Review

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A Diagnosis with Little Awareness in Adolescence: Menstrual Psychosis

Ergenlik Döneminde Farkındalığı Az Olan Bir Tanı: Menstruel Psikoz

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ABSTRACT

Menstrual psychosis has been described as a brief psychotic episode acute in its onset, rapid in its resolution, and marked by variable temporal boundaries within the menstrual cycle. It is a rare disorder with a crudely estimated prevalence of 1 in 10,000. To confirm a case with menstrual psychosis clinically, detailed dates regarding the association of the menstrual cycle and psychosis are necessary. Menstrual psychosis occurs most commonly in phases of the menstrual cycle where estrogen levels are low. It is thought to be caused by increased dopamine sensitivity during the low estrogen phases of the menstrual cycle. The mainstay of pharmacological treatment in menstrual psychosis is neuroleptics, mood stabilizers, and hormonal therapy. Antipsychotics and antidepressants have been reported to be helpful during acute psychotic states in menstrual psychoses, but have not been documented as successful monotherapy in the prevention of further episodes in the treatment of menstrual psychoses. Severe affective instability with evident psychosis during the menstrual cycle should be evaluated for menstrual psychosis. Further research is needed to describe most aspects of the disorder, including prevalence, pathophysiology, genetic risk, and evidence-based therapies. Menstrual psychosis is a distinct category of mental illness that should be managed by a multidisciplinary team. Education on menstrual psychosis should also be increased as it is likely to be missed clinically. Increased identification is important as the treatment is effective, and safe.

Keywords: Adolescent, menstruation, psychosis

ÖZ

Menstrüel psikoz, akut başlayan, hızlı çözülen ve adet döngüsü içinde değişken zamansal sınırlarla karakterize kısa bir psikotik epizod olarak tanımlanmıştır. Kabaca tahmin edilen prevalansı 10.000'de 1 olan nadir bir hastalıktır. Menstrüel psikozlu bir vakayı klinik olarak doğrulamak için menstrüel siklus ve psikoz ilişkisine ilişkin ayrıntılı tarihler gereklidir. Menstrüel psikoz, en sık östrojen seviyelerinin düşük olduğu adet dönemlerinde ortaya çıkar. Adet döngüsünün düşük östrojen fazları sırasında artan dopamin duyarlılığından kaynaklandığına düşünülmektedir. Menstrüel psikozda farmakolojik tedavinin temeli nöroleptikler, duygudurum düzenleyiciler ve hormon tedavisidir. Antipsikotikler ve antidepresanların, menstrüel psikozdaki akut durumlarda yardımcı olduğu bildirilmiş, ancak bu ilaçların gelecek atakların önlenmesinde monoterapi olarak faydalı olduğu belgelenmemiştir. Menstrüel psikoz tanısı için şiddetli afektif dengesizlik belirgin psikozla birlikte adet döngüsü sırasında değerlendirilmelidir. Prevalans, patofizyoloji, genetik risk ve kanıta dayalı tedaviler dahil olmak üzere bozukluğun birçok yönünü tanımlamak için daha fazla araştırmaya ihtiyaç vardır. Menstrüel psikoz, multidisipliner bir ekip tarafından yönetilmesi gereken ayrı bir ruhsal hastalık kategorisidir. Klinik olarak gözden kaçırılması muhtemel olduğundan, menstrüel psikoz eğitimi de artırılmalıdır. Gelişen tanımlamalar tedavinin etkili ve güvenli olabilmesi için önemlidir.

Anahtar sözcükler: Adölesan, menstrüasyon, psikoz

Introduction

The first case in the literature was a 21-year-old female who developed demon obsession once every 3-4 weeks as reported by Desmilleville in 1759. In this case, the patient was described as experiencing severe anger attacks and intense suffocation in the premenstrual period before these symptoms. Ply also reported a case in 1791, which periodically loses her memory in each menstrual period. Menstrual mood disorder was first used as a defense in a filicide case in 1827. In the incident that developed in Germany, a mother who caused the death of her 1-year-old child by jumping into the water was mentioned. During her execution, the prisoner told her cellmate that she had menstruation when she jumped into the water, felt anxious, and did not enjoy life during her menstrual periods. Thereupon, the prisoner was transferred to the hospital and it was found that the patient displayed tachycardia, tachypnea, anxiety, and deep melancholy symptoms during several

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menstrual periods. Thus, the prisoner's acquittal was decided (Brockington 1998, 2011).

