IJBPAS, April, 2026, 15(4): 1704-1719

ISSN: 2277–4998

International Journal of Biology, Pharmacy and Allied Sciences (IJBPAS)

'A Bridge Between Laboratory and Reader'

www.ijbpas.com

CURRENT PROSPECTIVES AND CHALLENGES IN THE MANAGEMENT OF NEUROLEPTIC DRUGS ASSOCIATED HORMONAL ALTERATIONS

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Received 20th Jan. 2025; Revised 19th Feb. 2025; Accepted 4th April 2025; Available online 1st April 2026

https://doi.org/10.31032/IJBPAS/2026/15.4.10058

ABSTRACT

Neuroleptic drugs, essential in treating psychiatric disorders, often cause hormonal alterations by disrupting the hypothalamic-pituitary axis through their effects on dopaminergic and serotonergic pathways. These disturbances can lead to conditions such as hyperprolactinemia, thyroid dysfunction, metabolic syndrome, and alterations in sex and stress hormones, which may exacerbate psychiatric symptoms and impair physical health. Effective management requires a comprehensive understanding of these effects and strategies such as switching to atypical antipsychotics with lower endocrine impact, dose optimization, or adjunctive therapies like dopamine agonists or hormonal treatments. However, challenges persist due to underdiagnosis, limited clinical guidelines, and variability in individual responses. Advancing research to elucidate the mechanisms behind these alterations and develop targeted interventions is crucial. A multidisciplinary approach involving psychiatrists, endocrinologists, and researchers is vital to address these complexities, improve patient outcomes, and minimize the burden of neuroleptic-associated hormonal side effects.

Keywords: Dopamine, Neuroleptic, psychiatric, endocrine etc.

INTRODUCTION

Neuroleptic drugs, also known as antipsychotics, are pivotal in the management of psychiatric disorders, particularly schizophrenia, bipolar disorder,

and other severe mental health conditions. These drugs exert their therapeutic effects primarily through modulation of dopaminergic and serotonergic pathways in the brain. Despite their efficacy in managing psychotic symptoms, neuroleptics are associated with a range of adverse effects, among which hormonal alterations represent a significant and often underrecognized challenge **[1]**.

This introduction explores the mechanisms, clinical manifestations, and implications of neuroleptic-induced hormonal alterations. It also highlights the importance of early detection and multidisciplinary management to mitigate these effects and improve the overall quality of life for patients undergoing long-term neuroleptic therapy **[2]**.

MECHANISMS UNDERLYING HORMONAL ALTERATIONS

Neuroleptic drugs primarily target dopamine receptors in the brain, a mechanism central to their therapeutic efficacy. Dopamine plays a crucial role in modulating prolactin release from the anterior pituitary gland by inhibiting its secretion. Neuroleptics, especially typical antipsychotics, block D2 receptors in the tuberoinfundibular pathway, removing this inhibitory control and resulting in elevated prolactin levels. Hyperprolactinemia is one of the most well-documented hormonal side effects of neuroleptic drugs **[3]**. In addition to prolactin dysregulation, neuroleptic drugs influence the broader HPA axis. Chronic exposure to these drugs can alter the secretion of corticotropin-releasing hormone (CRH), adrenocorticotropic hormone (ACTH), and cortisol **[4]**.

CLINICAL MANIFESTATIONS OF HORMONAL ALTERATIONS

The hormonal side effects of neuroleptic drugs manifest in diverse ways, affecting multiple physiological systems:

- **Hyperprolactinemia:** Common symptoms include galactorrhea (milk production unrelated to childbirth), amenorrhea (absence of menstruation), and gynecomastia (breast enlargement in men). In the long term, hyperprolactinemia can lead to infertility, sexual dysfunction, and decreased bone mineral density, increasing the risk of osteoporosis.
- **Thyroid Dysfunction:** Neuroleptic drugs can alter thyroid hormone levels, leading to hypothyroidism or subclinical thyroid dysfunction. Symptoms include fatigue, weight gain, depression, and cognitive impairment, which may exacerbate psychiatric conditions.
- **Cortisol Dysregulation:** Neuroleptics may alter cortisol secretion patterns, contributing to stress intolerance and mood disturbances. Prolonged cortisol

dysregulation can impair immune function and increase susceptibility to infections **[5, 6]**.

IMPLICATIONS FOR PATIENTS AND CLINICAL PRACTICE

The hormonal side effects of neuroleptic drugs have far-reaching implications for patients and clinicians. These alterations can exacerbate psychiatric symptoms, reduce adherence to medication, and compromise overall treatment outcomes. For example, sexual dysfunction, a common consequence of hyperprolactinemia and testosterone deficiency, often leads to decreased medication adherence in male patients.

