BIPOLAR AFFECTIVE DISORDER (BAR)

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Abstract. *Bipolar affective disorder (BAR) is an endogenous mental illness characterized by alternating affective phases: manic (or hypomanic) and depressive, and sometimes mixed states, in which the patient simultaneously experiences symptoms of mania (hypomania) and depression.*

Keywords: *manic-depressive psychosis, polydipsia and polyuria.*

For type I BAR (previously manic-depressive psychosis), the presence of expanded manic states is mandatory, while for type II BAR, distinct depressive episodes alternate with less pronounced periods of mood elevation – hypomania. The prevalence of BAR can reach 4-6.4% [1-4]. BAR, as a rule, occurs at a young age and continues throughout life, and is relatively common among women of childbearing age. The diagnosis and choice of pharmacotherapy for BAR seem to be a rather difficult task due to the different type of course of the disease (Table. 1) and the peculiarities of its course in persons of different sexes in different periods of life. In particular, in women, the diagnosis of BAR is complicated by the predominance of depressive symptoms both at the beginning of the disease and throughout life [6, 7]. Therapy of pregnant women with BAR is a particularly difficult task. This is due to the fact that, on the one hand, many drugs (AS) used to treat BAR have the potential of teratogenic action and can cause other adverse effects in the mother and newborn; and on the other hand, the cancellation of pharmacotherapy during pregnancy is associated with an increased risk of relapses of the disease. The lack of information on these issues and/or its unavailability for medical professionals is often the reason for unjustified termination of pregnancy, including on the recommendation of doctors [8]. The effect of pregnancy on the course of BAR The natural course of BAR during pregnancy has not been studied sufficiently, and the available data are contradictory [10]. According to the results of a number of observational studies, the state of euthymia can be maintained in pregnant women even if drug therapy is discontinued [11-13]. Moreover, data from one retrospective study suggested the presence of a protective effect of pregnancy on the course of BAR–1 in women responding to lithium therapy [14]. On the contrary, three other retrospective studies showed the absence of a protective effect of pregnancy and an increased risk of relapse during this period [15-17]. In these studies, exacerbation of BAR during gestation was observed in 45-52% of participants. The frequency of relapses was similar in women with type I and type II BAR, and the risk of relapse was highest in women, the effect of pregnancy on the course of BAR The natural course of BAR during pregnancy has not been sufficiently studied, and the available data are contradictory [10]. According to the results of a number of observational studies, the state of euthymia can be maintained in pregnant women even if drug therapy is discontinued [11-13]. Moreover, data from one retrospective study suggested the presence of a protective effect of pregnancy on the course of BAR–1 in women responding to lithium therapy [14]. On the contrary, three other retrospective studies showed the absence of a protective effect of pregnancy and an increased risk of relapse during this period [15-17]. In these studies, exacerbation of BAR during

