses and guidance documents. Prolactin liability varies substantially between drugs and doses, making conventional first- versus second-generation classifications insufficient for individual decisions. Assessment requires attention to symptoms, medication chronology, gonadal function and alternative causes of prolactin elevation. Monitoring recommendations remain inconsistent, particularly for asymptomatic patients. Among pharmacological interventions, adjunctive aripiprazole has the most consistent evidence for lowering prolactin while allowing continuation of the established antipsychotic. However, biochemical efficacy does not establish long-term protection against relapse, fractures or cancer, and optimal dosing and treatment duration remain uncertain. Dose reduction and switching can address the offending exposure but require consideration of previous treatment response, relapse consequences and alternative adverse effects. Dopamine agonists may lower prolactin, although conflicting psychiatric safety reports preclude routine reassurance. Evidence for metformin, high-dose vitamin B6 and herbal preparations is less secure. Specialist treatment of persistent hypogonadism and fertility counseling may be necessary alongside psychiatric management. The most defensible approach combines explicit therapeutic goals, shared decisions and parallel endocrine and psychiatric follow-up. Treatment should relieve clinically meaningful harm while preserving an effective, acceptable antipsychotic regimen whenever possible.

Keywords: Antipsychotics; Hyperprolactinemia; Aripiprazole; Psychiatric stability; Hypogonadism; Clinical psychopharmacology

1 INTRODUCTION

For a patient whose psychiatric illness has responded to an antipsychotic, the discovery of hyperprolactinemia creates a decision that cannot be resolved by the laboratory result alone. Menstrual disturbance, galactorrhea and sexual dysfunction may cause considerable distress, yet changing a successful regimen can jeopardize symptom control. Conversely, maintaining treatment without addressing adverse effects can undermine its acceptability. The clinical task is to assess endocrine harm and psychiatric vulnerability together, including the patient's experience of both illness and treatment. [1, 2, 3]

The literature has developed unevenly. Drug-specific prolactin effects and the biochemical efficacy of adjunctive aripiprazole are supported by quantitative syntheses, whereas monitoring schedules, intervention thresholds and long-term clinical outcomes remain less certain. Repeatedly favorable findings across reviews also require caution because these publications often revisit overlapping trials. A reduction in prolactin, improvement in symptoms and preservation of psychiatric stability are related but distinct outcomes. [4, 5, 6]

This narrative review asks how psychiatrists can identify, assess and manage antipsychotic-induced hyperprolactinemia while maintaining psychiatric stability and limiting endocrine complications. It draws on a predefined collection of clinical studies, reviews and guidance documents, with duplicate publications consolidated. Primary observational findings, secondary treatment evidence and guidance recommendations are distinguished throughout. The collection was not assembled through an independent systematic search, and this critical narrative synthesis does not establish an exhaustive account of the literature.

2 PHARMACOLOGICAL BASIS AND DIFFERENCES BETWEEN AGENTS

Dopamine normally inhibits prolactin secretion through D2 receptors on anterior pituitary lactotrophs. Antagonism at these receptors removes that inhibition. Persistently elevated prolactin can suppress hypothalamic gonadotropin-releasing hormone activity and downstream gonadal function, providing a mechanism for reproductive symptoms and sex-steroid deficiency. Differences in receptor activity, binding characteristics and access to the pituitary contribute to variation between antipsychotics; partial D2 agonism helps explain aripiprazole's prolactin-lowering properties. [1, 7]

These effects are better understood at the level of individual drugs than through the labels typical and atypical. In their dose-response meta-analysis, Lin and colleagues analyzed prolactin data from 68 studies involving 23,128 participants with acutely exacerbated schizophrenia. Risperidone and paliperidone showed particularly pronounced increases. Olanzapine also demonstrated a dose-related increase, whereas quetiapine, brexpiprazole, cariprazine and lumateperone showed negligible increases over the examined dose ranges. Aripiprazole generally reduced prolactin. The analysis contained no eligible prolactin-change data for amisulpride or clozapine, so their omission from its quantitative comparisons should not be interpreted as evidence of equivalence or absence of an effect. [4]