Causes of Psychosis

Psychosis, a condition characterized by a disconnection from reality, manifests through symptoms such as hallucinations, delusions, and disorganized thinking. The causes of psychosis are multifaceted, encompassing a combination of biological, psychological, and environmental factors. Biologically, psychosis often arises from imbalances in neurotransmitters, particularly dopamine and glutamate, which play critical roles in brain function. Genetic predisposition also plays a significant role, as individuals with a family history of psychotic disorders are at a higher risk **[7]**. Sleep deprivation and postpartum hormonal changes are other notable contributors. Furthermore, autoimmune disorders and nutritional deficiencies, such as vitamin B12 deficiency, have also been linked to psychosis. Early developmental insults, such as prenatal exposure to infections or malnutrition, can increase vulnerability later in life. Chronic stress, which disrupts the hypothalamic-pituitary-adrenal (HPA) axis, has been shown to heighten the risk of psychotic disorders. Social isolation, discrimination, and lack of support networks may further exacerbate the condition, particularly in marginalized populations. Emerging research also highlights the role of inflammation and immune dysregulation, as elevated levels of pro-inflammatory cytokines have been observed in individuals experiencing psychosis. This suggests a potential link between the immune system and brain function. Additionally, epigenetic mechanisms, where environmental factors influence gene expression, are increasingly recognized as contributors to psychotic disorders. The interplay of these factors underscores the complexity of psychosis, necessitating comprehensive diagnostic and therapeutic approaches to address its diverse etiologies and manifestations **[8]**.

Pathophysiology of Psychosis

Psychosis is a complex condition involving a disconnection from reality, characterized by symptoms such as hallucinations, delusions, and disorganized thinking. The pathophysiology of psychosis is multifactorial, involving intricate interactions among neurotransmitter

imbalances, neural circuitry dysfunction, genetic predisposition, and environmental influences.

Neuroanatomical studies reveal structural and functional brain abnormalities in individuals with psychosis, including reduced gray matter volume in regions such as the prefrontal cortex, hippocampus, and thalamus. These changes disrupt normal communication between brain regions, impairing cognitive processing and emotional regulation. Functional imaging studies demonstrate altered activity in neural networks, such as the default mode network (DMN) and salience network, which play critical roles in self-referential thinking and the allocation of attention, respectively. Dysregulation of these networks is thought to underlie the disorganized thinking and aberrant salience attribution seen in psychosis **[9]**.

The role of neuroinflammation and immune system dysfunction in psychosis is increasingly recognized. Elevated levels of pro-inflammatory cytokines and microglial activation are observed in individuals with psychotic disorders, suggesting a connection between inflammation and altered neural function. This is supported by findings of increased blood-brain barrier permeability, which may facilitate the entry of peripheral immune mediators into the central nervous system, further exacerbating neuro-inflammation. Chronic inflammation may also impair neurogenesis and synaptic plasticity, contributing to the progression of psychotic symptoms **[10]**.

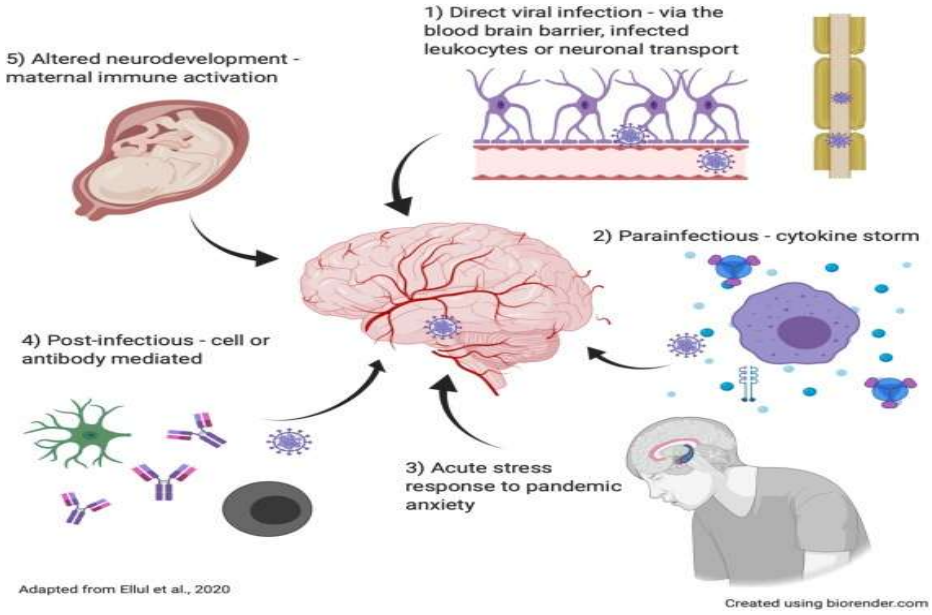

Figure 1: **Pathophysiology of psychosis**

Additionally, epigenetic modifications, such as DNA methylation and histone acetylation, may mediate the effects of environmental factors, such as prenatal

stress, infections, and substance use, on gene expression, thereby influencing the risk of developing psychosis **[11]**.