gestation was observed in 45-52% of participants. The recurrence rate was similar in women with type I and type II BAR, and the risk of relapse was highest in women who had a history of more than four episodes of the disease, as well as in those who abruptly or very quickly stopped lithium treatment. Thus, in a prospective study conducted within the framework of a specialized program for the provision of perinatal psychiatric care and included 89 women with type I and II BAR, the relapse rate in participants who continued treatment during pregnancy was 37%, and in participants who had pharmacotherapy canceled 6 months before conception or during the first trimester – 85.5% (Table. 2) [19]. In general, 70,8% of pregnant women developed relapses. The factors contributing to the increased risk of relapse were the cancellation of normotimics and unplanned pregnancy. Most of the new episodes of the disease developed in the early stages of pregnancy: the probability of their occurrence in the I, II and III trimesters was 47.2, 31.9 and 18.8%, respectively. In most cases (74%), episodes of depression or mixed states were noted. In women who abruptly (within 1-14 days) canceled the normotimic drug, the risk of relapse within 2 weeks was 50%. In women who canceled drugs more slowly, a similar level of risk was recorded 22 weeks after cancellation. In turn, rapid withdrawal of AS was significantly more often observed in women with unplanned pregnancy. Since this study was conducted within the framework of a specialized program and the vast majority of its participants had a sufficiently high social and educational level, the authors suggested that in real medical practice, relapses of BAR can be observed in a higher proportion of pregnant women suffering from this disease. The most dangerous period in terms of the risk of recurrence of the disease is the postpartum period. This was confirmed both in retrospective [14, 20] and in a prospective study [21]. The frequency of relapses in the postpartum period varies, according to different authors, from 32 to 67% [22]. Studies have demonstrated a significantly higher frequency of episodes of the disease in women who did not receive normotimics, compared with women who continued or resumed treatment with drugs of this group [17, 21]. In women who refused to continue lithium therapy during pregnancy, the risk of relapse in the postpartum period was 3 times higher than in non-pregnant women with BAR [17]. Relapse symptoms, as a rule, appeared in the late stages of pregnancy or in the first few days or weeks after childbirth and rapidly increased [21, 23]. Women with BAR also have a very high (10-20%) risk of developing postpartum psychosis, which is 100-200 times higher than the population level (0.05%). In general, pregnant women and maternity women suffering from BAR have a 2−fold higher risk of relapse than for non-pregnant women with BAR, and the risk of hospitalization due to an exacerbation of the disease is 7-fold [23]. The effect of BAR on the course and outcomes of pregnancy Data on the potential effects of BAR on the course /outcomes of pregnancy are limited. Since most relapses of the disease during pregnancy are episodes of depression 7 [17-19], it can be assumed that the potential risk of adverse outcomes in pregnant women with BAR is similar to that in women with depressive disorders. The undesirable consequences of untreated depression during pregnancy are summarized in Table 3. The negative effect of depression in the mother on the fetus/newborn was confirmed by the results of preclinical and clinical studies [29-31].In general, pregnant women and maternity women suffering from BAR have a 2−fold higher risk of relapse than for non-pregnant women with BAR, and the risk of hospitalization due to an exacerbation of the disease is 7-fold [23]. The effect of BAR on the course and outcomes of pregnancy Data on the potential effects of BAR on the course /outcomes of pregnancy are limited. Since most relapses of the disease during pregnancy are episodes of depression 7 [17-19], it can be assumed that the potential risk of adverse outcomes in pregnant

women with BAR is similar to that in women with depressive disorders. The undesirable consequences of untreated depression during pregnancy are summarized in Table 3. The negative effect of depression in the mother on the fetus/newborn was confirmed by the results of preclinical and clinical studies [29-31]. In addition, the fetuses of mothers with depression showed a change in the nature of the heart rhythm [40, 41]. Whether the described changes affect the development of the fetus and, if so, to what extent, remains unclear. The effect of depression on pregnancy outcomes may be due both directly to the disease itself and to indirect factors, such as decreased appetite, substance abuse and a lower level of use of medical care in the prenatal period [32]. Untreated mania is also associated with an increased prenatal risk, since in the manic phase a pregnant woman can commit impulsive actions that can cause significant harm to both her health and the condition of the fetus [33]. Risky behavior in an episode of mania also includes increased sexual activity and substance abuse. According to the results of a number of studies, the frequency of comorbid alcohol and substance abuse can reach 60% in patients with BAR, which is associated with a high potential risk of adverse pregnancy outcomes [42, 43]. In addition to the adverse effect of the relapse of the BAR itself on the course/outcomes of pregnancy, the administration of AS associated with a higher risk to the fetus than drugs discontinued during pregnancy may be required to relieve the manic state [44]. Efficacy and safety of medicines used for the treatment of BAR during pregnancy and lactation.

The main groups of AS used for the treatment of BAR, including during pregnancy, are:

- Lithium salts.

-Anticonvulsants (mainly carbamazepine, lamotrigine and valproic acid).

-Antipsychotics (typical and atypical).