The same analysis illustrates the limits of drug comparisons. Most trials were short, participants predominantly had multiepisode illness with an acute exacerbation, and previous medication could influence baseline and subsequent prolactin measurements. Female dose-response curves generally showed larger elevations, but formal statistical tests of sex differences were not performed. These findings can inform anticipatory prescribing and dose review, while providing less direct guidance on the consequences of changing treatment in a patient who has remained well for years. [4]

Prolactin liability therefore belongs within a broader assessment of antipsychotic suitability. An alternative drug may have a more favorable endocrine profile yet introduce other tolerability problems or fail to reproduce the individual's psychiatric response. Selection should incorporate previous efficacy, adverse effects and treatment preferences rather than treating prolactin liability as a sufficient prescribing criterion. [2, 8]

3 CLINICAL MANIFESTATIONS AND THEIR PSYCHIATRIC SIGNIFICANCE

3.1 Symptoms and patient experience

Clinical manifestations include menstrual irregularity or amenorrhea, galactorrhea, reduced libido, erectile difficulties and impaired fertility. Symptoms may reflect direct prolactin effects, secondary hypogonadism or several concurrent mechanisms. Sexual dysfunction warrants particular care in interpretation: psychiatric symptoms, depression, social circumstances and other pharmacological effects can contribute independently of prolactin. Neither an elevated result nor a symptom report alone establishes that the entire clinical problem is prolactin-mediated. [1, 8, 9]

Takechi and colleagues provide directly observed evidence of a symptom-biochemistry association. Their retrospective study included 83 women selected for prolactin testing, of whom 18 had menstrual disorders. Mean prolactin was 89.3 ± 36.9 ng/mL in those with menstrual disorders and 42.5 ± 54.5 ng/mL in those without them ($p < 0.001$). Chlorpromazine-equivalent doses did not differ significantly between groups ($p = 0.36$). The derived 60 ng/mL discrimination cut-off requires prospective validation; it cannot serve as a universal threshold for symptoms or intervention. Selection for testing, a small single-center sample and heterogeneous treatments further restrict generalization. [10]

Biochemical elevation is also frequently recorded without symptoms. In a retrospective study of 1,103 eligible records from two Omani tertiary hospitals, 753 patients (68.3%) had elevated prolactin according to hospital-specific reference ranges. Many elevated results occurred among patients classified as asymptomatic. This describes a selected clinical population with recorded baseline and follow-up measurements, rather than a universal prevalence estimate. It nevertheless shows why symptom inquiry and laboratory assessment answer different questions. [11]

The absence of a spontaneous complaint is insufficient evidence that treatment is acceptable. Patients may not connect menstrual or sexual changes with medication, or may be reluctant to discuss them. Explicit, respectful inquiry is therefore central to psychiatric care. Associations between sexual adverse effects and nonadherence are discussed in the clinical reviews, but they do not establish that lowering prolactin necessarily improves adherence or prevents relapse. Those outcomes should be assessed rather than presumed. [1, 2]

The patient's account also helps determine what constitutes improvement. Menstrual recovery, relief of breast symptoms and restoration of satisfactory sexual functioning are clinically different endpoints, and the relationship between prolactin and each is imperfect. Persistent sexual difficulties after a biochemical response should prompt reconsideration of other contributors rather than automatic escalation of prolactin-lowering treatment. The clinical reviews support a broader assessment of psychiatric, pharmacological and psychosocial influences on sexual function. [1, 8, 9]

3.2 Bone health and longer-term concerns

Persistent hypogonadism provides a clinically important reason to assess beyond immediate discomfort. The clinical reviews describe reduced bone mineral density in antipsychotic-treated populations, while emphasizing the contributions of gonadal deficiency, smoking, nutrition, physical activity and other factors. Prolactin concentration alone is consequently an incomplete measure of skeletal risk. Duration of endocrine disturbance, menstrual and gonadal status, fracture history and other risk factors should inform consideration of bone assessment and specialist involvement. [1, 8, 9, 12]