Adverse childhood experiences, such as trauma and abuse, have been linked to alterations in the hypothalamic-pituitary-adrenal (HPA) axis, leading to heightened stress reactivity and increased risk of psychosis. Increased oxidative stress, resulting from an imbalance between reactive oxygen species (ROS) production and antioxidant defences, can damage cellular components, including lipids, proteins, and DNA. Mitochondrial dysfunction may impair energy metabolism and exacerbate oxidative stress, further disrupting neuronal function and connectivity **[12, 13]**.

The concept of aberrant neurodevelopment is central to understanding the onset and progression of psychosis. Disruptions in synaptic pruning during adolescence, a critical period for brain maturation, may lead to the retention of redundant synaptic connections and impaired neural efficiency. These developmental abnormalities are thought to contribute to the emergence of psychotic symptoms during late adolescence or early adulthood, a common period for the onset of psychotic disorders. In addition to neurobiological factors, dysregulation of the gut-brain axis has gained attention as a potential contributor to psychosis **[14, 15]**. The gut microbiota influences brain function through the production of neuroactive compounds, modulation of immune responses, and regulation of the HPA axis. Alterations in gut microbiota composition, observed in individuals with psychotic disorders, may exacerbate systemic inflammation and impact neurotransmitter systems, further contributing to psychosis **[16]**.

Types of Psychiatric Disorders

Psychiatric disorders encompass a broad range of mental health conditions that affect mood, thinking, behaviour, and overall functioning. These disorders are classified into several categories based on their symptoms, aetiology, and clinical manifestations. Below are the main types of psychiatric disorders:

Generalized Anxiety Disorder (GAD) is a common psychiatric condition characterized by excessive, uncontrollable worry about various aspects of life, such as work, health, or personal relationships. Unlike situational anxiety, GAD involves persistent and pervasive worry that lasts for at least six months and interferes significantly with daily functioning. Individuals with GAD often experience physical symptoms, including muscle tension, restlessness, fatigue, and difficulty concentrating. Sleep disturbances, such as insomnia, are also prevalent, further exacerbating emotional distress **[17]**.

Figure 2: **Types of psychiatric Disorders**

Post-traumatic stress disorder (PTSD) is a psychiatric disorder that can develop after an individual experiences or witnesses a traumatic event, such as combat, sexual assault, accidents, or natural disasters. PTSD is characterized by a persistent sense of fear, anxiety, and distress that can interfere with daily functioning. Symptoms typically include flashbacks, nightmares, hypervigilance, emotional numbness, and avoidance of reminders of the trauma. PTSD is classified as an anxiety disorder in the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) but is also linked to other psychiatric conditions like depression, substance abuse, and dissociative disorders. The trauma can lead to alterations in brain function, particularly in areas like the hippocampus, amygdala, and prefrontal cortex, which affect memory, emotional regulation, and stress response **[18]**.

Major depressive disorder (MDD), also known as clinical depression, is a common and serious psychiatric condition that negatively affects how a person feels, thinks, and functions. It is characterized by persistent sadness, loss of interest or pleasure in activities, and a range of physical and emotional symptoms, including fatigue, difficulty concentrating, changes in appetite or sleep patterns, feelings of worthlessness, and thoughts of death or suicide. This disorder often co-occurs with other psychiatric conditions, including anxiety disorders, substance use disorders, and post-traumatic stress disorder. Left untreated, MDD can lead to significant impairment in daily life, including difficulties at work,

school, or in relationships, and an increased risk of suicide **[19]**.

Binge eating disorder (BED) is a psychiatric disorder characterized by recurrent episodes of consuming large amounts of food in a short period, accompanied by a lack of control over eating. Unlike bulimia nervosa, individuals with BED do not engage in compensatory behaviors such as vomiting or excessive exercise. Treatment for binge eating disorder typically includes psychotherapy, such as Cognitive Behavioral Therapy (CBT), and sometimes medication, including antidepressants or anti-obesity drugs. Early intervention and support are vital for managing symptoms and improving quality of life **[20, 21]**.