In addition, drugs of other groups are often used in BAR therapy in practice, most often antidepressants and anxiolytics. The frequency of congenital anomalies in the use of the most widely used psychotropic drugs is shown in Table 6 (the frequency of congenital anomalies in the general population is 2-4%). Below are the data on the safety of normotimics during pregnancy. A more detailed description of the safety of drugs of other pharmacological groups used for the treatment of BAR is presented in other sections devoted to the treatment of mental illnesses in pregnant women. Safety of normotimics during pregnancy Lithium safety According to the FDA classification lithium belongs to category D. This means that its use during pregnancy has demonstrated a significant risk to the fetus, but in certain situations, the potential benefits of its use may outweigh this risk. Concerns about the association between the use of lithium preparations during pregnancy and congenital anomalies in the child arose shortly after their introduction into widespread medical practice, which led to the creation of the Register of Lithium Babies (Register of Lithium Babies) – a database containing voluntary reports from doctors about the effects of prenatal lithium exposure on the fetus/newborn. The results of the first analysis of the register suggested that in children whose mothers took lithium during pregnancy, the risk of congenital cardiovascular defects, especially Ebstein's anomaly, increased by 400 times compared to the general population [47]. However, subsequent studies have shown that the frequency of this congenital anomaly when taking lithium is 0.05–0.1% and exceeds the frequency of its development in the general population by no more than 20-40 times [48, 49]. Thus, the absolute risk of developing congenital heart abnormalities when using lithium during pregnancy is quite low. Moreover, Ebstein's anomalies develop only when the effect of lithium on the fetus coincides with the period of heart formation during organogenesis (mainly 3-6 weeks of gestation). When

lithium is exposed to the fetus in the second and third trimesters, goiter may develop [50, 51].In late pregnancy and during childbirth, due to changes in the pharmacokinetics of lithium, the risk of toxic effects in the mother and fetus / newborn is increased. The use of lithium can lead to the development of hypothyroidism (in rare cases, hyperthyroidism) in the mother. Lithium can aggravate polydipsia and polyuria, which are common in pregnant women, cause kidney damage and nephrogenic (non-sugar) diabetes in pregnant women [52-54]. Polyhydramnios may develop [55-57]. The toxic effects of lithium in a newborn are usually manifested by lethargy and floppy baby syndrome, which is characterized by respiratory disorders, cyanosis and decreased muscle tone. These symptoms are dose-dependent and develop against the background of high levels of lithium in the blood in late pregnancy. They are usually light and transient in nature [50, 51, 58] Cases of cardiomegaly, hypotension, bradycardia, atrial flutter, T wave inversion on ECG, diabetes insipidus, hypothyroidism, hepatomegaly, gastrointestinal bleeding, convulsions and shock have been described in the child [55, 57, 59-60]. Most of the undesirable effects resolved themselves within 12 weeks, which coincides with the half-life of the drug in newborns, which is 68-96 hours [60]. However, in the two cases described, nephrogenic diabetes persisted for 2 months or more [60]. In fetuses exposed to lithium, an increase in the level of choline, which is a metabolic precursor of acetylcholine, was found in erythrocytes [66]. The clinical significance of this fact is unclear, but perhaps the accumulation of choline contributes to the development of the teratogenic effect of lithium, since choline affects the cellular transport of the drug. Data on the effect of lithium on the subsequent development of children are extremely limited. No neurobehavioral toxicity was detected in two small studies [49]. In a recently published systematic review, which included information from electronic databases, books and other sources, it was not possible to formulate a definite conclusion about the effect of lithium on long-term outcomes of children's development due to a lack of information.

REFERENCES

1. Sarkisova V. ASPECTS OF THE STATE OF THE AUTONOMIC NERVOUS SYSTEM IN HYPOXIA //Science and innovation. – 2022. – T. 1. – №. D8. – C. 977-982.
2. Vladimirovna S. V. Epidemiology, Theories Of The Development, Conservative And Operative Treatment Of The Endometriosis //The Peerian Journal. – 2023. – T. 15. –C. 84-93.
3. Саркисова В., Абдурахманова К. Астено-вегетативные нарушения, оценка качества жизни у женщин климактерического возраста с гиперпластическими процессами в матке //Журнал вестник врача. – 2014. – Т. 1. – №. 01. – С. 163-166.
4. Vladimirovna S. V. About the Causes of Endometrial Hyperplasia and Forms of Endometrial Hyperplasia //Global Scientific Review. – 2023. – T. 12. – C. 25-32.
5. Sarkisova V., Xegay R. CAUSES, DIAGNOSIS, CONSERVATIVE AND OPERATIVE TREATMENT OF UTERINE MYOMA //Science and innovation. – 2022. – T. 1. – №. D8. – C. 198-203.
6. Саркисова В., Джуманов Б., Исроилова Г. Анализ репродуктивного и соматического здоровья женщин, госпитализированных по поводу гиперплазии эндометрия и маточных кровотечений //Журнал вестник врача. – 2014. – Т. 1. – №. 01. – С. 169-170.
7. Саркисова В., Абдурахманова К. Роль гормональных препаратов в терапии гиперпластических процессов эндометрия и в частности при миоме матки //Журнал вестник врача. – 2014. – Т. 1. – №. 01. – С. 167-168.

