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Risperidone-Induced Polymenorrhea: An under Recognized Endocrine Adverse Reaction

Samridhi Sharma[1], Girish Joseph[2], Neena Bhatti[2*], Dinesh Kumar Badyal[3] and Pallavi Abhilasha[4]

[1]MBBS Student, Phase III Part 2, Christian Medical College & Hospital, Ludhiana
[2]Assistant Professor, Department of Pharmacology, Christian Medical College & Hospital, Ludhiana
[3]Professor & Head, Department of Pharmacology, Christian Medical College & Hospital, Ludhiana
[4]Associate Professor, Department of Psychiatry, Christian Medical College, Ludhiana

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Abstract

Background: *Antipsychotic medications, particularly risperidone, are widely used in the management of psychotic disorders due to their efficacy and favorable side effect profile compared to typical antipsychotics. However, endocrine and reproductive adverse effects such as hyperprolactinemia are increasingly recognized, yet often underdiagnosed.*

Methodology: *The Department of Pharmacology, CMC Ludhiana, is an ADR reporting centre. The case was reported to ADR Centre from the Psychiatry Ward as a part of Pharmacovigilance Elective in MBBS Third Prof Part-1.*

Conclusion: *Polymenorrhea is a rare but significant adverse effect of risperidone that may impair quality of life and treatment adherence. Routine surveillance and early recognition of endocrine side effects, coupled with interdisciplinary management, are essential for optimizing patient care in psychiatric settings.*

***Corresponding author:** Neena Bhatti, Assistant Professor, Department of Pharmacology, Christian Medical College & Hospital, Ludhiana, India.

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Introduction

Psychotic disorders, including schizophrenia, pose a major health burden worldwide. The World Health Organization (WHO) estimated in 2022 that approximately 24 million individuals suffer from psychosis, making it a significant health burden [1]. Antipsychotic medications like risperidone are frontline treatments for such conditions, with proven efficacy in symptom management. However, the increasing use of these drugs has been paralleled by a growing recognition of their adverse effects, particularly those involving the endocrine and reproductive systems [2].

Risperidone was first synthesized in 1984 by Janssen Pharmaceuticals and approved for clinical use in the United States by the Food and Drug Administration (FDA) in 1993 [3]. Risperidone is an atypical antipsychotic with high affinity for several neurotransmitter receptors. The dopamine D2 receptors blockade reduces psychotic symptoms by inhibiting dopaminergic neurotransmission in the mesolimbic pathway. The serotonin 5-HT2A receptors cause antagonism at these receptors enhances dopaminergic activity in the nigrostriatal pathway, reducing extrapyramidal side effects. The alpha-adrenergic receptors contribute to sedation and hypotension, while histamine H1 receptors antagonism leads to weight gain and sedation [4]. As a second-generation (atypical) antipsychotic, it has a reduced risk of extrapyramidal side effects compared to typical antipsychotics like haloperidol, therefore also referred as an 'atypical anti-pyschotic'. The introduction of risperidone marked a significant advancement in the pharmacological management of psychiatric disorders, offering broader symptom control with improved tolerability. Its clinical applications soon expanded beyond schizophrenia to include bipolar mania and behavioral symptoms in autism spectrum disorders [5].

Despite its success, risperidone's pharmacological profile presents a double-edged sword. While it offers significant symptom relief, the risk of adverse effects especially endocrine disorders like hyperprolactinemia has gained attention. These hormonal imbalances can result in menstrual disorders such as polymenorrhea, amenorrhea, and galactorrhea, which are often underdiagnosed or misattributed [6]. The other Adverse Drug Reactions (ADRs) of Risperidone include neurological symptoms such as Extrapyramidal symptoms, dystonia, akathisia, parkinsonism, metabolic such as weight gain, hyperglycemia, lipid abnormalities, cardiovascular such as orthostatic hypotension, QT interval prolongation and gastrointestinal such as nausea, constipation, dry mouth [7].