Bipolar disorder is a psychiatric condition characterized by extreme mood swings, including episodes of mania or hypomania (elevated, expansive, or irritable mood) and depression. These mood changes can significantly impact an individual's behavior, energy levels, and ability to function. There are two main types: Bipolar I, which involves manic episodes lasting at least seven days or requiring hospitalization, and Bipolar II, marked by hypomanic episodes and major depressive episodes. The exact causes of bipolar disorder are not fully understood but are believed to involve a combination of genetic, neurobiological, and environmental factors. Family history and imbalances in neurotransmitters like serotonin and dopamine contribute to its development. Treatment typically involves a combination of mood-stabilizing medications (such as lithium), antipsychotics, and antidepressants, along with psychotherapy (e.g., Cognitive Behavioral Therapy). Early intervention, continuous treatment, and support can help individuals manage the disorder and lead fulfilling lives **[22]**.

Schizophrenia is a severe psychiatric disorder characterized by distorted thinking, perceptions, emotions, and behaviors. Common symptoms include hallucinations (hearing or seeing things that aren't there), delusions (false beliefs), disorganized speech and thinking, and impaired functioning in daily activities. Individuals with schizophrenia may also experience cognitive impairments, such as difficulty with memory, attention, and decision-making. The exact cause of schizophrenia is unknown, but it is thought to result from a combination of genetic, biochemical, and environmental factors. Early diagnosis and consistent treatment are crucial in managing the disorder and improving long-term outcomes **[23]**.

Schizoaffective disorder is a psychiatric condition characterized by symptoms of both schizophrenia (e.g., hallucinations, delusions, disorganized thinking) and mood disorders, such as depression or mania. The disorder is classified into two types: bipolar

type, which involves episodes of mania or hypomania, and depressive type, which includes only major depressive episodes. Treatment typically involves antipsychotic medications to manage psychosis and mood stabilizers or antidepressants for mood symptoms. Psychotherapy, such as Cognitive Behavioral Therapy, is also helpful in improving coping strategies and functional outcomes. Early treatment is essential for managing symptoms and enhancing quality of life **[24]**.

Borderline personality disorder (BPD) is a psychiatric condition characterized by intense emotional instability, impulsive behaviors, and unstable relationships. Individuals with BPD often experience extreme mood swings, fear of abandonment, difficulty maintaining relationships, and a distorted self-imageTreatment for BPD typically involves psychotherapy, with Dialectical Behavior Therapy (DBT) being particularly effective. DBT helps individuals develop skills for emotional regulation, mindfulness, and interpersonal effectiveness. Medications, such as antidepressants or mood stabilizers, may also be used to manage symptoms. Early diagnosis and treatment are crucial for improving long-term outcomes and helping individuals lead more stable, fulfilling lives **[25]**.

Narcissistic personality disorder (NPD) is a psychiatric condition marked by a pattern of grandiosity, a need for admiration, and a lack of empathy for others. Individuals with NPD often have an inflated sense of their own importance, a belief that they are unique or special, and a preoccupation with success or powerTreatment for NPD typically involves psychotherapy, such as Cognitive Behavioral Therapy (CBT), which helps individuals develop healthier patterns of thinking and behavior. Therapy can address underlying insecurities and help improve interpersonal skills. Medication may be used to manage symptoms like depression or anxiety, though it's not a primary treatment for NPD itself **[26]**.

Medical conditions that can cause psychosis: Psychosis, characterized by a distorted perception of reality, often manifests through symptoms like hallucinations, delusions, and disorganized thinking, and it can be caused by a wide range of medical conditions **[27]**. Dementia with Lewy bodies, another type of dementia, is particularly associated with vivid visual hallucinations and fluctuating cognitive impairments, leading to psychotic episodes. Multiple sclerosis (MS), a condition that affects the central nervous system, can cause psychosis due to lesions in the brain and disruption of neural pathways involved in perception and thought. Traumatic brain injuries (TBI), resulting from physical impact to the brain, can lead to cognitive dysfunction and psychotic symptoms,