The first definitions of psychosis were used by Brière de Boismont in 1842 and 1851. In 1858 and 1862, Marcé observed the effect of menstruation on postpartum psychosis. In 1874; Berthier wrote a descriptive study presenting 242 cases classified according to symptoms, related to all menstrual disorders; including dysmenorrhea, menorrhagia, amenorrhea, and menopause. In 1890, Icard wrote his thesis that summarized 261 cases classified under symptoms (eg Kleptomania, pyromania, dipsomania, nymphomania, homicidal mania). Schlager reviewed the impact of menstrual bleeding on epilepsy, mental illness and mental hospitalization, suicide rates, and crime comprehensively (Brockington 1998).

In 1878, Krafft-Ebing made one of his two major contributions to the literature with his article describing 19 cases, and in 1902 he wrote the main text on menstrual psychosis (MP). He classified his cases according to their temporal associations under the titles of menstrual developmental psychosis, ovulation psychosis (single, recurrent and periodic), and periodic menstrual psychosis. Jolly revised Krafft-Ebing's classification in 1914 by focusing on the stage of reproductive life (cases beginning before menarche/beginning with menarche/beginning with menopause, recurrent psychosis associated with menstruation, and periodic cases). Despite the excellence of these studies and the reputation of Krafft-Ebing as a forensic psychiatrist and sexologist, the concept was not particularly accepted by Kraepelin followers, and psychiatrists lost interest in the subject. This notion reappeared depending on the Japanese clinical and endocrinological studies conducted between 1959-1984 (Brockington 1998).

'Menstrual psychosis, periodic psychosis, cycloid psychosis, catamenial psychosis, recurrent psychotic episodes, recurrent affective psychosis, brief psychosis' keywords were scanned using 'Google', 'Google Scholar', 'Pubmed' search engines, and 36 articles were included in our review article. MP is a clinical condition with relatively poor recognizability and lack of clear criteria in psychiatric diagnosis systems (DSM/ICD diagnostic systems). In this review, it is aimed to present information about the clinical symptoms, pathogenesis, differential diagnosis and treatment of MP in the light of the literature.

Definition and Epidemiology

MP diagnosis requires meeting the criteria specified below:

- Acute onset of symptoms despite the absence of any psychiatric illness in the past history
- Complete recovery after short-term symptoms
- Psychotic features: Confusion, delusions, hallucinations, stupor, mutism or manic episode
- A cyclic rhythm that repeats with menstruation (Brockington 2011).

For the diagnosis of MP, episodes of the disease need to be repeated. Women aged 13-50 live at least 1/3 of their lives in a premenstrual/menstrual period. In cases, it is necessary to determine the association between the onset of at least a few episodes and the menstrual period. Unfortunately, although there are more than 200 cases in the literature; many authors are not able to fully define this association. Therefore; these cases are only considered as 'probable' (Brockington 2011). Despite the limited literature, the prevalence rate was 1 in 1,000 applications in a study dated 1888; but it is estimated to be 1 in 10,000 in recent studies.

Although MP is classified by both the timing and stage of reproductive life, only timing-related classification is common in the literature. Definitions in this classification are as follows: premenstrual psychosis, symptoms that begin in the second half of the menstrual cycle; catamenial psychosis, symptoms that begin with the onset of menstruation; paramenstrual psychosis symptoms occurring at different times of the menstrual cycle. On the other hand, epochal menstrual psychosis is a picture that includes psychotic features which continue throughout the menstrual period and bipolar disorder features that vary in the range of depression/mania. (Heinzman and Buckingham 2019)

Pathogenesis

Menstrual psychosis(MP) appears to be associated with the pituitary-ovarian axis as well as with anovulatory cycles. To better understand this connection, it would be helpful to examine the menstrual cycle. The menstrual cycle begins as estrogen decreases and progesterone induces menstruation. Then, follicle-stimulating hormone (FSH) causes the granulosa cells in the ovary to secrete estrogen. Estrogen stimulates the proliferation of the endometrial part of the uterus. When estrogen peaks, it triggers the LH surge, causing ovulation. Subsequently, the corpus luteum (post-ovulation follicle) produces progesterone. If fertilization does not occur, both estrogen and progesterone levels drop and menstrual bleeding begins (Heinzman and Buckingham 2019).