Breast-cancer findings require similarly proportionate interpretation. Bird's meta-analysis of 15 observational studies reported a pooled summary association of 1.19 (95% confidence interval [CI] 1.10–1.30) for antipsychotic exposure, with substantial heterogeneity ($I^2 = 79\%$). A subgroup restricted to highly prolactin-increasing drugs yielded 1.59 (95% CI 1.37–1.85), but comprised only two studies. Differences in exposure definitions and comparators, and residual confounding, limit causal interpretation. These associations do not establish that prolactin mediates the observed risk or that a prolactin-lowering intervention prevents cancer. They warrant discussion without converting an uncertain long-term association into an automatic indication to abandon effective psychiatric treatment. [13]

The distinction between biological plausibility and demonstrated prevention is particularly relevant here. Bird discusses both circulating and locally produced prolactin, while the epidemiological analyses concern medication exposure rather than an intervention that selectively lowers circulating prolactin. The pooled estimate also combines studies reporting different risk measures. It should therefore be described as a summary association, with its methodological qualifications retained. The practical implication is an informed discussion of uncertainty and attention to breast-health assessment, rather than a claim that a specific antipsychotic change has proven cancer-preventive benefit. [13]

4 ASSESSMENT AND MONITORING WITHIN PSYCHIATRIC CARE

4.1 Establishing the clinical context

Assessment begins with medication chronology and a symptom history. Previous prolactin results, antipsychotic initiation or dose increases, concomitant medicines and the onset of menstrual, breast or sexual changes help determine plausibility. Baseline prolactin measurement can make subsequent interpretation easier, while a baseline sexual and menstrual history prevents pre-existing problems being attributed retrospectively to treatment. Laboratory reference intervals and sampling conditions matter because physiological variation and stress can influence results. [1, 2, 7]

An unexpected or modest elevation should be interpreted in context and repeated under appropriate conditions when a transient rise is plausible. Medication review should extend beyond the antipsychotic to other potential contributors, including antiemetics and antidepressants. Depending on the presentation, pregnancy, hypothyroidism, renal or hepatic disease and pituitary pathology require consideration. Macroprolactin assessment can be relevant when the biochemical result and clinical picture are discordant. Gonadal evaluation is particularly pertinent when symptoms or persistent elevation suggest hypogonadism. [1, 2, 7, 9]

The magnitude of elevation cannot reliably identify its cause. Although drug-related values often fall within a moderate range, some medications can produce much higher concentrations; conversely, structural lesions may cause elevations overlapping the medication-associated range. Headache, visual disturbance, an atypical chronology or otherwise unexplained persistent elevation strengthens the case for endocrine evaluation and pituitary imaging. The reviewed guidance varies in its numerical imaging thresholds, favoring interpretation of the whole presentation over reliance on a single cut-off. [1, 7, 9]

A diagnostic interruption of treatment poses a separate psychiatric question. Some endocrine-oriented recommendations describe short withdrawal and retesting, but Grigg and colleagues explicitly question this approach because of relapse risk and limited supporting evidence. Prolactin normalization also differs by drug and formulation; effects of some depot preparations may persist for months. Routine withdrawal simply to establish causation is therefore difficult to justify in a vulnerable, stable patient. When the drug cannot safely be withheld, investigation and specialist discussion can proceed while treatment continues. [1, 2, 7]

4.2 Monitoring without overstating consensus

There is no uniform monitoring schedule across the reviewed guidance. Grigg and colleagues found that eight of twelve guidelines recommended baseline prolactin testing, with substantial disagreement about subsequent laboratory surveillance and management of asymptomatic elevation. The Korean adaptation by Kim and colleagues retained baseline testing but replaced routine testing at three months with symptom assessment and testing when adverse effects were suspected. These differences partly reflect local applicability and resource considerations, as well as uncertainty in the evidence. [2, 12]