especially when the injury occurs in areas that regulate mood and perception. Strokes, which interrupt blood flow to the brain, can cause psychosis depending on the region of the brain affected; for example, strokes in the temporal lobe can lead to hallucinations or delusions. Brain infections like encephalitis, which is inflammation of the brain usually caused by a viral infection, can lead to psychosis due to direct inflammation and damage to brain tissue, resulting in altered mental status, delusions, and hallucinations. Meningitis, another infection of the brain's protective membranes, can cause confusion, delusions, and psychotic symptoms as the infection spreads. In individuals with HIV/AIDS, psychosis can develop as a result of the virus's direct effects on the brain, as well as due to complications such as HIV-associated dementia, which can manifest as memory loss, confusion, and hallucinations **[28, 29]**. This is particularly common in conditions like hepatic encephalopathy, where the liver fails to detoxify the blood, leading to confusion, altered mental status, and psychosis. Wernicke-Korsakoff syndrome, caused by a thiamine deficiency often related to chronic alcohol abuse, is a neurocognitive disorder that can lead to psychosis, particularly through memory impairment, confabulation, and hallucinations. Substance abuse and withdrawal are significant contributors to psychosis **[30, 31]**. For instance, drugs such as methamphetamines, cocaine, LSD, and other hallucinogens can induce psychotic episodes during use, with effects ranging from visual and auditory hallucinations to delusional thinking. Long-term drug use can lead to persistent psychosis even after the drug has left the system, a condition known as substance-induced psychosis. Alcohol withdrawal, particularly when it is severe (delirium tremens), can also result in psychosis, with symptoms including tremors, hallucinations, agitation, and confusion. Autoimmune disorders like systemic lupus erythematosus (SLE), which causes the immune system to attack the body's own tissues, can result in psychiatric symptoms, including psychosis, particularly when the central nervous system is involved **[32]**. Cancer treatments, including chemotherapy and radiation, can sometimes cause cognitive disruptions and psychosis as side effects due to the toxic impact on the brain or hormonal changes. Finally, certain psychiatric disorders, while not strictly medical conditions, can overlap with medical causes of psychosis. Schizophrenia, a primary psychotic disorder, is one of the most common causes of psychosis, but psychotic episodes can also be triggered or exacerbated by medical conditions, making it important to differentiate between primary psychiatric causes and secondary medical causes of psychosis **[33]**.

Antipsychotics induced hormonal alterations

Antipsychotics, particularly atypical antipsychotics, can induce a range of hormonal alterations that affect various endocrine systems. These effects are important to consider as they may contribute to side effects, including metabolic changes, sexual dysfunction, and disruptions in reproductive health. The hormonal alterations induced by antipsychotics are primarily due to their interaction with neurotransmitter systems, particularly dopamine, which plays a key role in regulating the secretion of several hormones **[34, 35]**.

1. **Prolactin Elevation**: One of the most common hormonal changes associated with antipsychotic use, particularly with first-generation antipsychotics (e.g., haloperidol) and some second-generation (atypical) antipsychotics (e.g., risperidone), is an increase in prolactin levels. Antipsychotics block dopamine receptors in the tuberoinfundibular pathway, a region of the brain responsible for inhibiting prolactin release. When dopamine is blocked, prolactin secretion increases, which can lead to conditions such as hyperprolactinemia. This can cause menstrual disturbances (amenorrhea) in women, galactorrhea (inappropriate lactation), and sexual dysfunction, including erectile dysfunction and decreased libido in both men and women. Long-term hyperprolactinemia can also contribute to bone density loss, leading to an increased risk of osteoporosis **[36]**.
2. **Insulin Resistance and Glucose Metabolism**: Many atypical antipsychotics, such as olanzapine, clozapine, and quetiapine, are associated with metabolic side effects, including insulin resistance and impaired glucose metabolism. These medications can lead to an increase in blood glucose levels, raising the risk of type 2 diabetes. The mechanism behind this is not fully understood, but it is thought to involve alterations in insulin sensitivity and an increase in appetite, which can lead to weight gain. Additionally, changes in the secretion of insulin and leptin (a hormone involved in appetite regulation) may contribute to these metabolic disturbances **[37]**.
3. **Thyroid Function**: Antipsychotics can also affect thyroid function. For example, some studies have reported that second-generation antipsychotics, such as olanzapine and quetiapine, may cause mild alterations in thyroid hormone levels, including elevated TSH (thyroid-stimulating hormone) levels, which can indicate hypothyroidism. However, significant thyroid

dysfunction is rare. The mechanisms by which antipsychotics affect thyroid function remain unclear, but it is believed to be related to changes in dopamine and serotonin, which influence the hypothalamic-pituitary-thyroid axis **[38]**.

4. **Sex Hormones**: Antipsychotic-induced hormonal alterations can also affect the balance of sex hormones. For example, the increased prolactin levels caused by antipsychotics may disrupt the hypothalamic-pituitary-gonadal axis, leading to reduced levels of estrogen in women and testosterone in men. This can result in menstrual irregularities, decreased libido, and infertility in women, as well as reduced sexual drive and erectile dysfunction in men. The impact on sex hormones can also affect mood and quality of life **[39]**.
5. **Adrenal Hormones**: Some studies have suggested that antipsychotics, particularly atypical ones like clozapine and olanzapine, may affect adrenal function. Specifically, these medications may influence cortisol levels, which are involved in the body's stress response.
6. **Growth Hormone**: Antipsychotics may also influence growth hormone (GH) secretion, although this is less commonly discussed. Some studies have shown that medications such as risperidone and clozapine may alter GH levels, potentially leading to changes in metabolism and growth. However, the clinical significance of these changes is not well understood, and more research is needed to determine the long-term impact **[40]**.

