

A pregnant patient with schizophrenia – dilemmas of treatment and care. A problem still not only for psychiatrists

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Summary

Pregnancy is a special period in any women's life. A pregnant woman who suffers from schizophrenia is a special patient and a huge challenge both for the psychiatrist and gynecologist. Such pregnancy is associated not only with the higher level of risk because of inappropriate diet, insufficient prenatal care and smoking but also because of the risk of possible mental degradation of a pregnant woman – occurrence or exacerbation of psychotic symptoms. Moreover, pharmaceutical treatment during pregnancy and its influence on fetus rises doubts and controversy. The aim of the study is to show three stories of pregnant patients treated for schizophrenia in a context of up to date knowledge on anti-psychotic treatment and to pay attention to the need of interdisciplinary approach to this special group of patients. Every pregnant woman suffering from schizophrenia requires individual approach in terms of treatment and care. The problem, which is still ignored, is the need of effective and constant cooperation between the doctors: a psychiatrist and a gynecologist since the very beginning of pregnancy, in order to assess the risk factors associated with pregnancy and periparturient period.

Key words: pregnancy, schizophrenia, treatment

Introduction

Pregnancy is a special period in any women's life, however, it is associated with huge physical changes and stress related to concerns about a baby, its development, and the fear of labor [1]. A pregnant woman suffering from schizophrenia is a special patient who needs special, individual approach. Mental illness does not impair reproductive function, however, the analyses show lower fertility rates in a group of women suffering from schizophrenia [2, 3]. Fertility is not, however, lowered because of pathophysiological mechanisms of schizophrenia but because of specificity

of the disorder, which has an impact on poorer social functioning of this group of women [4]. Psychotic symptoms may significantly limit the patients in their social functioning, searching for support during pregnancy, denial of pregnancy, drinking alcohol, smoking, and not using appropriate obstetric care. Untreated psychosis may result not only in the negligence of self-care but also in pregnancy complications [5]. Introducing into treatment a new generation of narcoleptics highly influenced the quality of patients' lives. Thus they are more frequently in relationships, and as a result they plan to have children [5]. This is the reason why the research shows that the number of pregnant women suffering from schizophrenia is rising [3]. Some studies even state that the number of schizophrenic patients who will get pregnant may reach 50% [6]. It was observed that among pregnant patients suffering from schizophrenia, even without any treatment, there was a higher risk of giving birth to a child with malformations than among pregnant women who are mentally healthy [7, 8]. Risk factors for malformations are: obesity, diabetes, the intake of alcohol and other psychoactive substances, smoking, and low socioeconomic status of patients. However, the influence of schizophrenic process in the mother's organism on fetal development is also not clear [9].

Knowledge concerning the effects of medications and their influence on fetus is based on research conducted on animals and on case studies concerning treatment of pregnant women with schizophrenia. Guidelines concerning procedures for treatment of mental disorders in pregnant patients have not changed for years [10–13]:

- (1) Pharmacological treatment should be introduced only if the potential advantages coming from the intake of medicines outweigh the potential harms caused by pharmacotherapy.
- (2) It is always necessary to consider the risk associated with the cessation of medications – which might cause greater risk for the mother and the fetus than pharmacotherapy.
- (3) Avoid medications in the first trimester of pregnancy, discontinue therapy about a week before labor.
- (4) Use the medication of the least teratogenic potential, in the lowest but effective dose divided for a day.
- (5) It is necessary to adjust the dose of the medication to the altered pharmacokinetics of individual stages of pregnancy.
- (6) In the case of exacerbation of the disorder, the patient should be hospitalized.
- (7) The condition of the newborn and the mother should be monitored in a period after the labor.

Despite the above findings, there are still discussions concerning the treatment of a pregnant, schizophrenic woman, how to evaluate whether the pharmacotherapy is safe. No account is taken of the need of cooperation between doctors: a psychiatrist and a gynecologist in order to lower the risk of complications during pregnancy and labor, associated with monitoring of somatic and mental conditions of the mother and the development of the fetus.

The aim of the paper is to show three stories of pregnant patients treated for schizophrenia and to pay attention to the aspect of anti-psychotic treatment, as well as to pay attention to maternity care during pregnancy and in the perinatal period.

Case studies

Case 1

A 33 years old woman, married, with secondary education qualifications, receiving psychiatric treatment for schizophrenia for fifteen years, hospitalized thrice due to this reason, three pregnancies in the past – two children (9 and 11 years old) and one miscarriage in the 9th week. Before two pregnancies (one ended in a miscarriage and the other in a natural delivery) and during them the patient was treated with risperidone in a dose of 1mg/day. During the third pregnancy, it was decided to discontinue the medication during the first trimester of pregnancy, the patient had a spontaneous delivery and breast-fed the baby for five months. After this period, the patient restarted the treatment and was treated systematically. She was treated with quetiapine in a dose of 300 mg/day and sodium valproate in a dose of 300 mg/day. On 9th August, she informed her psychiatrist that she might be pregnant. After performing a pregnancy test, the patient decided to discontinue sodium valproate. On account of pregnancy, it was decided to change the treatment – the dose of quetiapine was lowered to 200 mg/day. In a few days the patient had a gynecological appointment in order to confirm the pregnancy.