8. Саркисова В. В. Патогенетические отношения артериальной гипертензии и сопротивления инсулина //IQRO JURNALI. – 2023. – Т. 2. – №. 1. – С. 727-731.
9. Vladimirovna S. V. PATHOGENETIC RELATIONSHIPS OF ARTERIAL HYPERTENSION AND INSULIN RESISTANCE //IQRO JURNALI. – 2023. – Т. 2. – №. 1. – С. 685-691.
10. Sarkisova V., Regina X. РОЛЬ БРАДИКИНИНА В ПРОТЕКАНИИ ОСНОВНЫХ ЖИЗНЕННЫХ ПРОЦЕССОВ //Science and innovation. – 2022. – Т. 1. – №. D8. – С. 587-593.
11. Sarkisova V., Numonova A., Xegay R. АНТИБИОТИКОРЕЗИСТЕНТНОСТЬ ИЛИ БОРЬБА С ГЛОБАЛЬНОЙ УГРОЗОЙ XXI ВЕКА //Science and innovation. – 2022. – Т. 1. – №. D8. – С. 232-241.
12. Sarkisova V., Numonova A., Xegay R. АСПЕКТЫ СОСТОЯНИЯ ВЕГЕТАТИВНОЙ НЕРВНОЙ СИСТЕМЫ ПРИ ГИПОКСИИ //Science and innovation. – 2022. – Т. 1. – №. D8. – С. 228-231.
13. Sarkisova V. et al. UTERINE ARTERY EMBOLIZATION AS A METHOD OF TREATMENT OF UTERINE FIBROIDS //Science and innovation. – 2023. – Т. 2. – №. D3. – С. 115-121.
14. Vladimirovna S. V. ABOUT THE CAUSES OF ENDOMETRIAL HYPERPLASIA AND FORMS OF ENDOMETRIAL HYPERPLASIA //ResearchJet Journal of Analysis and Inventions. – 2022. – Т. 3. – №. 11. – С. 66-72.
15. Шерназаров Фаррух,Шерназаров Самандар,Курбаниязова В.Е.,Виктория Саркисова Владимировна. (2023). Клиническое значение микробиоты кишечника у новорожденных с геморрагической болезнью. *IQRO JURNALI*, *2*(2), 867–877. Retrieved from http://wordlyknowledge.uz/index.php/iqro/article/view/893
16. Шерназаров Фаррух,Шерназаров Самандар,Курбаниязова В.Е.,Виктория Саркисова Владимировна. “Клиническое значение микробиоты кишечника у новорожденных с геморрагической болезнью”. *IQRO JURNALI*, vol. 2, no. 2, Apr. 2023, pp. 867-7, http://wordlyknowledge.uz/index.php/iqro/article/view/893.
17. Vladimirovna S. V. et al. PREGNANCY WITH CONGENITAL HEART DISEASE //Science and innovation. – 2023. – Т. 2. – №. D4. – С. 127-136.
18. Sarkisova V., Xegay R., Numonova A. ENDOCRINE CONTROL OF THE DIGESTION PROCESS. GASTROINTESTINAL ENDOCRINE CELLS //Science and innovation. – 2022. – Т. 1. – №. D8. – С. 582-586.
19. Sarkisova V. et al. ESSENTIAL ROLE OF BRADIKININ IN THE COURSE OF BASIC LIFE PROCESSES //Science and innovation. – 2022. – Т. 1. – №. D8. – С. 576-581.
20. Джуманов Б. и др. Применение инструментальных методов исследование в диагностике острого аппендицита у беременных //Журнал проблемы биологии и медицины. – 2014. – №. 1 (77). – С. 9-12.
21. Vladimirovna S. V. et al. Adenomyosis as an Independent Unit of Dysfunction of the Endometrium and Uterine Myometrium //Scholastic: Journal of Natural and Medical Education. – 2023. – Т. 2. – №. 3. – С. 85-91.
22. Вахидова А., Стреляева А., Садыков В. Грибы рода Paecilomyces и их роль в развитии эхинококкоза //Журнал проблемы биологии и медицины. – 2011. – №. 3 (66). – С. 43-47.