The hormonal side effects of antipsychotic medications vary between individuals and depend on factors such as the specific antipsychotic used, dosage, duration of treatment, and individual susceptibility. In some cases, switching to a different antipsychotic with a more favourable endocrine profile (e.g., aripiprazole, ziprasidone) may reduce the risk of hormonal side effects **[41]**. Additionally, adjunctive treatments such as dopamine agonists may be used to mitigate prolactin-related side effects. Monitoring endocrine function through regular blood tests and clinical evaluations is important for individuals on antipsychotic treatment, particularly those on medications known to affect metabolic and hormonal systems **[42]**.

CURRENT PROSPECTIVES AND CHALLENGES

The management of neuroleptic drugs, particularly their associated hormonal alterations, presents both current prospects and challenges in clinical practice. Neuroleptics, or antipsychotics, are widely used to treat a range of psychiatric disorders, including schizophrenia, bipolar disorder, and other mood-related conditions. Over the

years, second-generation antipsychotics (SGAs) have emerged as the first-line treatment due to their superior efficacy and better side-effect profile compared to first-generation antipsychotics (FGAs). However, these drugs are not without significant adverse effects, particularly hormonal disruptions that can negatively impact patient health **[43, 44]**. One of the most prominent concerns with neuroleptic medications is their ability to elevate prolactin levels, leading to conditions such as hyperprolactinemia, which can cause menstrual irregularities, galactorrhoea, sexual dysfunction, and infertility. In some cases, prolonged hyperprolactinemia may lead to bone mineral density loss and osteoporosis **[45]**. Additionally, atypical antipsychotics are also linked to metabolic side effects, such as weight gain, insulin resistance, and an increased risk of type 2 diabetes, which further complicates patient care. These metabolic disturbances are often exacerbated by changes in insulin and leptin regulation, contributing to long-term health risks like cardiovascular disease and metabolic syndrome **[46, 47]**.

Despite these challenges, there are some promising developments in the management of neuroleptic drug-induced hormonal alterations. Efforts to develop new antipsychotic drugs with a more favourable endocrine side-effect profile are ongoing, with medications like aripiprazole and ziprasidone emerging as alternatives that exert less impact on prolactin and metabolic processes. Pharmacogenetic testing may also offer new insights into predicting individual responses to antipsychotic medications, enabling more personalized and effective treatment strategies. Additionally, adjunctive therapies, such as dopamine agonists, can be used to address prolactin-related issues, while careful monitoring of metabolic parameters (such as blood glucose levels, cholesterol, and weight) can help mitigate the risk of metabolic disturbances **[48, 49]**.

CONCLUSION

In conclusion, the management of neuroleptic drug-induced hormonal alterations remains a complex and evolving challenge in clinical practice. While antipsychotics, particularly second-generation (atypical) antipsychotics, have revolutionized the treatment of psychiatric disorders, their associated endocrine side effects, such as hyperprolactinemia, insulin resistance, thyroid dysfunction, and sexual hormone imbalances, can significantly impact patients' physical health and quality of life. These hormonal disturbances require careful monitoring and individualized management strategies to mitigate long-term health risks, such as osteoporosis, metabolic syndrome, and reproductive complications. Although newer antipsychotics tend to have a more

favourable hormonal profile, the risk of adverse endocrine effects cannot be entirely eliminated. Current therapeutic approaches include dose adjustments, switching to medications with a lower propensity for endocrine disruption (e.g., aripiprazole), and adjunctive treatments, such as dopamine agonists or medications to manage metabolic disturbances. However, despite these strategies, there is still a need for more targeted, evidence-based interventions to address the underlying mechanisms of hormonal alterations induced by neuroleptics. Additionally, educating healthcare providers and patients about the potential endocrine side effects and the importance of regular monitoring is essential for improving long-term treatment outcomes. Future research should focus on better understanding the pharmacological mechanisms involved in antipsychotic-induced hormonal changes, as well as developing novel drugs with reduced endocrine risks. Ultimately, a balanced approach that carefully weighs the therapeutic benefits of antipsychotic medications against their potential hormonal side effects is crucial for optimizing patient care in psychiatric settings.

REFERENCES

[1] Larsen PR, Kronenberg HM, Melmed S, *et al*., editors. Williams textbook of endocrinology. 10th ed. Philadelphia (PA): Saunders, 2003.

[2] Polishuk WZ, Kulcsar S. Effects of chlorpromazine on pituitary function. J Clin Endocrinol Metab 1956; 16: 292–3.