There are many etiological theories about MP:

1. Psychodynamic theory: The difficulty experienced by a woman in accepting her sexual identity may cause castration anxiety, and this negative attitude may also mediate the breakdown of the ego structure (Thippaiah et al. 2018).
2. Genetic Theory: It has been reported that many MP cases have a history of MP in their first-degree relatives. (Thippaiah et al. 2018).
3. Hormonal Theory: There is not a single hormonal mechanism to explain MP, but it is thought to be caused by a disorder in the pituitary-ovarian axis. A non-specific relationship is mentioned with the overactivity of the Hypothalamic-Pituitary-Adrenal (HPA) axis and some hormones secreted from the pituitary. So, it is clear that

menstruation-related psychosis is linked to ovulation cycles. Findings such as decreased dexamethasone suppression, changes in cortisol cycle, and changes in thyroid-stimulating hormone (TSH) response have led to the questioning of the involvement of the hypothalamic-pituitary-adrenal axis. Interestingly, these abnormalities are detected only in the active phase of MP and attenuate between episodes (Thippaiah et al. 2018, Al-Sibani et al. 2020).

4. Estrogen Hypothesis: Estrogen is generally considered a neuroprotective steroid hormone (Al-Sibani et al. 2020). It has been suggested that following the continuous rise of estrogen which has a triggering effect on the brain of susceptible women, a sudden decrement of estrogen during menstruation in the central nervous system can trigger menstrual psychosis. In the luteal phase, some women are more biologically sensitive to hormonal fluctuations (Thippaiah et al. 2018).

MP is thought to develop due to the increased dopamine sensitivity seen at low estrogen levels in the menstrual cycle. Estrogen is a modulator of tyrosine hydroxylase, which limits the rate of noradrenaline and dopamine synthesis. It is hypothesized that increased dopamine levels in the brains of MP-sensitive women during certain parts of a menstrual cycle associated with low estrogen precipitate psychotic symptoms. A study conducted on monkeys has shown that dopamine receptors (D2) are 12% more sensitive at low estrogen levels in the luteal phase of the menstrual cycle. There is also a case report of a patient with a damaged pituitary gland who developed symptoms after discontinuing hormone replacement therapy, which is thought to support the hypothalamic origin. (Ahern 2019).

Estrogen does not only have specific effects on the gonadal axis but also affects brain functions through neurotrophic and neuroprotective effects mediated by direct and indirect genomic pathways. It is also shown that estrogen can affect cholinergic, noradrenergic, serotonergic, and dopaminergic neurotransmitter systems in the brain. In addition; there is evidence that estrogen is effective in the prognosis of various diseases such as Parkinson's disease, Alzheimer's disease, depression, and schizophrenia. A study has shown that estradiol may have specific antipsychotic-like effects on the symptoms of schizophrenia. (Bergemann et al. 2007).

Clinical Features

It is accepted that cognitive deficits seen in MP play a central role in the severity and prognosis of the disease and shape the quality of life in patients with psychotic symptoms. (Al-Sibani ve ark. 2020). It has been reported that in some cases with MP, fear and bewilderment are the core symptoms, excessive dependence on family members and regression symptoms can be observed, and anxiety and affective symptoms can be seen together with psychotic symptoms (Aktepe et al. 2016). The clinical symptoms detected during the attack in adolescents with MP diagnosis in the literature are shown in Table 1. (Karatepe et al. 2010, Grünewald et al. 2012, Arteaga and Lopez 2013, Santos-Cubina et al. 2013, Ellison-Wright and O'Keane 2013, Fernando et al. 2014, Aktepe et al. 2016, Fatica et al. 2018, Kiel et al. 2018, Thippaiah et al. 2018, Ahern et al. 2019, Langer et al. 2019, Öztürk et al. 2019, Al-Sibani et al. 2020, Takahashi et al. 2020)

Family History Related to Mental Disease

Although there is no genetic study related to this subject in the literature, it is reported that 30 of 80 cases diagnosed with MP have a family history of mental illness. In this study, a history of postpartum depression or psychosis was found in the mothers of 3 cases and in the aunt of one case (Brockington 2011). It has been reported that the mental illnesses seen in families of adolescents with MP (mother/father/aunt/grandmother/great uncle) include bipolar disorder, depressive disorder, premenstrual symptoms, and postpartum depression (Stein et al. 2003, Grünewald et al. 2012, Ellison-Wright and O'Keane 2013, Fernando et al. 2014, Langer et al. 2019). However, there are also adolescent cases with no family history of psychiatric illness (Stein et al. 2003, Aktepe et al. 2016, Che 2016, Fatica et al. 2018).