A defensible clinical plan should state what is being monitored, by whom and for what purpose. Symptoms, menstrual or gonadal function, the trajectory of prolactin and psychiatric status should be considered together. Reassessment after treatment modification should establish whether the intended benefit occurred and whether new psychiatric or other adverse effects emerged. A small conference audit illustrates the implementation problem: six of 23 eligible patients had no prolactin test recorded. This abstract lacked standard journal peer review and cannot establish the effectiveness of a monitoring strategy or the frequency of skeletal complications. [2, 3, 14]

Different follow-up questions also require different evidence. A repeat result can help establish persistence or response, whereas a gonadal assessment addresses possible functional consequences and bone evaluation addresses a longer-term concern. One test cannot substitute for all three. Grigg and colleagues' proposed algorithms combine these domains, but remain an integrated interpretation of guidance and available research rather than a prospectively validated decision rule. Their detailed intervals and numerical categories should be read with that limitation in mind. [2, 9]

5 THERAPEUTIC MANAGEMENT AND PSYCHIATRIC CONTINUITY

5.1 Defining the treatment objective

Management should begin with an explicit objective: relieving distressing symptoms, addressing hypogonadism, supporting fertility or investigating unexplained biochemical elevation. These aims overlap but do not require identical interventions. The decision also depends on how much the current antipsychotic has helped, previous unsuccessful treatments, the consequences of relapse, anticipated treatment duration and the patient's priorities. A strategy justified by biochemical improvement may be unattractive if it replaces an effective treatment with an uncertain psychiatric response. [1, 2, 3]

For an asymptomatic patient, active surveillance may be reasonable after alternative causes and gonadal implications have been assessed. This requires a follow-up plan rather than dismissal of the result. Guidance disagrees about when asymptomatic elevations warrant treatment, and a symptom-free presentation does not resolve questions about prolonged hypogonadism or bone risk. Intervention should therefore be individualized rather than triggered solely by a laboratory category. [2, 7, 12]

The treatment hierarchy itself reflects different priorities. Inder and Castle favor switching where feasible; Tewksbury and Olander favor adjunctive aripiprazole when the patient is stable and relapse risk is high; Grigg and colleagues urge particular caution before switching stable patients. These positions should not be presented as interchangeable universal recommendations. Their clinically useful point of agreement is the need to consider whether the existing antipsychotic can realistically be replaced and what would be lost if the alternative were unsuccessful. [2, 3, 9]

5.2 Antipsychotic dose adjustment

Dose reduction avoids adding another drug and may be attractive when the current dose can be lowered without compromising the treatment objective. The dose-response findings support a pharmacological basis for considering this option for several agents. They do not, however, directly establish the success of dose reduction as a treatment for hyperprolactinemia in stable maintenance patients. Drug-specific plateaux and individual variability also mean that a smaller dose change may not produce a clinically meaningful endocrine improvement. [1, 4]

The psychiatric history is decisive. Previous deterioration at lower doses, incomplete symptom control or serious consequences of relapse can make reduction inappropriate. If pursued, the change should be treated as a monitored therapeutic trial with both endocrine and psychiatric outcomes, rather than assumed to be the simplest solution. Earlier reviews describe its prolactin-lowering effectiveness as unpredictable, and the treatment syntheses provide less direct comparative evidence for dose reduction than for adjunctive aripiprazole. [1, 3, 15]

Dose-equivalence measures should also be interpreted carefully. The absence of a significant difference in chlorpromazine-equivalent dose between women with and without menstrual disorders in Takechi and colleagues' study does not show that prolactin effects are dose-independent. The groups included different drugs, whose endocrine effects differ, and the study was retrospective. This observation can coexist with dose-response relationships for individual agents in the randomized-trial synthesis. A between-patient comparison of mixed treatments and a drug-specific dose-response analysis address different questions. [4, 10]

5.3 Switching to another antipsychotic

Switching addresses the offending exposure and may be especially appropriate when hyperprolactinemia accompanies inadequate efficacy or other unacceptable adverse effects. It can also avoid prolonged combination antipsychotic treatment. The case series describes prolactin normalization and symptom resolution after switching in three patients, while the treatment reviews summarize broader switching experience. Such observations support the possibility of benefit without establishing a reliable comparative relapse risk. [3, 15, 16]

