

阿立哌唑治疗帕利哌酮引起高泌乳素血症机制及研究进展

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摘要

精神分裂症是一种致残率较高的慢性疾病。帕利哌酮是常用的抗精神病药物, 高泌乳素血症是使用帕利哌酮时常见的副作用。在这种情况下, 联合使用阿立哌唑可以有效降低泌乳素水平。因此, 了解高泌乳素血症的产生机制、帕利哌酮导致高泌乳素血症的机制以及阿立哌唑降低泌乳素水平的作用机制, 对于改善患者的生存质量尤为重要。本文综述了阿立哌唑治疗帕利哌酮引起的高泌乳素血症的机制, 旨在探索有效的精神专科治疗方案。

关键词

精神分裂症, 高泌乳素血症, 帕利哌酮, 阿立哌唑

The Mechanism and Research Progress of Aripiprazole in the Treatment of Hyperprolactinemia Caused by Paliperidone

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Abstract

Schizophrenia is a chronic disease with a high morbidity rate. Paliperidone is a commonly used antipsychotic drug; however, hyperprolactinemia is a common side effect of paliperidone. In this setting, coadministration with aripiprazole may be effective in reducing prolactin levels. Therefore, understanding the mechanism of hyperprolactinemia, the mechanism of paliperidone causing hyperprolactinemia, and the mechanism of aripiprazole reducing prolactin levels is particularly important to improve the quality of life of patients. This article reviews the mechanism of aripiprazole in the treatment of paliperidone-induced hyperprolactinemia, aiming to explore effective psychiatric treatment options.

Keywords

Schizophrenia, Hyperprolactinemia, Paliperidone, Aripiprazole

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1. 背景

精神分裂症是致残率高的慢性疾病，表现为阳性症状、阴性症状和认知障碍，明显增加患者、家庭及社会负担[1]。帕利哌酮是常用治疗精神分裂症的抗精神病药之一，患者精神病性症状改善的同时，也会出现药物副反应，如体重增加、异常运动、代谢异常等[2]。其中高泌乳素血症是是使用帕利哌酮产生的常见副反应之一，可能导致月经紊乱、乳房发育、泌乳、性功能异常等[3]，影响患者正常的日常生活及社会功能。有文献报道[4]，阿立哌唑可以有效降低抗精神病药物引起的高泌乳素血症。2021年中国神经科学学会精神病学基础与临床分会精神分裂症临床研究联盟发布了关于抗精神病药物引起的高泌乳素血症管理的共识[5]，共识中指出，联合使用阿立哌唑，能够有效地降低抗精神病药导致的泌乳素水平。但目前阿立哌唑尚未批准纳入治疗帕利哌酮引起的高泌乳素血症，研究联用阿立哌唑治疗帕利哌酮引起的高泌乳素血症，对于改善患者的生存质量极为重要。

2. 高泌乳素血症

高泌乳素血症是一种复杂的内分泌科疾病，通常在血液检测时发现泌乳素超过正常范围[6]，男性和绝经后女性通常高于 20 ng/mL，绝经前女性通常高于 25 ng/mL [7]。泌乳素主要由脑垂体前叶的泌乳细胞分泌，主要刺激怀孕期间和产后母乳的生成[8]。多巴胺是泌乳素分泌最重要的抑制因子。多巴胺主要由下丘脑的肾上腺下神经元合成并释放，神经元将多巴胺释放到垂体门静脉，直接作用于垂体前叶的泌乳细胞，与泌乳素细胞表面的 D₂ 型受体结合，导致细胞内 cAMP 水平的降低，进而抑制泌乳素的释放和基因表达[9]。不同浓度的多巴胺，对泌乳素的分泌有着不同的生理作用，高浓度的多巴胺会抑制泌乳素的分泌，低浓度的多巴胺会促进泌乳素的分泌[10]。正常生理状态下，泌乳素也对多巴胺的分泌，会形成一种负反馈调节，这种机制在生理状态下维持了泌乳素的平衡[11]。精神科治疗精神分裂症时，使用抗精神病药，尤其是利培酮、帕利哌酮等药物，会导致泌乳素水平的增高[12]。高泌乳素血症的出现，会出现很多副反应。女性高泌乳素血症[13]，可能会有下列表现：(1) 月经不规律，比如稀发月经、闭经、周期

