澄 清 醫 護 管 理 雜 誌
CHENG CHING MEDICAL JOURNAL
Case Report

# Pharmacological Aspect and Challenges in Managing Amisulpride-Induced Hyperprolactinemia: A Case Report and Implications of Failed Normalization with Add-On Aripiprazole and the Risk of Mastitis

**Ya-Wen Lu[1], Hsaun-Ting Yu[1], Tsung-Chia Chen[2], Han-Ting Yeo Jillian[3]**

Department of Pharmacy[1], Division of Infectious Diseases[2], Taichung Hospital, Ministry of Health Welfare;
Centre for Medical Education, Yong Loo Lin School of Medicine, National University of Singapore[3]

## Abstract

**Purposes**

Hyperprolactinemia is a known adverse effect of antipsychotics, attributed to the blockade of dopamine $D_2$ receptors in the posterior pituitary. While previous studies have shown the potential of add-on aripiprazole, a partial agonist of $D_2$ receptors, to reduce atypical antipsychotic-induced hyperprolactinemia, this case report presents an instance where aripiprazole failed to alleviate amisulpride-induced hyperprolactinemia.

**Methods**

The case report describes a patient who developed mastitis attributed to hyperprolactinemia secondary to the use of antipsychotics, specifically amisulpride. The authors demonstrate the principles of using add-on aripiprazole to manage elevated prolactin levels. Furthermore, the article will discuss the reasons for the failure of aripiprazole to lower prolactin when combined with amisulpride from a pharmacological perspective.

**Results**

The difference in lipophilicity between amisulpride and aripiprazole is identified as a contributing factor to the varying affinities for dopamine $D_2$ receptors in the pituitary. This pharmacological distinction elucidates the inability of aripiprazole to regulate amisulpride-induced hyperprolactinemia.

**Conclusions**

This case highlights the paramount importance for healthcare professionals to remain vigilant regarding the risk of mastitis resulting from antipsychotic side effects. Regular monitoring of blood prolactin levels is crucial for patients on amisulpiride, particularly men and menopausal women. Furthermore, adopting a multidisciplinary team approach is essential for managing uncommon infections. Early identification and intervention of elevated prolactin levels induced by amisulpiride play a pivotal role in preventing further side effects. (Cheng Ching Medical Journal 2024; 20(1): 30-38)

***Keywords : Amisulpride, Aripiprazole, Mastitis, Hyperprolactinemia, Antipsychotic***

## Introduction

Schizophrenia is a chronic disease causing one of the top 15 disorders globally [1]. It can be characterized into positive and negative symptoms based on the behaviors. Negative symptoms dominate around 60% of psychosis [2]. In an earlier meta-analysis, Leucht and colleagues reported that the second-generation antipsychotics (SGA) amisulpride, clozapine, olanzapine, and risperidone were more efficacious than first-generation antipsychotics (FGA) [3]. The European Psychiatric Association (EPA)

Corresponding author : Ya-Wen Lu
Address: No. 199, Sec. 1, Sanmin Rd., West Dist., Taichung City, 403301, Taiwan (R.O.C.)
E-mail: tinalu1988@gmail.com

Received: January 2023; Accepted: July 2023

recommends that patients treated with an FGA who experience negative symptoms should be switched to an SGA, but it does not recommend a specific SGA [4]. Amisulpride, a SGA, is effect on both positive and negative symptoms. Unlike other SGA, amisulpride demonstrates efficacy in ameliorating negative symptoms. A 2018 systematic review and meta-analysis in patients with predominant or prominent negative symptoms found that amisulpride (mean dose 50-300mg/day) was the only antipsychotic superior to placebo [5]. However, amisulpride does not get into the brain easily which leads to a needed of higher oral dose (compared to other SGA). As a result, it is estimated that the relative hydrophilic characteristic of amisulpride has more effect on pituitary gland compared with other antipsychotics. Pituitary gland is responsible for the secretion of prolactin when lactotroph cells located at anterior gland received stimulation. Prolactin homeostasis is subjected to internal and external factors such as circadian rhythm, stress, estrogen, serotonin and dopamine. Those factors can directly or indirectly affect the lactotroph cells and affects the prolactin production. The primary physiological control mechanism for prolactin secretion is mediated by the inhibitory action of dopamine. Dopamine is secreted in hypothalamic periventricular zone and is released from neuronal projections in the nerve endings in the median eminence. It then travels to the anterior pituitary gland through portal vessels. Dopamine then binds to the $D_2$ receptors on lactotroph cells and inhibits prolactin release. This mechanism is called tuberoinfundibular dopamine (TIDA) pathway[6]. (Figure 1) The administration of antipsychotics, targets at blocking dopamine receptor, is known to be associated with decrease of dopamine concentration therefore increase the release of prolactin. A third-generation antipsychotic (TGA), aripiprazole, acts as a dopamine system stabilizer (DSS) and has been used as an add-on therapy to reverse elevated prolactin levels by competing with $D_2$ antagonists. Published literature has successfully reversed the increase in prolactin levels induced by risperidone and paliperidone with the concomitant use of aripiprazole [7,8]. However,