Comorbidity

It is known that some diseases such as asthma, diabetes, epilepsy, hypersomnia, migraine, and porphyria are exacerbated by menstruation, and none of these are common in patients with MP. Additionally, it is reported that MP is seen with menstrual disorders such as luteal phase defects, anovulatory cycles, and episodic amenorrhea (Brockington 2011). Since it is associated with menstrual disorders, gynecological evaluation is necessary in cases with MP. Correcting problems associated with menstruation can be an important part of treatment.

From the perspective of comorbid psychiatric disorders, it is astonishing that menstrual psychosis is not associated with menstrual mood disorder. The two disorders differ in almost every aspect (timing in the cycle, association with other disorders, and response to treatment). Unlike psychosis, menstrual mood disorder develops only in normal ovulatory cycles (Brockington 2011).

The disease most strongly associated with MP is postpartum psychosis. Many women with symptoms of MP are reported to have postpartum psychosis or another pregnancy-related mental disorder at another stage of their lives. These two disorders appear to be closely linked. Both diseases are associated with the female reproductive system and have a similar range of clinical symptoms belonging to the bipolar disorder group (Brockington 2011). It is also mentioned in the literature that premenstrual psychosis may be a predictive factor for future postpartum psychosis. Both diseases are rare and have similar clinical features. The symptoms of

Table 1.Clinical symptoms seen in adolescents with menstrual psychosis
Semistupor, stupor, bewilderment, distraction, delirium table, confusion, apathy
Hyperactivity, psychomotor agitation, restlessness, irritability, crying spells, hypersensitivity to sound
Hallucinations (visual / auditory / somatic), delusions (reference / persecution), paranoia, reference / persecution ideas, disorganized thought / behavior, Capgras Syndrome symptoms, bizarre behavior
Depressive symptoms, manic symptoms (euphoria, severe mood lability, grandiosity, pressured speech), depressed mood
Continuous or fluctuating sudden anxiety / fear (fear of the dark, inability to stay alone at home because of fear), destructive behavior, regressive behavior
Decrease in thinking and understanding skills, difficulty in remembering memories, prolonged response to verbal stimuli, impoverishment in thought content, forgetfulness, decrease in speed and amount of speech, difficulty in judgment skills, difficulty in performing daily routines (decreased self-care), disorganization in associations, decrease in psychomotor activity, withdrawal / focus on internal stimuli, stagnation, dealing with self-incriminating thoughts, perseveration
Somatic symptoms such as insomnia / increased sleep time, difficulty in falling asleep, loss of appetite, refusal to eat and drink, palpitations / inability to breathe / facial flushing/ lethargy / headache

an adolescent diagnosed with MP have been reported as similar to postpartum psychosis in the literature, and the case exhibits the symptoms of Capgras syndrome, which is quite common in postpartum psychosis. The nosological status of postpartum psychosis and menstrual psychosis is unclear. Considering the timing of attacks associated with both diseases, it has been reported that fluctuations in the concentrations of female reproductive hormones may have an etiological role. Hormonal changes that precede menstruation also recur during the early puerperium, and a sharp decrease in circulating estrogen and progesterone is observed in both diseases (Deuchar and Brockington 1998). An endocrine hypothesis has been proposed regarding premenstrual and postpartum psychosis. In this hypothesis, it is reported that rapid decreases in estrogen levels in susceptible individuals may reveal psychotic episodes (Ellison-Wright and O'Keane 2013).

Differential Diagnosis

1.Bipolar Disorder: Clinical symptoms defined in case reports with MP are compatible with bipolar disorder. It has been suggested by some authors that menstrual psychosis belongs to the family of manic-depressive psychosis, and menstruation is one of the factors that trigger bipolar periods. Psychotic symptoms are common in prepubertal major depressive disorder and adolescent mania. In addition, there are case reports of manic depressive disorder showing a monthly relapse rhythm. For this reason, it has been suggested that both psychotic characteristics and monthly cycles may be characteristics of some adolescents with mood disorders (Che 2016). However, one study has shown that cycloid psychosis is etiologically different from manic-depressive disorder and cannot be integrated into a spectrum of bipolar affective disorder. (Pfuhlmann et al. 2004).