延长等；(2) 乳房异常，比如乳房胀痛、泌乳等；(3) 卵巢功能的异常，比如排卵异常、不孕症等；(4) 性功能影响，比如性交疼痛、性欲下降等；(5) 其他，比如情绪变化、体重变化等。男性高泌乳素血症[14]，可能会有下列表现：(1) 性功能障碍，比如勃起功能障碍、性欲减退等；(2) 乳腺变化：比如乳腺增生、泌乳等；(3) 生育问题，比如精子生成和成熟受损、睾丸萎缩等；(4) 其他，比如情绪波动、体重变化、骨密度降低[15]等。

3. 帕利哌酮与高泌乳素血症

帕利哌酮是精神科常用的新型非典型抗精神病药，属于苯异噁唑类化合物，是利培酮的活性代谢产物，充分发挥利培酮的高疗效，主要治疗精神分裂症和其他伴有精神病性症状的精神疾病[16][17]。帕利哌酮拮抗中脑、纹状体和前额叶的多巴胺 D₂ 受体，降低多巴胺的活性，改善患者的阳性症状，如幻觉、妄想等症状；拮抗大脑皮层、海马和基底节的 5-HT_{2A} 受体，改善患者的阴性症状，如情感平淡、社交退化等症状。帕利哌酮不仅可以用于精神疾病患者急性期的治疗，迅速发挥作用，改善患者的阳性和阴性症状，还能够在后续维持治疗中，防止症状的复发，保持患者病情稳定。但是帕利哌酮在发挥治疗作用的同时，也会因为多巴胺的拮抗机制和其他受体出现药物副反应，如内分泌的影响、锥体外系综合征、代谢综合征等。而帕利哌酮对泌乳素的影响，主要是作用于下丘脑的结节漏斗通路，拮抗多巴胺 D₂ 受体，从而导致泌乳素增加，而且帕利哌酮穿过血脑屏障的能力弱，在屏障外保持的时间长，因为它的低脂溶性，所以在结节漏斗途径中作用更长时间，泌乳素水平升高更明显[18]，且泌乳素水平越高，副反应临床表现越明显[19]。国外有文献报道，使用帕利哌酮后，泌乳素的升高水平与使用帕利哌酮有明显剂量依赖性，高剂量的帕利哌酮导致更显著的泌乳素水平的升高，并且与血浆中药物浓度正相关[20]，泌乳素水平会相比基线升高 2~10 倍[21]，且女性比男性更容易升高[19]。国内有文献报道[22]，帕利哌酮片剂与注射剂型对于泌乳素水平的影响无显著差异，升高泌乳素水平有相同作用。