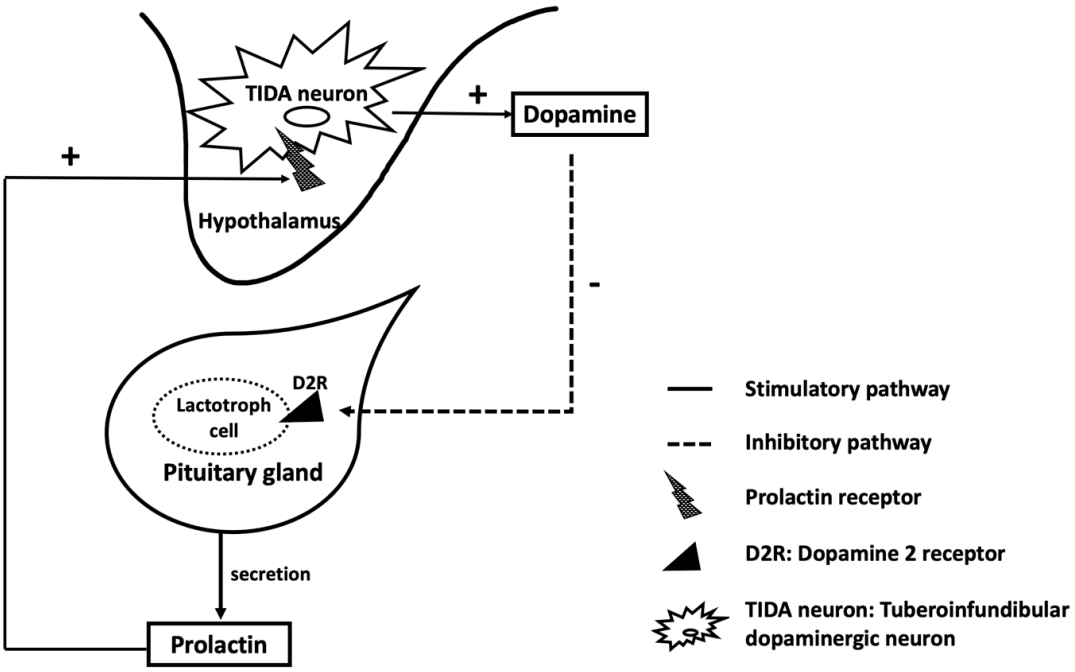



Figure 1 Tuberoinfundibular dopamine pathway: The TIDA neuron identifies the existence of prolactin, signaling the hypothalamus to release dopamine. The release of dopamine inhibits prolactin synthesis and secretion. This feedback loop regulation is called the tuberoinfundibular dopamine (TIDA) pathway

we herein present a case of mastitis attributed to hyperprolactinemia caused by amisulpride and failed to be managed by add-on aripiprazole. This article will explore the possible reasons for the discrepancy in effects of add-on aripiprazole between the literatures and discuss the implications for healthcare professionals.