Lu and colleagues found a significant prolactin reduction for a titrated switch to aripiprazole with gradual withdrawal of the previous agent in the subgroup with baseline prolactin above 50 ng/mL. However, the evidence was less certain than that for adjunctive aripiprazole, and results varied with switching strategy and analytical approach. This supports planned cross-titration as an option, rather than proving that switching is superior to retaining the antipsychotic and adding treatment. [5]

For a patient stable on a difficult-to-replace regimen, the rationale for switching needs to be particularly strong. Previous responses to alternatives, treatment resistance, adherence needs and the adverse-effect profile of the proposed drug all matter. Long-acting treatment adds formulation-specific considerations; prolactin may remain elevated after a preparation is stopped, so an early persistently high result does not by itself prove failure of the new regimen. Continuity planning and close psychiatric observation should accompany an agreed switch. [1, 2, 3]

5.4 Adjunctive aripiprazole

Adjunctive aripiprazole has the most consistent prolactin-lowering evidence among the pharmacological approaches in the treatment syntheses. Its principal clinical attraction is that the established antipsychotic can be retained. In Lu and colleagues' pairwise analysis, the mean difference versus placebo was −68.84 ng/mL (95% CI −85.65 to −52.04), although heterogeneity was substantial (I^2 = 89%). In their network subgroup with baseline prolactin above 50 ng/mL, adjunctive aripiprazole 5 mg/day was associated with a mean difference of −64.26 ng/mL (95% CI −87.00 to −41.37) versus placebo. These are average biochemical effects within the studied populations. [5]

The umbrella review by Jiang and colleagues likewise favored aripiprazole, but rated the five included evidence syntheses as low or very low quality using AMSTAR 2. The convergence of findings is clinically useful, yet is not equivalent to multiple independent sets of confirmatory trials. Moreover, the trials underlying the reviews predominantly concern schizophrenia and often involve risperidone; confidence should be lower when extrapolating to other diagnoses, prolonged maintenance treatment or less studied antipsychotic combinations. [5, 6, 15]

Dose selection remains unsettled. A 5 mg/day starting approach is supported by the clinical reviews and treatment analyses, while some secondarily reported trials suggest greater biochemical responses at higher doses. Those findings do not establish a universal optimum. Lu and colleagues' safety analysis associated adjunctive doses above 10 mg/day with more adverse effects than placebo (odds ratio 2.2, 95% CI 1.2–4.3). Escalation should therefore depend on response and tolerability rather than a presumption that additional prolactin reduction is always desirable. [3, 5, 15]

Baseline prolactin also complicates interpretation. Lu and colleagues found no statistically significant separation from placebo among the interventions evaluated in studies with baseline levels below 50 ng/mL. These aggregate subgroup findings do not establish that every patient below that level is asymptomatic, requires no evaluation or cannot benefit. Nor does statistical significance for one dose subgroup and its absence for another prove that the doses differ from each other. Symptoms, gonadal status and the reason for treatment remain necessary to interpret the result. [5, 10]

Psychiatric tolerability should be assessed independently of biochemical success. Reviews report no average worsening on symptom scales in several adjunctive trials, but also describe cases of symptom exacerbation and the limitations of short follow-up. Monitoring should include activation, akathisia, sedation and changes in psychotic or mood symptoms, alongside prolactin and the original endocrine complaints. Potential interactions affecting aripiprazole exposure also warrant review. Continued use is most defensible when a meaningful benefit is documented and the additional treatment remains acceptable. [2, 3, 15]

Response may also depend on the antipsychotic being retained. Small open-label studies summarized by Tewksbury and Olander suggest less consistent responses to adjunctive aripiprazole with amisulpride or sulpiride than with risperidone. These observations are insufficient for a definitive drug-by-treatment comparison, but argue against promising the same response for every regimen. The consultation review by Rusgis and colleagues also identifies interactions involving CYP2D6 and CYP3A4 as relevant to aripiprazole exposure, adding another reason to review the whole prescription before interpreting nonresponse or adverse effects. [3, 15]