4. 阿立哌唑与高泌乳素血症

阿立哌唑是精神科常用的新型非典型抗精神病药，属于喹啉酮衍生物，通常被用来治疗精神分裂症、情感性精神障碍等。阿立哌唑是一种多巴胺系统稳定剂，它能够调节多巴胺 D₂ 水平，而不是简单地阻断多巴胺 D₂ 受体。阿立哌唑在多巴胺 D₂ 受体上表现为部分激动剂的特性，可以增强多巴胺的活动，而在多巴胺活性过高的情况下，它又可以起到抑制作用[23]，对于精神分裂症的阳性症状和阴性症状均有改善；阿立哌唑还是 5-HT_{1A} 受体的部分激动剂和 5-HT_{2A} 受体的拮抗剂，有助于改善精神分裂症的阴性症状和情感性精神障碍的焦虑抑郁情绪[24]。阿立哌唑独特的机制，副反应发生相对较少，但部分患者使用后仍会出现锥体外系综合征、静坐不能等副反应[25][26]，上述反应可能与阿立哌唑单药治疗的精神分裂症患者时，离子转运蛋白和离子通道有关[27]。而阿立哌唑几乎不升高泌乳素，甚至会部分抑制泌乳素的分泌，可能跟多巴胺 D₂ 受体部分激动剂特性有关，它在一定程度上激活 D₂ 受体，从而部分抑制泌乳素的分泌[28]。有研究[29][30]显示，血浆中的阿立哌唑及其代谢物脱氢阿立哌唑血药浓度与泌乳素水平呈负相关。但是也有部分个案报道，阿立哌唑会升高泌乳素水平，可能跟缺乏竞争性 D₂ 拮抗剂和存在多巴胺(天然激动剂)的情况下，阿立哌唑可作为功能性拮抗剂，从而升高泌乳素水平[31]。在一项随机双盲的临床试验[32]中显示：阿立哌唑与显著的血清泌乳素水平下降相关。

5. 国内外关于阿立哌唑治疗帕利哌酮引起的高泌乳素血症的研究

阿立哌唑治疗帕利哌酮引起的高泌乳素血症的作用机制，帕利哌酮是多巴胺 D₂ 受体拮抗剂，作用于结节漏斗通路时，拮抗多巴胺 D₂ 受体，多巴胺的活性被降低，而阿立哌唑是一种多巴胺受体部分激动剂，

在一定程度上平衡帕利哌酮在结节漏斗通路的对多巴胺 D₂ 受体的影响,从机制上可以诠释阿立哌唑如何治疗帕利哌酮引起的高泌乳素血症。在精神科选择使用阿立哌唑治疗帕利哌酮引起的高泌乳素血症,优于使用多巴胺激动剂(如溴隐亭),原因可能是多巴胺受体激动剂和抗精神病药的作用机制上在一定程度上是矛盾的,可能加重精神症状[33],而阿立哌唑具有双重作用,既是抗精神病药物又是多巴胺 D₂ 受体部分激动剂,且有荟萃分析[34]进一步证明,阿立哌唑是首选。国内有大量研究[35]-[38]显示阿立哌唑可以降低帕利哌酮引起的高泌乳素血症,国外也有大量研究[39]-[42]显示阿立哌唑联合帕利哌酮可以降低泌乳素水平。相关荟萃分析[34][43]显示,阿立哌唑有效降低帕利哌酮引起的泌乳素水平,而且在临床应用中,整体安全性较高,副反应较小。降低抗精神病药物引起的泌乳素水平,低剂量阿立哌唑是优于高剂量,这可能与低剂量阿立哌唑已经占据纹状体中的大多数 D₂ 受体有关[44]。相关荟萃分析[45]显示:阿立哌唑治疗后催乳素水平正常化率为 79.11%,并探讨出最佳治疗剂量为 5 mg,该结果与另一项荟萃分析[43]结果一致,高剂量阿立哌唑(>5 mg/d)比低剂量(<5 mg/d)对于泌乳素的恢复,差异无统计学意义。在一项阿立哌唑辅助治疗高泌乳素血症患者的随机双盲试验[46]中,对 2 周、4 周、8 周的患者进行随访,研究显示,所有剂量的阿立哌唑在治疗结束时均导致泌乳素水平显著降低,且这种降低在第 2 周就已开始显现,因此小剂量阿立哌唑的辅助治疗,对于因使用帕利哌酮而出现高泌乳素血症的患者来说尤为重要,在早期就能避免高泌乳素血症的发生,改善患者的生存质量。