**Case Report**

A 46-year-old nonpuerperal female presented to infectious diseases ward with the symptom of redness, pain, swelling and hard lump of the right breast (Figure. 2). She had no alcohol nor tobacco use history. She had a history of schizophrenia with negative symptoms and was currently under control with amisulpride 200mg four times daily for approximately one year. She had no known allergy to any medication and did not smoke and consume alcohol. She was nulliparous and not pregnant. Ultrasonography-guided aspiration biopsy as well as incision and drainage (I& D) were performed. The findings from breast biopsy showed no evidence of malignancy. The pus from I& D was sent and the culture yielded methicillin susceptible staphylococcus aureus (MSSA). The pathology report confirmed acute mastitis. Under the diagnosis of right breast mastitis, she was given intravenous oxacillin 2 grams every six hours. However, with no obvious trauma or skin lesion was noted, mastitis caused by endogenous risk factor was suspected. To find out the reason of mastitis, medication review was done by pharmacist. The possible side effect of amisulpride was raised and prolactin level checked was suggested. Serum level of prolactin was confirmed high and stood at 111.49ng/ml (reference level: 2.74-19.64ng/ml). New symptom of galactorrhoea was noted three days after the diagnosis of hyperprolactinemia (Figure. 3). A psychiatrist was consulted regarding medication adjustment to manage the raised level of serum prolactin. As per recommendation by psychiatrist, aripiprazole 5mg once daily was prescribed in combination with amisulpride. After 21 days of oxacillin treatment, there was a decrease in the amount of pus discharged from her right breast. The patient was discharged and followed-up at outpatient department. Prior to her discharged, her serum

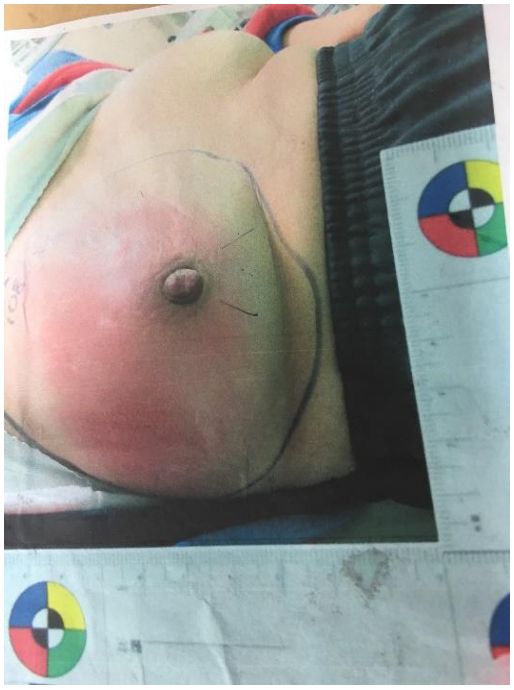


Figure 2. Right breast of the patient presented redness and swelling without skin lesion

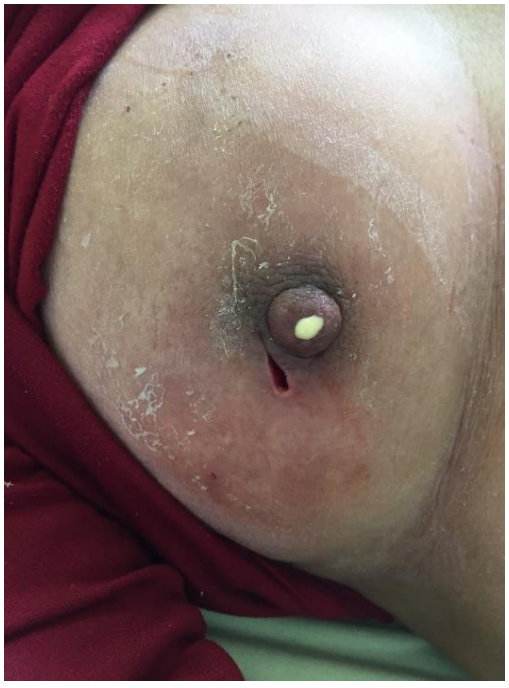


Figure 3. The milk lactated from right breast

prolactin was measured and showed 113.68ng/ml after 15 days of aripiprazole. Amisulpride was discontinued after the third consecutively high prolactin level (169.96ng/ml). After discontinuing amisulpride for 22 days, the patient's prolactin level returned back to normal (3.44ng/ml).