2.Psychotic disorder associated with medical conditions: Metabolic diseases should be considered in the differential diagnosis, especially in patients whose mental status periodically changes. Hereditary metabolic disorders are an important cause of psychiatric diseases in adolescents. (Wilson's disease, remethylation disorders, and porphyria). Psychiatric symptoms can be observed years before appearing organic symptoms in some hereditary metabolic diseases. Diagnosis and treatment of the disease at the stage where psychiatric symptoms are detected can prevent the occurrence of irreversible consequences of the disease. Although it is hard to diagnose hereditary metabolic diseases that appear entirely with psychiatric symptoms, psychiatrists need to be aware of these possible differential diagnoses. (Che 2016).

3.Substance/Drug-induced psychotic disorder: Substance-induced psychosis is typically defined as hallucinations and / or delusions caused by intoxication or withdrawal of a substance (Beckmann et al. 2020). The use or abuse of substances with psychomimetic properties, such as cocaine, amphetamines, hallucinogens, and cannabis can trigger psychotic reactions that resemble a primary psychotic illness (Fiorentini et al. 2011).

4.Premenstrual dysphoric disorder: According to DSM-V, in order to diagnose premenstrual dysphoric disorder, the symptoms must be present in the last week before the onset of menstruation and must be observed in the majority of the menstrual cycles. These symptoms start to recover within a few days of the onset of the menstrual period, and the week after the menstrual period, they become much less or disappear. Among the observed symptoms are: marked emotional lability/depressed mood/hopelessness, feeling anger/nervousness/ frustration, decreased interest in usual activities, subjective difficulty in focusing, lethargy/easy fatigue, appetite/sleep changes, and somatic symptoms (breast sensitivity or swelling, joint or muscle pain) (Özdel et al. 2015). Considering the psychotic symptoms seen in MP, it appears to differ from symptoms associated with premenstrual dysphoric disorder. (Brockington 2011, Kiel et al. 2018)

5.Chronic psychotic disorder that worsens during menstruation: The exacerbation of chronic psychosis during menstruation should be excluded from the diagnosis of MP. The diagnosis of MP is based on accurate dating of the episode onset. It is very difficult to make this assessment for patients who do not fully

heal between episodes (Brockington 2011). In the literature, it has been reported that the symptoms of psychiatric disorders such as schizophrenia worsen before menstruation and psychiatric admissions increase during these periods. On the other hand in MP, psychotic symptoms are seen before / during menstruation and these symptoms disappear after menstruation ends (Türkçapar and Türkçapar 2011). As a result, the diagnostic distinction between MP and schizophrenic episodes is made according to the determination of the relationship between MP episodes and the menstrual cycle, and the self-limiting course of MP (Grünewald et al. 2012).

Treatment

It is reported that the hypothalamic-pituitary-ovarian axis has an impact on women's mental health through its effects on mood and psychotic symptoms. Beneficial effects of estrogen on psychosis-like behavior have been demonstrated in studies with rats. Additional estrogen therapy has been reported as an alternative treatment for women with schizophrenia/ schizoaffective disorder who are resistant or do not respond adequately to antipsychotics. However, it is recommended that hormonal treatment decisions should be made by considering the profit/loss relationship, especially in young people (Ward et al. 2020).

The estrogen hypothesis states that estrogen is protective for psychosis and that a decrease in estrogen can worsen or precipitate psychosis. The putative neuroprotective effect of estrogen is thought to be the basis for the later onset of psychotic disorders in women than in men, the increased incidence of psychosis in postmenopausal women (following a decrease in estrogen levels), and the more severe psychotic symptoms in the late period.

Moreover, various interventions associated with estrogen withdrawal can precipitate episodes of psychosis. These include termination of pregnancy, removal of a hydatidiform mole, discontinuation of estrogen medication, administration of estrogen receptor antagonists, and administration of gonadotropin-releasing hormone agonists that inhibit estrogen release. Similarly, the postpartum period causes a sudden drop in estrogen and progesterone levels and carries a 23-fold increase in relative risk for emotional psychotic episodes (Reilly et al. 2020).