6. 总结与展望

阿立哌唑在治疗帕利哌酮引起的高泌乳素血症方面显示了良好的疗效和安全性,通过个体化治疗策略的不断探索和实践,可以更好地满足患者的需求,提高治疗的有效性。随着研究的深入,未来有望为高泌乳素血症患者提供更为精确和个性化的治疗方案。但目前阿立哌唑尚未获批进行临床治疗帕利哌酮引起的高泌乳素血症,我们还需要做出更多的探索:(1) 大规模临床试验:需要更多的随机对照试验来验证阿立哌唑的长期疗效与安全性,长期联合使用阿立哌唑患者能否进一步获益;(2) 基因组学研究:探索不同患者基因背景下,阿立哌唑对帕利哌酮引起的高泌乳素血症治疗反应的影响,实现个体化医疗;(3) 多中心合作研究:通过多中心的合作研究,积累更全面的数据支持,为临床实践提供更加可靠的依据。

参考文献

- [1] Dawn, I.V. and Subramanyeshwar, R. (2023) The Epidemiology and Global Burden of Schizophrenia. *The Journal of Clinical Psychiatry*, **84**, MS21078COM5.
- [2] Piparva, K.G., Buch, J.G. and Chandrani, K.V. (2011) Analysis of Adverse Drug Reactions of Atypical Antipsychotic Drugs in Psychiatry OPD. *Indian Journal of Psychological Medicine*, **33**, 153-157. <https://doi.org/10.4103/0253-7176.92067>
- [3] Halbreich, U. and Kahn, L.S. (2003) Hyperprolactinemia and Schizophrenia: Mechanisms and Clinical Aspects. *Journal of Psychiatric Practice*, **9**, 344-353. <https://doi.org/10.1097/00131746-200309000-00003>
- [4] Austen, Y. and Mujeeb, U.S. (2020) Aripiprazole for the Management of Antipsychotic-Induced Hyperprolactinemia A Retrospective Case Series. *The Primary Care Companion for CNS Disorders*, **22**, 19br02536.
- [5] 中国神经科学学会精神病学基础与临床分会精神分裂症临床研究联盟. 抗精神病药所致高泌乳素血症干预对策的专家共识[J]. 中华精神科杂志, 2021, 54(3): 163-169.
- [6] Nicholas, A.T. and Anne, K. (2015) Hyperprolactinemia. *JAMA*, **314**, 1742-1743.
- [7] Schlechte, J.A. (2003) Prolactinoma. *New England Journal of Medicine*, **349**, 2035-2041. <https://doi.org/10.1056/nejmcp025334>
- [8] Begon, E. and Bernard, V. (2022) Prolactin and Its Receptor: From Animal Models to Pituitary Pathophysiology. *Biology Aujourd'hui*, **216**, 105-110. <https://doi.org/10.1051/jbio/2022019>
- [9] Fitzgerald, P. and Dinan, T.G. (2008) Prolactin and Dopamine: What Is the Connection? A Review Article. *Journal of Psychopharmacology*, **22**, 12-19. <https://doi.org/10.1177/0269216307087148>

