Use of Antipsychotics and Polycystic Ovarian Syndrome

A Review of Current Evidence

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BACKGROUND

Antipsychotics are a class of medications used to treat conditions such as psychosis, mood disorders, and agitation. The typical, or 1st generation, antipsychotics are defined by their antagonism of dopamine receptors, while atypical, or 2nd generation, antipsychotics exhibit both dopamine antagonism and serotonergic partial agonism. Atypical antipsychotics have long been associated with the side effects of weight gain, diabetes, and metabolic syndrome.

Polycystic Ovarian Syndrome (PCOS) is the most common endocrinological pathology affecting women of childbearing age worldwide (between 4 and 20% globally)[1]. The pathogenesis involves hypersecretion of androgens by the ovaries, leading to altered ovulation and masculinization. This dysregulation can be caused by insulin excess, as insulin alters LH receptors in ovarian Theca cells leading to an upregulation in steroidogenesis. Excess obesity further contributes due to the peripheral conversion of excess androgens into estrogens, worsening the ovulatory dysfunction in PCOS syndrome. While it has been well established that antipsychotics may cause metabolic syndrome, and that insulin excess and obesity may cause PCOS, the relationship between antipsychotics and PCOS remains unclear.

METHODS

- Literature search of Pubmed, Embase and Cochrane Library
- The search used MeSH keywords "PCOS", "polycystic ovary syndrome", "antipsychotic(s)", "dopamine antagonist(s)"
- Search was conducted through March 2024
- Relevant literature was reviewed in full text
- Studies were limited to human subjects

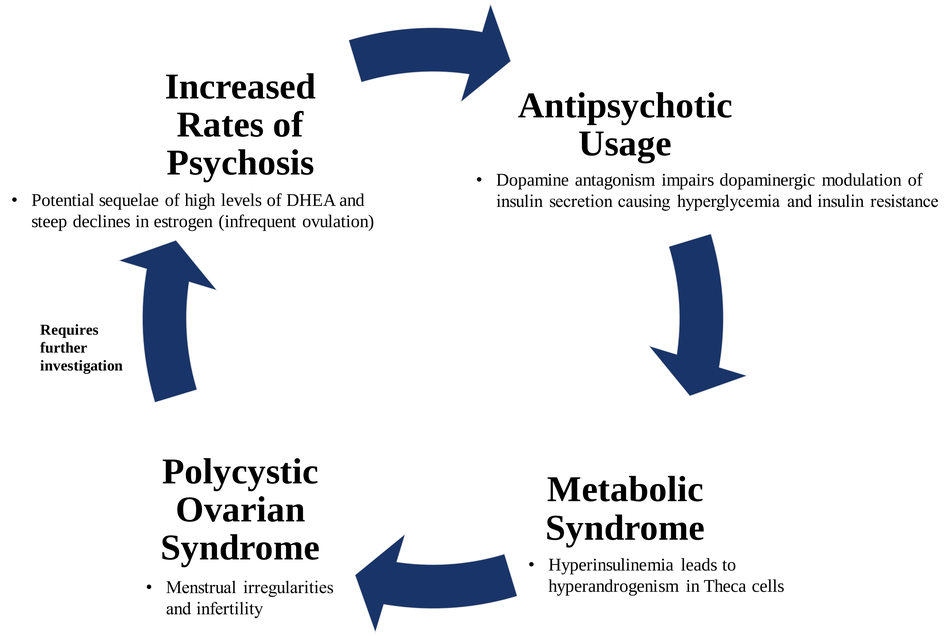

Figure 1: Diagram of the potential complex relationship between antipsychotic use and PCOS

RESULTS

Our literature search revealed limited evidence supporting a causal relationship, however many studies provide evidence for an overlap between antipsychotic use, psychosis and PCOS.

- Antipsychotics, particularly olanzapine and clozapine, exhibit metabolic effects seen in PCOS such as gut microbiota changes, hyperinsulinemia, elevated triglycerides and LDL.[2-3]
- Hyperprolactinemia is a common cause of menstrual irregularity and infertility in both psychosis patients using antipsychotics and PCOS patients.[2-3]
- A case control study of 225 patients in Sri Lanka found women on atypical antipsychotics were more likely to have PCOS than controls (21.6% vs 8.1%, p=0.04).[4]
- A retrospective cohort study in Taiwan found increased occurrence of PCOS in patients initiated on antipsychotics, particularly ziprasidone (105.2 per 1,000 person year) and haloperidol (51.7 per 1,000 person year).[5]
- One study found women with bipolar disorder controlled by atypical antipsychotics reported a greater rate of current or past menstrual abnormalities versus those on mood stabilizer therapy (80% versus 55%, p = 0.013).[6]
- Several studies have suggested that high levels of DHEA and the steep declines in estrogen during infrequent ovulation causes vulnerability to psychosis.[2,7]
- One study showed that women with PCOS had a three-fold increase in risk for psychosis by age 50, possibly indicating an increased need for antipsychotics in this population.[8]

CONCLUSIONS

There is limited evidence supporting a direct relationship between antipsychotic use and PCOS. The overlap of clinical presentation often makes it difficult to distinguish PCOS from adverse effects of antipsychotics.

Hyperandrogenism and rapid changes in estrogen levels seen in PCOS can increase risk for psychosis and subsequent antipsychotic need. Appropriate discussion with reproductive age women regarding potential reproductive impacts of antipsychotic use is crucial. Collaboration with obstetrics and gynecology providers should be considered with those at risk for PCOS.

Further study should prospectively monitor the development of PCOS in patients on antipsychotic therapy to investigate a causal relationship.

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