The two clinical reviews discuss reassessment over the first few weeks, with different suggestions about when an insufficient response should lead to dose escalation. This variation reinforces the absence of a single validated titration schedule for hyperprolactinemia. An initial plan can specify the symptoms and biochemical changes being sought, together with the adverse effects that would limit further treatment. Adding aripiprazole should remain a purposeful intervention with review of its ongoing value, rather than an automatic permanent addition to the regimen. [3, 15]

5.5 Dopamine agonists

Bromocriptine and cabergoline can reduce prolactin, but their use in antipsychotic-treated patients raises a specific concern about psychiatric destabilization. Reports include both successful treatment without worsening and psychotic exacerbations. Lertxundi and colleagues emphasized that the actual incidence of exacerbation and comparative psychiatric safety of the two agents were unknown. The absence of spontaneous pharmacovigilance reports in their database search could not settle that question. [3, 17]

Later syntheses do not eliminate the uncertainty. Jiang and colleagues drew relatively reassuring conclusions, while also reporting psychopathological worsening with some dopamine agonists and low methodological quality in the underlying review literature. Rusgis and colleagues described a cabergoline series with increased psychosis exacerbation, whereas other reports were more favorable. Because the primary reports were not independently evaluated here and populations and methods differ, these accounts cannot support a reliable pooled psychiatric risk estimate or a claim that cabergoline is uniformly safe in this setting. [6, 15]

The clinically proportionate position is selective specialist consideration when symptoms or endocrine consequences warrant intervention and better-supported or more acceptable options are unsuitable. Psychiatrist–endocrinologist coordination, an explicit discussion of uncertainty and close mental-state follow-up are essential elements of that approach. Potential nonpsychiatric adverse effects, including cardiovascular concerns discussed in the clinical reviews, also enter the decision. Prolactin-lowering efficacy in prolactinomas or idiopathic hyperprolactinemia should not be used as direct evidence of psychiatric safety in this population. [9, 12, 15, 17]

5.6 Metformin and less established adjunctive strategies

Metformin has a less consistent evidence base. Rusgis and colleagues summarized a four-trial meta-analysis showing a modest prolactin reduction, accompanied by substantial heterogeneity. Jiang and colleagues considered the findings promising but insufficiently established, while Lu and colleagues did not find a significant network effect. Differences between analyses prevent a firm treatment ranking. Metformin may be relevant when metabolic problems also influence management, but its prolactin effect should not be assumed equivalent to aripiprazole's or relied upon without checking the endocrine response. [5, 6, 15]

More specifically, the four-trial synthesis reported by Rusgis and colleagues included 509 participants and a weighted mean difference of −6.87 μg/L (95% CI −13.24 to −0.51), with I^2 = 80%. This finding provides a biochemical signal, while leaving uncertainty about its consistency and clinical magnitude. It is secondary evidence within the consultation review, not an independently evaluated primary trial dataset in the present synthesis. The broader metabolic rationale discussed by the authors may influence treatment selection, but it cannot establish reliable correction of prolactin-related symptoms in a particular patient. [15]

High-dose vitamin B6 produced a favorable prolactin estimate in Lu and colleagues' network analysis, but that evidence depended on one study. Herbal preparations, including peony–glycyrrhiza decoction, have heterogeneous findings and limitations in preparation, safety reporting and generalizability. Neither strategy has sufficiently developed evidence on sustained psychiatric and endocrine outcomes to occupy the same position as adjunctive aripiprazole. They are better presented as research questions than as routine solutions to a stable patient's treatment dilemma. [5, 6, 15]