- [10] Kirsch, P., Kunadia, J., Shah, S. and Agrawal, N. (2022) Metabolic Effects of Prolactin and the Role of Dopamine Agonists: A Review. *Frontiers in Endocrinology*, **13**, Article 1002320. <https://doi.org/10.3389/fendo.2022.1002320>
- [11] Lv, C., Mo, C., Liu, H., Wu, C., Li, Z., Li, J., et al. (2018) Dopamine D2-Like Receptors (DRD2 and DRD4) in Chickens: Tissue Distribution, Functional Analysis, and Their Involvement in Dopamine Inhibition of Pituitary Prolactin Expression. *Gene*, **651**, 33-43. <https://doi.org/10.1016/j.gene.2018.01.087>
- [12] Ángel, L.M., Buch, B., López, M.J., et al. (2022) Hormonal Alterations Due to Antipsychotic-Related Hyperprolactinemia. *European Psychiatry*, **65**, S782.
- [13] Katharina, W. (2021) Hyperprolactinemia in Women. *Journal für Gynäkologische Endokrinologie/Österreich*, **31**, 102-105. <https://doi.org/10.1007/s41974-021-00195-7>
- [14] Maggi, M., Buvat, J., Corona, G., Guay, A. and Torres, L.O. (2013) Hormonal Causes of Male Sexual Dysfunctions and Their Management (Hyperprolactinemia, Thyroid Disorders, GH Disorders, and DHEA). *The Journal of Sexual Medicine*, **10**, 661-677. <https://doi.org/10.1111/j.1743-6109.2012.02735.x>
- [15] Yun, S.J., Sang, H., Park, S.Y. and Chin, S.O. (2024) Effect of Hyperprolactinemia on Bone Metabolism: Focusing on Osteopenia/Osteoporosis. *International Journal of Molecular Sciences*, **25**, Article 1474. <https://doi.org/10.3390/ijms25031474>
- [16] Katsuya, T., Katsumi, S. and Akio, S. (2019) Paliperidone/Risperidone. *Reactions Weekly*, **1466**, 34.
- [17] Minwalla, H.D., Wrzesinski, P., Desforges, A., Caskey, J., Wagner, B., Ingrassia, P., et al. (2021) Paliperidone to Treat Psychotic Disorders. *Neurology International*, **13**, 343-358. <https://doi.org/10.3390/neurolint13030035>
- [18] Montejo, Á.L., Arango, C., Bernardo, M., Carrasco, J.L., Crespo-Facorro, B., Cruz, J.J., et al. (2017) Multidisciplinary Consensus on the Therapeutic Recommendations for Iatrogenic Hyperprolactinemia Secondary to Antipsychotics. *Frontiers in Neuroendocrinology*, **45**, 25-34. <https://doi.org/10.1016/j.yfrne.2017.02.003>
- [19] Besnard, I., Auclair, V., Callery, G., Gabriel-Bordenave, C. and Roberge, C. (2014) Antipsychotic-Drug-Induced Hyperprolactinemia: Physiopathology, Clinical Features and Guidance. *L'Encéphale*, **40**, 86-94. <https://doi.org/10.1016/j.encep.2012.03.002>
- [20] Duval, F., Guillon, M., Mokrani, M., Crocq, M. and Garcia Duarte, F. (2008) Relationship between Prolactin Secretion, and Plasma Risperidone and 9-Hydroxyrisperidone Concentrations in Adolescents with Schizophreniform Disorder. *Psychoneuroendocrinology*, **33**, 255-259. <https://doi.org/10.1016/j.psyneuen.2007.10.010>