[3] Wieck A, Haddad PM. Antipsychotic-induced hyperprolactinaemia in women: pathophysiology, severity and consequences: selective literature review. Br J Psychiatry 2003; 182: 199–204.

[4] Bushe C, Shaw M. Prevalence of hyperprolactinemia in a naturalistic cohort of schizophrenia and bipolar outpatients during treatment with typical and atypical anti-psychotics. J Psychopharmacol 2007; 21: 768–9.

[5] Langer G, Sachar EJ, Nathan RS, *et al*. Dopaminergic factors in human prolactin regulation: a pituitary model for the study of a neuroendocrine system in man. Psychopharmacology 1979; 65: 161–4.

[6] Fowlie S, Burton J. Hyperprolactinaemia and nonpuerperal lactation associated with clomipramine. Scott Med J 1987; 32: 52–3.

[7] Barbaro D, Faggionato F, Pallini S, *et al*. Verapamil acute administration: a new dynamic test in hyperprolactinemic states. Metabolism 1999; 48: 1351–6.

[8] Ziambaras K, Dagogo-Jack S. Tumor-grade hyperprolactinemia induced by multiple medications in the setting of renal failure. Endocrinol Pract 1999; 5: 139–42.

[9] Molitch ME. Disorders of prolactin secretion. Endocrinol Metab Clin North Am 2001; 30: 586–610.

[10] Orlando G, Brunetti L, Vacca M. Ritonavir and saquinavir directly stimulate anterior

pituitary prolactin secretion, in vitro. Int J Immunopathol Pharmacol 2002; 15: 65–8.

[11] Papakostas GI, Miller KK, Petersen T, *et al*. Serum prolactin levels among outpatients with major depressive disorder during the acute phase of treatment with fluox-etine. J Clin Psychiatry 2006; 67: 952–7.

[12] Monteleone P, Maj M, Ariano MG, *et al*. Prolactin response to sodium valproate in schizophrenics with and without tardive dyskinesia. Psychopharmacology 1988; 96: 223–6.

[13] Marken PA, Haykal RF, Fisher JN. Management of psychotropic-induced hyperprolactinemia. Clin Pharm 1992; 11: 851–6.

[14] Hirschfeld RM. Management of sexual side effects of antidepressant therapy. J Clin Psychiatry 1999; 60Suppl. 14: 27–35.

[15] El Khoury A, Tham A, Mathe AA, *et al*. Decreased plasma prolactin release in euthymic lithium-treated women with bipolar disorder. Neuropsychobiology 2003; 48: 14–8.

[16] Van Cauter E, Linkowski P, Kerkhofs M, *et al*. Circadian and sleep-related endocrine rhythms in schizophrenia. Arch Gen Psychiatry 1991; 48: 348–56.

[17] Kopacek M, Bares M, Svarc J, *et al*. Hyperprolactinemia after low dose of amisulpride. Neuroendocrinol Lett 2004; 25: 419–22.

[18] Paparrigopoulos T, Liappas J, Tzavellas E, *et al*. Amisulpride-induced hyperprolactinemia is reversible following discontinuation. Prog Neuropsychopharmacol Biol Psychiatry 2007; 31: 92–6.

[19] Melkersson KI. Prolactin elevation of the antipsychotic risperidone is predominantly related to its 9-hydroxy metabolite. Hum Psychopharmacol 2006; 21: 529–32.

[20] Lai YC, Chou CC, Chen CH, *et al*. Significant elevations of prolactin levels in patients who shifted from conventional depot antipsychotics to long-acting risperidone. J Clin Psychopharmacol 2007; 27: 523–4.

[21] Maguire GA. Prolactin elevation with antipsychotic medications: mechanisms of action and clinical consequences. J Clin Psychiatry 2002; 63 Suppl. 4: 56–62.

[22] Baldessarini RJ, Tarazi FI. Chapter 18: pharmacotherapy of psychosis and mania. In: Brunton LL, Lazo JS, Parker KL, editors. Goodman and Gilman's the pharmacological basis of therapeutics. 1 1th ed. New York: McGraw-Hill Press, 2005: 461–500.

[23] Costa AM, de Lima MS, Faria M. Naturalistic, ninemonth follow-up, comparing olanzapine and conventional antipsychotics on sexual function and hormonal profile for males with schizophrenia. J Psychopharmacol 2007; 21: 165–70.

[24] Saldana SN, Delgado SV. Ziprasidone-associated galactorrhea in an adolescent female. J Child Adolesc Psychopharmacol 2007; 17: 259–60.

[25] Kim KS, Pae CU, Chae JH, *et al*. Effects of olanzapine on prolactin levels of female patients with schizophrenia treated with risperidone. J Clin Psychiatry 2002; 63: 408–13.