In this case the patient presented with polymenorrhoea after consuming Risperidone. Polymenorrhea is defined as a menstrual cycle lasting less than 20 days [8]. According to Vigiaccess database, there are only 6 reported cases of polymennorhoea, although a huge proportion of cases (13%) belong to the class of reproductive system and breast disorders [9]. This article presents a rare case of polymenorrhea induced by risperidone and expands on the drug's pharmacodynamics, mechanism of action, ADRs, contraindications, and management strategies. With the limited number of similar reports in literature, this case underscores the importance of pharmacovigilance and individualized patient care.

Case Report

A 32-year-old married woman from Ludhiana, Punjab, presented to the psychiatric outpatient department with complaints of fear, decreased sleep, social withdrawal, crawling sensations, and poor eye contact. She was diagnosed with psychosis and started on therapy with risperidone. While her psychiatric symptoms improved over a few weeks, she reported experiencing menstruation twice a month, i.e. Polymenorrhea, her Serum prolactin levels was elevated at 43ng/ml, while the normal range is 2-19ng/dl. Suspecting risperidone-induced polymenorrhea the drug was replaced with aripiprazole. Despite this, prolactin levels remained high, leading to the discontinuation of aripiprazole as well. The patient continued other medications and is under follow-up. The Naranjo Adverse Drug Reaction Probability Scale scored 6, indicating a probable relationship between risperidone and the adverse event. Ten elements make up the validated, structured Naranjo Probability Scale, which is used to determine the probability that an adverse event is caused by a particular medication. According to the direction and strength of the evidence, each item is given a score based on the response "Yes," "No," or "Do not know" with corresponding point values of -1, 0, +1, or +2. The probability of an ADR is classified as

definite (scoring ≥9), probable (score 5-8), possible (score 1-4), or doubtful (score ≤0) based on the cumulative score. The total score, which represents the degree of causation vary from -4 to +13 [10].

Discussion

World Health Organization (WHO) defines adverse drug reaction (ADR) as "a response to a medication that is noxious and unintended and occurs at doses normally used in man." In both primary care and tertiary care institutions, ADRs are prevalent. ADRs not only have an effect on patients' quality of life, but they also put more strain on the healthcare system. Their high rates of illness and mortality make them a serious public health issue [11]. In this case, the patient developed polymenorrhea after starting on therapy with Risperidone. Considering Risperidone being an atypical antipsychotic, it is imperative to understand the mechanism. The hypothalamic-pituitary-gonadal axis regulates menstrual cycles. Dopamine acts as a prolactin-inhibitory factor; thus, antagonism of D2 receptors in the pituitary leads to elevated prolactin levels. Hyperprolactinemia disrupts the pulsatile secretion of gonadotropin-releasing hormone (GnRH), impairing follicle-stimulating hormone (FSH) and luteinizing hormone (LH) secretion. This hormonal imbalance results in irregular ovulation and menstrual disturbances like polymenorrhea [12]. Another mechanism postulated is that dopamine blockade in the tuberoinfundibular pathway leads to increased prolactin secretion, a central feature in the development of hyperprolactinemia-related ADRs [7].

Therefore, polymenorrhea can significantly affect the quality of life, causing anemia, fatigue, and emotional distress. In patients with psychiatric disorders, such symptoms may exacerbate psychological issues or lead to non-compliance with treatment. Therefore, it is important to incorporate menstrual history in psychiatric evaluations and periodically monitor serum prolactin levels in patients on antipsychotics as increased prolactin levels can lead to polymenorrhoea [7,12,13]. The immediate treatment is stopping of the offending drug and shifting the patient to aripiprazole which is a partial D2 agonist as a meta-analysis has demonstrated that there is no strong evidence of prolactin increase with aripiprazole. It is also important to encourage inter-disciplinary collaboration between psychiatrists, gynaecologists and clinical pharmacists to report patients presenting with raised prolactin, as increased prolactin levels can lead to a multitude of cases.

Conclusion

This case report highlights a rare but important adverse effect of risperidone polymenorrhea likely resulting from hyperprolactinemia. While risperidone remains a cornerstone in the treatment of psychotic disorders, its potential impact on the endocrine and reproductive systems must not be overlooked. Routine monitoring of prolactin levels and menstrual patterns should be integrated into psychiatric care, especially in female patients. Early recognition of such adverse effects and prompt interdisciplinary management can improve patient outcomes, enhance adherence to therapy, and contribute to more holistic mental health care.

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