- [21] Einarson, T.R., Hemels, M.E., Nuamah, I., Gopal, S., Coppola, D. and Hough, D. (2012) An Analysis of Potentially Prolactin-Related Adverse Events and Abnormal Prolactin Values in Randomized Clinical Trials with Paliperidone Palmitate. *Annals of Pharmacotherapy*, **46**, 1322-1330. <https://doi.org/10.1345/aph.1r123>
- [22] 金圭星, 王岚, 于鲁璐, 等. 不同剂型帕利哌酮对精神分裂症患者泌乳素水平影响的研究[C]//中华医学会第十一次全国精神医学学术会议暨第三届亚洲神经精神药理学学术会议论文集. 2013: 149-150.
- [23] Kikuchi, T., Maeda, K., Suzuki, M., Hirose, T., Futamura, T. and McQuade, R.D. (2021) Discovery Research and Development History of the Dopamine D₂ Receptor Partial Agonists, Aripiprazole and Brexpiprazole. *Neuropsychopharmacology Reports*, **41**, 134-143. <https://doi.org/10.1002/npr2.12180>
- [24] Potkin, S.G., Saha, A.R., Kujawa, M.J., Carson, W.H., Ali, M., Stock, E., et al. (2003) Aripiprazole, an Antipsychotic with a Novel Mechanism of Action, and Risperidone vs Placebo in Patients with Schizophrenia and Schizoaffective Disorder. *Archives of General Psychiatry*, **60**, 681-690. <https://doi.org/10.1001/archpsyc.60.7.681>
- [25] Soria-Chacartegui, P., Villalpos-García, G., Zubiaur, P., Abad-Santos, F. and Koller, D. (2021) Genetic Polymorphisms Associated with the Pharmacokinetics, Pharmacodynamics and Adverse Effects of Olanzapine, Aripiprazole and Risperidone. *Frontiers in Pharmacology*, **12**, Article 711940. <https://doi.org/10.3389/fphar.2021.711940>
- [26] Bernagie, C., Danckaerts, M., Wampers, M. and De Hert, M. (2016) Aripiprazole and Acute Extrapyramidal Symptoms in Children and Adolescents: A Meta-Analysis. *CNS Drugs*, **30**, 807-818. <https://doi.org/10.1007/s40263-016-0367-y>
- [27] Wang, X., Mei, D., Lu, Z., Zhang, Y., Sun, Y., Lu, T., et al. (2023) Genome-wide Association Study Identified Six Loci Associated with Adverse Drug Reactions to Aripiprazole in Schizophrenia Patients. *Schizophrenia*, **9**, Article No. 44. <https://doi.org/10.1038/s41537-023-00369-6>
- [28] Shapiro, D.A., Renock, S., Arrington, E., Chiodo, L.A., Liu, L., Sibley, D.R., et al. (2003) Aripiprazole, a Novel Atypical Antipsychotic Drug with a Unique and Robust Pharmacology. *Neuropsychopharmacology*, **28**, 1400-1411. <https://doi.org/10.1038/sj.npp.1300203>
- [29] Ma, B., Zhao, W., Fan, H., Yun, Y., Qi, S., An, H., et al. (2023) Relationship between Plasma Aripiprazole and Dehydroaripiprazole Concentrations and Prolactin Levels in Chinese Children and Adolescents. *Journal of Child and Adolescent Psychopharmacology*, **33**, 27-33. <https://doi.org/10.1089/cap.2022.0068>
- [30] Tasaki, M., Yasui-Furukori, N., Kubo, K., Yokoyama, S., Shinozaki, M., Sugawara, N., et al. (2021) Relationship of Prolactin Concentrations to Steady-State Plasma Concentrations of Aripiprazole in Patients with Schizophrenia.