[26] Wahl R, Ostroff R. Reversal of symptomatic hyperprolactinemia by aripiprazole. Am J Psychiatry 2005; 162: 1542–3.

[27] Shim JC, Shin JG, Kelly DL. Adjunctive treatment with a dopamine partial agonist, aripiprazole, for antipsychoticinduced hyperprolactinemia: placebo-controlled trial. Am J Psychiatry 2007; 164: 1404–10.

[28] Wolf J, Fiedler U. Hyperprolactinemia and amenorrhea associated with olanzapine normalized after addition of aripiprazole. J Clin Pharm Ther 2007; 32: 197–8.

[29] Molitch M. Medication-induced hyperprolactinemia. Mayo Clin Proc 2005; 80: 1050–7.

[30] Staller J. Effect of long-term antipsychotic treatment on prolactin. J Child Adolesc Psychopharmacol 2006; 16: 317–26.

[31] Kinon BJ, Gilmore JA, Liu H, *et al*. Hyperprolactinemia in response to antipsychotic drugs: characterization across comparative clinical trials. Psychoneuroendocrinology 2003; 28: 55–68.

[32] Alpert M, Diamond F, Kesselman M. Correlation between extrapyramidal and therapeutic effects of neuroleptics. Compr Psychiatry 1977; 18: 333–6.

[33] Stevens JR, Kysmissis PI, Baker AJ. Elevated prolactin levels in male youths treated with risperidone and quetiapine. J Child Adolesc Psychopharmacol 2005; 15: 893–900.

[34] Holzer M, Eap CB. Risperidone-induced symptomatic hyperprolactinaemia in adolescents. J Clin Psychopharmacol 2006; 26: 167–71.

[35] Lee BH, Kim YK. Relationship between prolactin response and clinical efficacy of risperidone in acute psychotic inpatients. Prog Neuropsychopharmacol Biol Psychiatry 2006; 30: 658–62.

[36] Misra M, Papakostas GI, Klibanski A. Effects of psychiatric disorders and psychotropic medications on prolactin and bone metabolism. J Clin Psychiatry 2004; 65: 1607–18.

[37] Haddad PM, Wieck A. Antipsychotic-induced hyperprolactinaemia: mechanisms, clinical features and management. Drugs 2004; 64: 2291–314.

[38] Thangavelu K, Geetanjali S. Menstrual disturbance and galactorrhea in people taking conventional antipsychotic medications. Exp Clin Psychopharmacol 2006; 14: 459–60.

[39] Loh C, Leckband SG, Meyer JM. Risperidone-induced retrograde ejaculation: case report and review of the literature. Int Clin Psychopharmacol 2004; 19: 111–2.

[40] Aleem M, Choudhari J, Padwal V. Hyperprolactinemia affects spermiogenesis in adult male rats. J Endocrinol Invest 2005; 28: 39–48.

[41] Whalley LJ, Christie JE, Blackwood DH, *et al*. Disturbed endocrine function in the psychoses: disordered homeostasis or disease process? Br J Psychiatry 1989; 155: 455–61.

[42] Harvey PW, Everett DJ, Springall CJ. Hyperprolactinaemia as an adverse effect in regulatory and clinical toxicology: role in breast and prostate cancer. Hum Exp Toxicol 2006; 25: 395–404.

[43] Correll CU, Carlson HE. Endocrine and metabolic adverse effects of psychotropic medications in children and adolescents. J Am Acad Child Adolesc Psychiatry 2006; 45: 771–91.

[44] Nakajima M, Terao T, Iwata N. Switching female schizophrenic patients to quetiapine from conventional antipsychotic drugs: effects on hyperprolactinemia. Pharmacopsychiatry 2005; 38: 17–9.

[45] Kinon MJ, Ahl J, Liu-Siefert H. Improvement in hyperprolactinemia and reproductive comorbidities in patients with schizophrenia switched from conventional anti-psychotics or risperidone to olanzapine. Psycho-neuroendocrinology 2006; 31: 577–88.

[46] Holt RI. A context for psychiatrists: medical causes and consequences of hyperprolactinemia. J Psycho-pharmacol 2002; 22(2 Suppl.): 28–37.

[47] Ellison DH, Berl T. Clinical practice: the syndrome of inappropriate antidiuresis. N Engl J Med 2007; 356: 2064–72.

[48] Dundas B, Harris M, Narasimhan M. Psychogenic polydipsia review: etiology, differential, and treatment. Curr Psychiatry Rep 2007; 9: 236–41.

[49] Kalantar-Zadeh K, Nguyen MK, Chang R, *et al*. Fatal hyponatremia in a young woman after ecstasy ingestion. Nat Clin Pract Nephrol 2006; 2: 283–8.