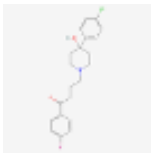
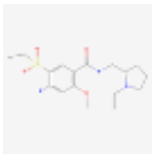
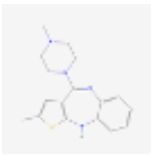
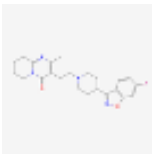
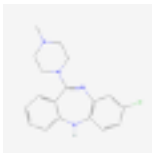
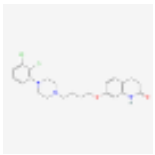
**Discussion and Implication**

Non-puerperal mastitis can be difficult to manage. The relapse rate of mastitis was 11% to 38.3% in Europe as well as America [9]. Diagnosis challenges attributed from the complex aetiology of mastitis which resulted in the difficulties to treatment and cure. Medications related adverse effect were rarely discussed as a causation of mastitis. According to our case experience, it is worth to shed light on medication related mastitis. The potential side effects from FGA and some SGA including galactorrhoea, sexual dysfunction, menstrual irregularities, decrease in bone density, pituitary tumor, breast and prostate cancer had been discussed in the published literatures [10,11]. In addition, infectious mastitis in our case. This can be pharmacologically explained by the blockage of dopaminergic receptor that might cause the rise in prolactin levels. There are five different dopaminergic receptor subtypes: $D_1$, $D_2$, $D_3$, $D_4$ and $D_5$. Antipsychotic exerts its effects mainly by $D_2$ receptor blockade, which is recognized as a main stay of schizophrenia therapy [12]. The ventral striatal region, situated in the subcortical brain, contains crucial $D_1$ and $D_2$ receptors that are associated with psychosis. These receptors play a significant role in regulate the value of stimuli, indicating the presence or anticipation of rewards, and encoding errors and outcomes resulting from predictive processes. Psychotic symptoms occur when dysregulated in dopamine releases and consequently resulted in chaos stimuli of striatum [15]. Antipsychotics can be categorized into three generations based on their actions on different receptors: FGA block the $D_2$ receptor, SGA block the $D_2$ and serotonin 5-$HT_{2A}$ receptors, and TGA exhibit partial agonist activity at the $D_2$ and serotonin 5-$HT_{1A}$ receptor. In addition, the clinical doses of antipsychotics are correlated with their affinities to the $D_2$ receptor. Antipsychotics with stronger affinities to the $D_2$ receptor have smaller inhibitory constants (Ki). This can be explained by the fact that a smaller Ki indicates that the drug can occupy 50% of the $D_2$ receptors even at lower concentrations of the antipsychotic [13,14]. The affinity of antipsychotics to $D_2$ in pituitary is possibly associated with the rise in serum prolactin levels as well [16,17]. The incidence rate varies among different antipsychotics. It is known that the FGA have a higher affinity to the dopaminergic $D_2$ subtype receptor compared with second- and third-generation antipsychotics. Therefore, hyperprolactinemia is more common among FGA. Evidence has shown that the use of SGA such as quetiapine and clozapine does not result in significant or sustained increases in prolactin levels. However, some SGAs have been reported with elevated prolactin levels include amisulpride, olanzapine and risperidone [10,18-21]. Findings from Lee et al. (2012) also suggested that even low dose of amisulpride (50mg per day) could cause hyperprolactinemia [19]. This strengthens the notion that hyperprolactinemia is associated with the degree of $D_2$ receptor blockade rather than being indicative of different antipsychotic generations.

Aripiprazole characterized as a TGA or DSS. The mechanism of its efficacy on schizophrenia is thought to be a combination of partial agonist of dopamine $D_2$ and serotonin $5HT_{1a}$ receptors and antagonist of serotonin $5HT_{2a}$ receptors [22]. Aripiprazole has very low Ki (0.95) to $D_2$ receptor, providing it a strong receptor binding characteristic. Aripiprazole bindings to the receptor easily and releasee quickly, providing it a functional agonist or antagonist to $D_2$ receptor depending on the surrounding levels of dopamine [23]. Therefore, both an increase and a decrease in serum prolactin levels had been observed in aripiprazole's clinical trials when comparing to baseline levels. Therefore, aripiprazole has been used as an add-on therapy to reverse elevated prolactin level caused by