Clifford and Rowland (2011) have reported that estrogen is effective on recurrent affective psychoses through dopamine blockade and prolactin-inducing effects. The significant decrement of estrogen level seen in the premenstrual period may mediate the hyperdopaminergic state associated with psychosis. It has also been reported that the decrease in estrogen may affect catecholaminergic and serotonergic pathways through its effects on ion channels, calcium balance, and neuronal excitability (Ward et al. 2020).

The levels of estrogen, progesterone and their metabolites decrease in the premenstrual (late luteal) phase and remain low in the menstrual (early follicular) phase. These gonadal steroids are known to regulate the functions of central neurotransmitters such as serotonin, dopamine, norepinephrine, and GABA. It has been suggested that as the levels of gonadal steroids change throughout the menstrual cycle, psychiatric symptoms may be affected. Suppression of menstruation in MP has also been considered as a solution to prevent the syndrome, which starts a few days before menstrual bleeding, so oral contraceptive agents have been used in the treatment. It has been suggested that in the treatment with contraceptives with a more dominant estrogen ratio, estrogen changes the norepinephrine levels in the synapses by decreasing the monoamine oxidase activity, and thus the disease can be controlled. Danazol and steroid derivatives, which are agents that can suppress ovulation and menstruation, are also groups of agents that have been used in the treatment and have achieved results. (Karatepe et al. 2010).

There is no treatment guide for MP, and it is reported that physicians should make arrangements on a case-by-case basis and treatment may take years (Heinzman and Buckingham 2019, Colak et al. 2020). Many drugs (antipsychotic agents, mood stabilizers, estrogen, androgen, progesterone, oral contraceptive agents, thyroid hormone, clomiphene, antidepressant agents, electroconvulsive therapy, benzodiazepines, bromocriptine) have been used in MP so far. (Colak et al. 2020).

The treatment of MP is directed towards the menstrual cycle, which is the underlying cause of the psychosis. It is focused on both hormone replacement and suppression of the menstrual cycle with antipsychotics in the acute psychotic period. (Heinzman and Buckingham 2019). Based on trial and error, some authors have suggested the use of treatments used in bipolar disorder together with endocrine therapy in MP cases. (Ellison-Wright and O'Keane 2013). A case diagnosed with menstrual psychosis in the literature has been diagnosed with bipolar disorder spectrum disorder over time and responded positively to lithium treatment. (Ahern et al. 2019). Antipsychotic drugs have proven useful for acute treatment by shortening the duration of the episode, but the response to maintenance therapy is unclear (Langer et al. 2019).

It has been reported that high and sustained estrogen levels in anovulatory cycles may lead to increased dopaminergic receptors and thus increased sensitivity (Wieck et al. 2003). While the use of psychotropic treatment in MP with anovulation is considered inconclusive, it has been reported that hormonal agents may be effective (Stein et al. 2003).

Recurrence of psychotic symptoms during adequate antipsychotic treatment and resolution of the symptoms after discontinuation of antipsychotics in some cases in the literature show that the syndrome can go into spontaneous remission, and long-term satisfactory results can be encountered after drug-free follow-up (Karatepe et al. 2010).