- Therapeutic Drug Monitoring*, **43**, 589-592. <https://doi.org/10.1097/ftd.0000000000000843>
- [31] Joseph, S.P. (2016) Aripiprazole-Induced Hyperprolactinemia in a Young Female with Delusional Disorder. *Indian Journal of Psychological Medicine*, **38**, 260-262. <https://doi.org/10.4103/0253-7176.183082>
- [32] Kelly, D.L., Wehring, H.J., Earl, A.K., Sullivan, K.M., Dickerson, F.B., Feldman, S., *et al.* (2013) Treating Symptomatic Hyperprolactinemia in Women with Schizophrenia: Presentation of the Ongoing DAAMSEL Clinical Trial (Dopamine Partial Agonist, Aripiprazole, for the Management of Symptomatic Elevated Prolactin). *BMC Psychiatry*, **13**, Article No. 214. <https://doi.org/10.1186/1471-244x-13-214>
- [33] Snellen, M., Power, J., Blankley, G. and Galbally, M. (2016) Pharmacological Lactation Suppression with D₂ Receptor Agonists and Risk of Postpartum Psychosis: A Systematic Review. *Australian and New Zealand Journal of Obstetrics and Gynaecology*, **56**, 336-340. <https://doi.org/10.1111/ajo.12479>
- [34] Labad, J., Montalvo, I., González-Rodríguez, A., García-Rizo, C., Crespo-Facorro, B., Monreal, J.A., *et al.* (2020) Data of a Meta-Analysis on Pharmacological Treatment Strategies for Lowering Prolactin in People with a Psychotic Disorder and Hyperprolactinaemia. *Data in Brief*, **31**, Article ID: 105904. <https://doi.org/10.1016/j.dib.2020.105904>
- [35] 黄锦, 朱丞. 帕利哌酮缓释片联合阿立哌唑对精神分裂症精神病性症状、认知功能和催乳素的影响[J]. 中华全科医学, 2022, 20(10): 1688-1690, 1791.
- [36] 王飞, 车清磊, 王蕊, 等. 阿立哌唑对部分抗精神病药物所致高泌乳素血症疗效对比[J]. 中外医疗, 2022, 41(16): 67-70.
- [37] 汪毅, 甘明远, 刘华清, 等. 帕利哌酮缓释片与阿立哌唑治疗青少年首发精神分裂症的疗效和催乳素变化[J]. 中国心理卫生杂志, 2019, 33(8): 592-597.
- [38] 朱峰, 梅其一, 沈建红, 等. 阿立哌唑对帕利哌酮引起的高泌乳素水平的影响[C]//中华医学会第十次全国精神医学学术会议论文集. 2012: 140-141.
- [39] Jiang, Q., Li, T., Zhao, L., Sun, Y., Mao, Z., Xing, Y., *et al.* (2024) Treatment of Antipsychotic-Induced Hyperprolactinemia: An Umbrella Review of Systematic Reviews and Meta-Analyses. *Frontiers in Psychiatry*, **15**, Article 1337274. <https://doi.org/10.3389/fpsy.2024.1337274>
- [40] Sá Esteves, P., Mota, D., Cerejeira, J., Mendes, F., *et al.* (2015) Low Doses of Adjunctive Aripiprazole as Treatment for Antipsychotic-Induced Hyperprolactinemia: A Literature Review. *European Psychiatry*, **30**, 393.
- [41] 陈景旭, 王宁, 卞清涛, 等. 阿立哌唑对利培酮所致高催乳素血症的疗效[J]. 临床精神医学杂志, 2009, 19(2): 127-129.
- [42] Qiao, Y., Yang, F.Z., Li, C.B., *et al.* (2016) Add-On Effects of a Low-Dose Aripiprazole in Resolving Hyperprolactinemia Induced by Risperidone or Paliperidone. *Psychiatry Research*, **237**, 83-89.
- [43] Meng, M.L., Li, W., Zhang, S.W., *et al.* (2015) Using Aripiprazole to Reduce Antipsychotic-Induced Hyperprolactinemia: Meta-Analysis of Currently Available Randomized Controlled Trials. *Shanghai Arch Psychiatry*, **27**, 4-17.
- [44] Krøigaard, S.M., Clemmensen, L., Tarp, S. and Pagsberg, A.K. (2022) A Meta-Analysis of Antipsychotic-Induced Hypo- and Hyperprolactinemia in Children and Adolescents. *Journal of Child and Adolescent Psychopharmacology*, **32**, 374-389. <https://doi.org/10.1089/cap.2021.0140>
- [45] Li, X., Tang, Y. and Wang, C. (2013) Adjunctive Aripiprazole versus Placebo for Antipsychotic-Induced Hyperprolactinemia: Meta-Analysis of Randomized Controlled Trials. *PLOS ONE*, **8**, e70179. <https://doi.org/10.1371/journal.pone.0070179>
- [46] Chen, J., Su, Y., Bian, Q., Wei, L., Zhang, R., Liu, Y., *et al.* (2015) Adjunctive Aripiprazole in the Treatment of Risperidone-Induced Hyperprolactinemia: A Randomized, Double-Blind, Placebo-Controlled, Dose-Response Study. *Psychoneuroendocrinology*, **58**, 130-140. <https://doi.org/10.1016/j.psyneuen.2015.04.011>