FGA and SGA [7,8,23-25]. The hyperprolactinemia was failed to manage by add-on aripiprazole in our case. The difference in pharmacological profile of amisulpride and aripiprazole could provide a possible explanation. Amisulpride, a relatively hydrophilic drug, is less likely to cross the blood brain barrier [17]. The LogP is the log of the partition coefficient of a solute between octanol and water, and it provides a quantitative index for determining the hydrophilic or lipophilic properties of drugs. The higher the LogP, the more lipophilic the drug [26]. Amisulpride has a LogP value of 1.06 [27] The ideal lipophilic character for optimal brain concentrations is associated with a LogP value over 2.16. The lower the logP, the greater the need for higher therapeutic dose to achieve central nerve concentration [28] The correlation coefficient between LogP and blood-brain barrier (BBB) penetration is estimated at 0.557, which can be considered moderately correlated [29]. Therefore, the occupancy of amisulpride within the pituitary, which is outside the BBB is higher compared to that of a less hydrophilic drug, such as aripiprazole (logP 5.21). (Table 1.) The less affinity of aripiprazole to receptors in the pituitary provides explanations for management failure of hyperprolactinemia due to amisulpride. Aripiprazole occupied more $D_2$ receptors in brain. Raveendranathan et al. (2018) reported a significant reduction in prolactin levels, with an average reduction of 51.5 ng/ml, after adding aripiprazole 5-10mg per day to risperidone, amisulpride, or olanzapine. However, the final prolactin levels remained higher than the normal reference range. This might be attributed to the nature of the study's calculation approach. The study did not separately calculate the difference in prolactin reduction among the three antipsychotics. The variations in BBB penetration ability among risperidone, amisulpride and olanzapine leading to different ability of aripiprazole reverse effect in the study [30] As per recommendations by

**Table 1 Comparison of Antipsychotic**

| Features \ Drug | Haloperidol | Amisulpiride | Olanzepine | Risperidone | Clozapine | Aripiprazole |
|---|---|---|---|---|---|---|
| **Chemical Structure** |  |  |  |  |  |  |
| **Generation** | First | Second | Second | Second | Second | Third |
| **Dose-response for Positive or Negative Symptoms** | Similar | Higher dose for positive | Higher dose for negative | Similar | Similar | Similar |
| **Chemical Properties** | | | | | | |
| Lipophilicity (logP) | 4.3 | 1.06 | 4.094 | 3.27 | 3.23 | 5.21 |
| **Receptor Affinity** | | | | | | |
| $D_2$R Ki | 2.00 | 1.30 | 72.00 | 4.90 | 431.00 | 0.95 |
| 5-$HT_{2A}$R Ki | 118.600 | ND | 4.900 | 0.481 | 9.150 | 17.500 |
| **Clinical Effective Dose (mg)** | 2-15 | Schizophrenia: 400-800 Postoperative nausea and vomiting: 5-10 | 10-20 | 2-8 | 12.5-900 | 5-30 |
| **Effect on Prolactin in Literatures** | Increased | Increased | Increased/ Decreased | Increased | Increased/ Decreased | Increased/ Decreased |

LogP: Octanol-Water Partition Coefficient, high positive LogP value means a drug with low aqueous solubility and high lipophilicity; ND: no data. D2R: dopamine 2 receptor; 5-HT2A R: 5HT Serotonin $_{2A}$ Receptor; Ki value: dissociation constant of binding affinity between the inhibitor and the receptor, with lower values indicating stronger affinity. Data taken from [20,21,27,29,34-41]

the American Psychiatric Association guidelines, screening for prolactin level should be conducted in the presence of symptoms related to hyperprolactinemia [31]. It is also worthy to noted that in many literatures, most of the clinical cases of hyperprolactinemia were asymptomatic leading to the difficulty of early detection [10,11,17-20].

According to the findings in our case and previous literatures, it is justifiable to emphasize precaution on the use of amisulpride. Firstly, there is a safety concern in the use of amisulpride in women with menopause and men. Abnormal prolactin level may present with irregular or abrupt absent of menstrual period. In our case, the hyperprolactinemia was not promptly identified due to the patient's failure to report her breast inflammation, which was likely influenced by her mental health condition and concurrent menopause. Additionally, men have no menopause to act as an early identify signal. Moreover, no regular checks for the prolactin level were conducted and the absence of signs of irregular menstrual period all contributed to the late discovery of prolactin abnormality which then leaded to her mastitis. Secondly, literatures had documented several serious consequences associated with hyperprolactinemia, including irreversible adverse events such as an increased risk of precancerous cells or potential progression to breast cancer [10,11,32]. Thirdly, although there are several strategies reported in managing hyperprolactinemia, such as decreasing the dose of antipsychotics, adding a dopamine agonist agent (i.e bromocriptine) or changing to other antipsychotics [33]. However, these methods could put the patient at risk of disease instability. An add-on of partial dopaminergic agent of aripiprazole was regarded as a relative safe approach compared to other strategies. However, the management of amisulpride related hyperprolactinemia with add-on aripiprazole had failed in our case. As a result, the discontinuation of amisulpride and restarting a new antipsychotic were inevitable in this patient.