Table 2. Drug treatments used in female adolescents diagnosed with Menstrual Psychosis and the follow-up process		
Author (Year)	**Age; Treatment**	**The follow-up process**
Ambelas / Kat (1998)	13 years old; progesterone	18-month stable course with progesterone therapy
Stein et al. (2003)	14 years old; perphenazine/penfluridol	Improvement in psychotic symptoms with penfluridol, no psychotic symptoms from the 2nd menstrual cycle after penfluridol was discontinued, and a stable course at 3-year follow-up
Stein et al. (2003)	14 years old; perphenazine / venlafaxine / combined OCs	2-year stable course with combined OCs therapy
Kobayashi / Kato (2009)	18 years old; haloperidol / diazepam / lithium	Significant improvement in symptoms with lithium treatment
Karatepe et al. (2010)	17 years; risperidone / chlorpromazine / quetiapine	Clinical improvement with risperidone and chlorpromazine treatment, relief in psychotic symptoms with quetiapine treatment. 3-year stable course in the case followed by discontinuing drug therapy
Grunewald et al. (2012)	12 years; combined OCs	Asymptomatic course at 10-month follow-up without medication after 3 months of combined OCs therapy
López Arteaga / Loro López (2013)	13 years old; risperidone /fluoxetine	Reduction in symptoms with risperidone and fluoxetine treatment, risperidone was discontinued due to sedation, asymptomatic course without treatment in the last 5 months in a 2-year follow-up
Santos Cubina et al. (2013)	13 years old; quetiapine	6-month stable course
Wright / O'Keane (2013)	14 years old; risperidone / quetiapine / OCs containing progesterone	Symptom control was achieved with quetiapine and OCs treatment
Fernando et al. (2014)	14 years old; combined OCs /leuprolide / sertraline / clonidine	Complete improvement in psychotic symptoms after OCS and leuprolide treatment, leuprolide treatment was discontinued after 18 months, 1 year stable course with OCS and fluoxetine treatment
Aktepe et al. (2016)	14 years old; risperidone / valproate	Asymptomatic course for 3 cycles from the 2nd menstrual cycle after risperidone and valproate treatment
Metin et al. (2016)	14 years old; drug-free follow-up	Asymptomatic course in 4 consecutive menstrual cycles
Che (2016)	12 years; risperidone	2-year stable course
Kiel et al. (2018)	14 years old; combined OCs	Asymptomatic course
Fatica et al. (2018)	15 years old; olanzapine / combined OCs	Symptoms completely disappeared after menstruation. After 1 month, olanzapine treatment was discontinued. Asymptomatic course with OCs therapy
Ahern et al. (2019)	13 years old; aripiprazole / risperidone / lithium	Asymptomatic course with risperidone and lithium therapy
Langer et al. (2019)	14 years old; risperidone / benztropine / olanzapine	Asymptomatic course with risperidone therapy
Öztürk et al. (2019)	16 years old; quetiapine	4-month symptom-free course with quetiapine therapy used only in the menstrual cycle in 2 consecutive menstrual cycles
Takakashi et al. (2020)	16 years old; lithium carbonate	2-year stable course with lithium therapy
Ray / Paul (2020)	14 years old; olanzapine and OCs	2-year stable course after treatment
OCs: Oral Contraceptives		

Table 2 summarizes the drug treatments and follow-up processes used in female adolescents diagnosed with MP in the literature. (Ambelas and Kat 1998, Stein et al. 2003, Kobayashi and Kato 2009, Karatepe et al. 2010, Grünewald et al. 2012, Arteaga and Lopez 2013, Ellison-Wright and O'Keane 2013, Santos-Cubina et al. 2013, Fernando et al. 2014, Aktepe et al. 2016, Che 2016, Metin et al. 2016, Fatica et al. 2018, Kiel et al. 2018, Ahern et al. 2019, Langer et al. 2019, Öztürk et al. 2019, Ray and Paul 2020, Takahashi et al. 2020).

Conclusion

Menstrual psychosis is a rare disease and its recognizability by psychiatrists is relatively low. The key to diagnosis is the identification of periodic recurrent psychotic episodes associated with the menstrual cycle. To establish the link, both menstrual periods and the onset of psychotic episodes must be accurately dated for at least a few episodes. Although the etiology of menstrual psychosis is still unknown, it has been suggested that it may be associated with fluctuations in

the concentration of female reproductive hormones produced during the menstrual cycle. The disease most strongly associated with MP is postpartum psychosis. Many women with symptoms of MP are reported to have postpartum psychosis or another pregnancy-related mental disorder at another stage of their lives. If the diagnosis of MP is ignored in terms of periodic adolescent psychosis, a diagnosis of mood disorders, schizophrenia, or premenstrual dysphoric disorder will diagnose. Especially if schizophrenia or premenstrual dysphoric disorder is diagnosed, there will be great differences in pharmacological treatment and prognosis in terms of MP diagnosis. Many drugs (antipsychotic agents, mood stabilizers, estrogen, androgen, progesterone, oral contraceptive agents, thyroid hormone, clomiphene, antidepressant agents, electroconvulsive therapy, benzodiazepines, bromocriptine) have been used in MP so far. There is no treatment guide for MP, and it is reported that physicians should make arrangements on a case-by-case basis and treatment may take years. More research is needed to define most aspects of the disorder, including prevalence, pathophysiology, genetic risk, and evidence-based treatments. Menstrual psychosis education should also be increased because the diagnosis is clinically overlooked.

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