For vitamin B6, a favorable network estimate should not obscure the limited number of independent observations supporting it. For herbal preparations, biochemical and symptom findings have not always agreed, and studies outside antipsychotic-induced hyperprolactinemia are not directly transferable. Rusgis and colleagues additionally discuss variability in product quality and potential interactions. These limitations concern the reproducibility and interpretation of treatment as well as its efficacy; the absence of reported adverse events in small studies does not settle longer-term tolerability. [5, 15]

5.7 Endocrine consequences and fertility

When clinically important hypogonadism persists and changing psychiatric treatment is unsuitable, specialist sex-steroid replacement may address consequences of deficiency. This differs from removing the cause of prolactin elevation and does not necessarily relieve symptoms such as galactorrhea. Selection depends on gonadal status, contraindications and reproductive goals; treatment should not be presented as an interchangeable substitute for prolactin-lowering strategies. Bone assessment and management should likewise reflect the individual's broader risk profile. [1, 2, 7, 9]

Successful treatment can restore fertility, which should be discussed before intervention rather than after an unintended pregnancy. Contraception and pregnancy intentions belong in the management conversation, including counseling of male patients. Follow-up should return to the initial objectives: whether symptoms improved, gonadal concerns were addressed, prolactin changed as expected and psychiatric benefit was maintained. A lower laboratory value is an incomplete success if the patient experiences activation, recurrent psychosis or an unacceptable new treatment burden. [2, 3]

6 CLINICAL CONTROVERSIES AND RESEARCH PRIORITIES

The most consequential evidence gap concerns the joint outcome of endocrine improvement and sustained psychiatric stability. Many studies prioritize prolactin concentration, whereas clinicians need comparative information on symptom relief, sexual functioning, adherence, relapse, hospitalization and treatment continuation. Longer follow-up is also required before biochemical changes can be linked to skeletal outcomes. The treatment syntheses do not demonstrate that any prolactin-lowering strategy prevents fractures or breast cancer. [2, 5, 6, 15]

Future studies should compare clinically relevant choices, particularly adjunctive aripiprazole versus switching in patients whose current medication is effective. Drug and formulation, previous treatment failures, baseline prolactin, gonadal status and sex require explicit consideration. The acute-treatment findings of Lin and colleagues should not substitute for maintenance evidence, and subgroup effects based on aggregate data need confirmation at the individual-patient level. Optimal adjunctive dose, duration, subsequent withdrawal and the management of patients who do not respond remain unresolved. [4, 5, 15]

Monitoring also needs outcome-based evaluation. More frequent testing may detect otherwise unrecognized elevations, but its clinical value depends on whether the resulting decisions improve meaningful outcomes without unnecessary treatment disruption. Guideline variation, locally adapted recommendations and incomplete implementation reinforce the need for studies of monitoring pathways, patient acceptability and service responsibility. Shared decision-making is especially important where recommendations depend more on consensus than on direct comparative evidence. [2, 12]

These uncertainties should shape how reassurance is offered. A patient can be told that several approaches lower prolactin and may improve related symptoms, while being informed that the best strategy for preserving their own psychiatric response is not established by the biochemical rankings. Likewise, a clinician can acknowledge an unresolved long-term risk without presenting treatment interruption as obligatory. This approach follows the

individualized, collaborative reasoning of the clinical guidance and makes the remaining uncertainty part of the decision rather than concealing it behind a treatment algorithm. [1, 2, 3]

7 CONCLUSION

Antipsychotic-induced hyperprolactinemia requires an assessment of endocrine consequences and psychiatric treatment value in the same decision. Symptoms, gonadal function, alternative causes and patient priorities should guide intervention. Adjunctive aripiprazole has the strongest consistent biochemical evidence when retaining the effective antipsychotic is desirable; dose reduction and switching remain reasonable options when the psychiatric context supports them. Dopamine agonists and less established adjuncts require greater caution. Close follow-up must establish both clinical endocrine benefit and continued psychiatric stability, while acknowledging that long-term protection against skeletal or malignant outcomes remains unproven.

STATEMENTS ON COMPLIANCE WITH ETHICAL STANDARDS

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Disclosure of conflict of interest

The authors declare no conflicts of interest regarding this manuscript.

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