We demonstrated an infectious mastitis case manage under infectious disease physician. The pharmacist played a vital role in facilitating communication between different experts, assisting in identifying the underlying cause of the patient's mastitis, and providing a discussion and recommendations to the psychiatrist regarding the pharmacology of aripiprazole and amisulpride. The aim was to understand the failure of the add-on therapy. Ultimately, the psychiatrist decided to switch the medication directly. The different areas of expertise contributed to the early identification and timely management of complicated cases.

**Conclusions**

It is important to note that amisulpride might predispose individuals to acute mastitis due to its side effect of hyperprolactinemia. Additionally, patients who combine aripiprazole with amisulpride might still experience persistent elevated prolactin levels, which could contribute to the inevitable discontinuation of amisulpride, thereby increasing the patient's risk of disease instability. Despite the pharmacological theory discussed, the failure to reduce prolactin level by an add-on aripiprazole treatment in our case still need more studies. There is still a knowledge gap regarding the timing of add-on aripiprazole and its failure to control prolactin. Furthermore, inventions are needed to optimize the chemical structure (more lipophilic) of amisulpride in order to minimize the effect on prolactin.

To summarized, we advocate the periodic screening of prolactin level in patient using amisulpride regardless of dose and hyperprolactinemia symptoms. Additionally, multidisciplinary team, including different medical expertise and clinical pharmacists, in managing unusual infection is worth to be addressed. The lessons learned from this case emphasize the importance of early identification of rising prolactin levels in order to prevent further risks of mastitis and other complications associated with hyperprolactinemia.

**Acknowledgments**

I would like to express my gratitude to Cheng, Wei-Yuan, who provided me technical help. I would

also like to extend my appreciation to Yeo Han Ting Jillian, who gave me writing and editing assistance. This study would not have been possible without the support of the Taichung Hospital whom had provided the timely and relevant resources for the completion of my study.

## References

1. Jablensky A: Epidemiology of schizophrenia: the global burden of disease and disability. Eur Arch Psychiatry Clin Neurosci 2000; 250(6): 274-285.
2. Rabinowitz J, Werbeloff N, Caers I, et al.: Negative symptoms in schizophrenia-the remarkable impact of inclusion definitions in clinical trials and their consequences. Schizophrenia Research. 2013; 150(2-3): 334-338.
3. Leucht S, Corves C, Arbter D, et al.: Davis JM. Second-generation versus first-generation antipsychotic drugs for schizophrenia: a meta-analysis. Lancet 2009; 373(9657): 31-41.
4. Galderisi S, Mucci A, Dollfus S, et al.: EPA guidance on assessment of negative symptoms in schizophrenia. European Psychiatry 2021; 64(1): e23.
5. Krause M, Zhu Y, Huhn M, et al.: Antipsychotic drugs for patients with schizophrenia and predominant or prominent negative symptoms: a systematic review and meta-analysis. European Archives of Psychiatry and Clinical Neuroscience 2018; 268(7): 625-639.
6. Torre DL, Falorni A: Pharmacological causes of hyperprolactinemia. Ther Clin Risk Manag 2007; 3(5): 929-951.
7. Niari Khams P, Ranjbar F, Arfaie A, et al.: Adjunctive treatment with aripiprazole for risperidone-induced hyperprolactinemia. Neuropsychiatric Disease and Treatment 2015: 549-555.
8. Zhi P, Wang Y, Quan W, et al.: Aripiprazole combination for reversal of paliperidone-induced increase in prolactin level. Neuropsychiatr Dis Treat 2018; 14: 2175-2179.
9. Taffurelli M, Pellegrini A, Santini D, et al.: Recurrent periductal mastitis: surgical treatment. Surgery 2016; 160(6): 1689-1692.
10. Byerly M, Suppes T, Tran Q, et al.: Clinical implications of antipsychotic-induced hyperprolactinemia in patients with schizophrenia spectrum or bipolar spectrum disorders. Journal of Clinical Psychopharmacology 2007; 27(6): 639-661.
11. Kaneda Y: The impact of prolactin elevation with antipsychotic medications on subjective quality of life in patients with schizophrenia. Clinical Neuropharmacology 2003; 26(4): 182-184.
12. Martel JC, Gatti McArthur S: Dopamine receptor subtypes, physiology and pharmacology: new ligands and concepts in schizophrenia. Front Pharmacol 2020; 11: 1003.
13. Helion C, Krueger SM, Ochsner KN: Chapter 14- emotion regulation across the life span. Mark D'Esposito, Jordan H. Grafman. Handbook of Clinical Neurology. Amsterdam, Netherlands: Elsevier. 2019: 257-280.
14. Richtand NM, Welge JA, Logue AD, et al.: Dopamine and serotonin receptor binding and antipsychotic efficacy. Neuropsychopharmacology 2007; 32(8): 1715-1726.
15. Preskorn SH: Clinical relevance of relative receptor binding affinity: quetiapine and ziprasidone as examples. J Psychiatr Pract 2007; 13(6): 393-398.
16. Fitzgerald P, Dinan T: Prolactin and dopamine: what is the connection? A Review Article. Journal of Psychopharmacology 2008; 22(Suppl. 2): 12-19.
17. Kutsuna S, Mezaki K, Nagamatsu M, et al.: Two cases of granulomatous mastitis caused by corynebacterium kroppenstedtii infection in nulliparous young women with hyperprolactinemia. Internal Medicine 2015; 54(14): 1815-1818.
18. Paulzen M, Gründer G: Amisulpride-induced hyperprolactinaemia is not reversed by addition of aripiprazole. The International Journal of Neuro-psychopharmacology 2006; 10(1):149-151.
19. Lee B, Kang S, Kim T, et al.: Hyperprolactinemia induced by low-dosage amisulpride in Korean psychiatric patients. Psychiatry and Clinical Neurosciences 2012; 66(1): 69-73.
20. Dehelean L, Romosan AM, Papava I, et al.: Prolactin response to antipsychotics: an inpatient study. PLoS One 2020; 15(2): e0228648.
21. Alexander T, Julia E, Maria A, et al.: Is second-generation antipsychotic-induced hyperprolactinemia due to biologically active prolactin or to biologically inactive macroprolactin? Results from a prospective study. J Clin Psychiatry 2009; 70(2): 293-294. Retrieved from https://bit.ly/3PU9zzB

22. Stahl S: Dopamine system stabilizers, aripiprazole, and the next generation of antipsychotics, part 1: "Goldilocks" actions at dopamine receptors. The Journal of Clinical Psychiatry 2001; 62(11): 841-842.
23. Tuplin EW, Holahan MR: Aripiprazole, a drug that displays partial agonism and functional selectivity. Curr Neuropharmacol 2017; 15(8): 1192-1207.
24. Byerly M, Marcus R, Tran Q, et al.: Effects of aripiprazole on prolactin levels in subjects with schizophrenia during cross-titration with risperidone or olanzapine: analysis of a randomized, open-label study. Schizophrenia Research 2009; 107(2-3): 218-222.
25. Joseph SP: Aripiprazole-induced hyperprolactinemia in a young female with delusional disorder. Indian Journal of Psychological Medicine 2016; 38(3): 260-262.
26. Sona L, Sharat S, Sourav D. et al.: Chapter 6 - coumarin derivatives: biomedicinal properties and interactions with carrier proteins. Studies in Natural Products Chemistry, Elsevier 2022; 73: 173-220.
27. National Center for Biotechnology Information. PubChem Compound Summary for CID 2159, Amisulpride. 2023. Retrirved from https://bit.ly/45nrNPz
28. Timmermans PB, Brands A, van Zwieten PA: Lipophilicity and brain disposition of clonidine and structurally related imidazolidines. Naunyn Schmiedebergs Arch Pharmacol 1977; 300(3): 217-226.
29. Idowu S, Adeyemo M. Balogun F: Lipophilicity descriptors correlate uniquely with pharmacokinetic and blood-brain barrier penetration parameters for selected antipsychotic drugs. African Journal of Biomedical Research 2021; 24(2): 173-179.
30. Raveendranathan D, Rao NP, Rao MG, et al.: Add-on aripiprazole for atypical antipsychotic-induced, clinically significant hyperprolactinemia. Indian J Psychol Med 2018; 40(1): 38-40.
31. Lehman A: Practice guideline for the treatment of patients with schizophrenia. Washington, DC: American Psychiatric Association, 2004.
32. Halbreich U, Kinon BJ, Gilmore JA, et al.: Elevated prolactin levels in patients with schizophrenia: mechanisms and related adverse effects. Psychoneuroendocrinology 2003; 28 (Supp I): 53-67.
33. Bliesener N, Yokusoglu H, Quednow B, et al.: Usefulness of bromocriptine in the treatment of amisulpride-induced hyperprolactinemia. Pharmacopsychiatry 2004; 37(4): 189-191.
34. Sabe M, Zhao N, Crippa A, et al.: Antipsychotics for negative and positive symptoms of schizophrenia: dose-response meta-analysis of randomized controlled acute phase trials. NPJ Schizophr 2021; 7(1): 43.
35. Sokoloff P, Andrieux M, Besançon R, et al.: Pharmacology of human dopamine D3 receptor expressed in a mammalian cell line: comparison with D2 receptor. Eur J Pharmacol 1992; 225(4): 331-337.
36. National Center for Biotechnology Information: PubChem compound summary for CID 3559, Haloperidol. 2023. Retrieved from https://bit.ly/3ZQBDIE
37. National Center for Biotechnology Information: PubChem Compound Summary for CID 135398745, Olanzapine. 2023. Retrieved from https://bit.ly/48Nye1i
38. National Center for Biotechnology Information: PubChem Compound Summary for CID 5073, Risperidone. 2023. Retrieved from https://bit.ly/3rD4qE5
39. National Center for Biotechnology Information: PubChem Compound Summary for CID 60795, Aripiprazole. 2023. Retrieved from https://bit.ly/3ZNdgM1
40. Lawler CP, Prioleau C, Lewis MM, et al.: Interactions of the novel antipsychotic aripiprazole (OPC-14597) with dopamine and serotonin receptor subtypes. Neuropsychopharmacology 1999; 20(6): 612-627.
41. Besnard J, Ruda GF, Setola V, et al.: Automated design of ligands to polypharmacological profiles. Nature 2012; 492(7428): 215-220.

# Amisulpride引起之高泌乳激素血症處置之藥理學觀點與挑戰：Aripiprazole附加療法失效且合併感染風險之個案報告與啓示

盧雅紋[1]、尤暄婷[1]、陳宗家[2]、Han-Ting Yeo Jillian[3]
衛生福利部臺中醫院 藥劑科[1]、感染科[2]、新加坡國立大學楊潞齡醫學院醫學教育中心[3]

## 摘要

### 目的

高泌乳激素血症是抗精神病藥物的不良反應之一，原理是阻斷腦下垂體體後葉的多巴胺$D_2$受體。根據先前研究，添加Aripiprazole可有效降低非典型抗精神病藥物引起的高泌乳素血症，因爲Aripiprazole是$D_2$受體部分致效劑。然而，我們報告了一例使用Aripiprazole卻無法降低Amisulpride引起之高泌乳激素血症的個案。

### 方法

作者將描述一例因抗精神病藥物引起的高泌乳激素血症而導致乳腺炎的案例，並說明添加 Aripiprazole 應用在調節高泌乳激素方面的原理。此外，我們還會從藥理學理論的角度討論添加 Aripiprazole 但未能降低本案泌乳激素的失敗原因。

### 結果

由於藥物親脂性之不同，造成Amisulpride和Aripiprazole對腦下垂體$D_2$受體的親和力不同，兩藥的藥理學上的差異解釋了Aripiprazole無法調節Amisulpride引起之高泌乳激素血症的原因。

### 結論

此個案向醫療專業人員提供了一個重要的暗示，即抗精神病藥物的高泌乳激素副作用可能導致乳腺感染風險。在使用 Amisulpride 時，需要定期檢查泌乳激素血中濃度，特別是在停經後的婦女與男性。也因此，遇到不尋常的感染時，跨團隊的共同照護需特別提倡，及早的識別並處理 Amisulpride 引起的升高泌乳素血症對於預防進一步副作用非常重要。（澄清醫護管理雜誌 2024；20（1）：30-38）

關鍵詞：Amisulpride、Aripiprazole、乳腺炎、高泌乳激素血症、抗精神病藥物

受理日期：2023 年 1 月；接受刊載：2023 年 7 月