On account of the remission of psychotic symptoms for three years and appropriate cooperation, it was decided to discontinue pharmacological treatment on 16th August. Subsequent appointments were planned every 2–4 weeks, or when necessary. The patient was obliged to inform her gynecologist about her illness and current recommendations. For this purpose, the psychiatrist gave her an appropriate medical certificate. During the pregnancy period, the patient visited the psychiatrist regularly, showed the gynecological examination results and her pregnancy card. The patient's mental condition was balanced, only at times did she suffer from irritability and anxiety associated with everyday responsibilities and taking care of other children in a situation of being pregnant. Since 15th March, the patient's well-being deteriorated. The patient complained of fear and anxiety, she had trouble falling asleep. Four days later, after consulting a gynecologist, she presented to the Gynecology and Obstetrics Ward for further recommendations (according to her pregnancy card, her due date was 31st March). After being admitted to the ward, the patient called her attending psychiatrist, who recommended her to ask the doctor on duty for a psychiatrist consultation on the ward. Unfortunately, the consultation did not take place because of the beginning of the weekend. Unfortunately, doctors on the ER also ignored the certificate provided by the psychiatrist, which informed about the patient's schizophrenic history and need for special care. However, because of the 38th week of pregnancy, the doctor decided to start natural delivery, the patient received oxytocin and a Foley's catheter was inserted. During the night of 19th to 20th March, the patient could no sleep and was very irritated.

After few hours, psychotic symptoms appeared – phantasmia (the patient smelled strange odors in the ward); the patient also reported insecurity and even tried to call the prosecutor's office. On 20th March 2011 at about 6 a.m., the doctor on duty called her psychiatrist to get further recommendations. The psychiatrist again asked for the psychiatric consultation in the ward (unfortunately, the psychiatric consultant was unavailable) and suggested C-section because of strong psychotic symptoms. Gynecologist, however, maintained his decision of a natural delivery. The patient did not cooperate with the staff, her mental state continued to exacerbate: she became more irritated and tense, spoke delusional content of persecution, she threw a ring at her husband. Finally, another doctor, after observing the patient and consulting her psychiatrist again, decided to conduct C-section. The C-section was conducted without complications, under general anesthesia. A female baby was born with weight 3,100 g and got 9 APGAR points. After delivery, the patient received 5 mg of diazepam and 5 mg of olanzapine. Despite receiving medications she was still suspicious, anxious, and in one moment she did not want to give her child to the midwife. Due to her psychotic symptoms, she was sent to the psychiatric ward. There she had consultation with a gynecologist, and the suppression of lactation was recommended.

Case 2

A 30 years old woman, single, high school education, second pregnancy, one miscarriage in the eighth week, informed her psychiatrist that she was 4 weeks pregnant.

Earlier, she was several times hospitalized in a psychiatric ward (last hospitalization in January 2017). After the last hospitalization, she received the following recommendations: aripiprazole 15 mg/day, haloperidol 3 mg/day, carbamazepine 600 mg/day, and haloperidol injections 1 ampoule every 14 days. Before the hospitalization the patient showed pregnancy delusion. After being informed about pregnancy, the psychiatrist decided to discontinue two medications: haloperidol injections and carbamazepine. The next appointment was scheduled within a week. In the meantime, the patient was taken to the gynecology ER due to the possible uterine bleeding. After the tests, the threat of miscarriage was excluded. The patient came to the psychiatric appointment, however, did not have her hospital discharge card from the ER. Because of the early stage of her pregnancy, the doctor decided to reduce doses of medications: cessation of oral haloperidol and lowering the dose of aripiprazole to 7.5 mg/day. On the next appointment the patient was mentally stable. She did not show positive symptoms of schizophrenia, this is why the doctor decided to reduce the dose of aripiprazole to 3.75 mg/day since 13th July. The patient was informed about the need of constant contact with her psychiatrist. Moreover, because of the diagnosis of hypothyroidism during the last hospitalization, the patient received thyroid hormones. Since 8th September there appeared episodes of mood swings toward depression, which were completely self-resolving. The next appointment was the emergency one on 24th November – after the patient's stay in a gynecology ward. The patient was treated there with the diagnosis "Observation

toward thrombosis – negative. Hypotonia of the pelvicalyceal system on the left side”. During her stay on the ward, she fell on the wet floor and got hurt.

During the medical appointment on the ward, the patient reported anxiety, however, there was no psychiatric consultation during the hospitalization. She had a meeting with a psychologist and was given a sedative mixture. Since the beginning of December the patient suffered from: racing thoughts, anxiety and fear; the patient became effusive, she would call her family at night because of the feeling of insecurity, this is why the doctor decided to provide pharmacological treatment (29th week of pregnancy) in the form of pernazine 25 mg/day. The patient informed her gynecologist about that fact. The next appointment was also an emergency one – 4th January, due to irritability and anxiety. The patient received the recommendation to increase the dose of pernazine to 50 mg/day. As she did not feel the baby’s movements for few hours she reported to the gynecologist. On 23rd January, patient’s mental condition deteriorated again, again she felt anxiety and fear since few days. The psychiatrist recommended the increase of the dose of pernazine to 50 mg/day again, as the patient lowered the previous dose by herself. Because of the deterioration of the patient’s mental condition and the end of 36th week of pregnancy, the gynecologist decided to hospitalize the patient. On 2nd February 2018, the patient delivered the baby by C-section as the contraction was not progressing. A female baby was born with the weight of 2,470 g, APGAR at 1 minute – 8 points, 3 minutes – 9 points, the baby was observed toward FHR; needed breathing stimulation. The patient was consulted with a psychiatrist, pernazine in the dose of 5 mg/day was recommended. The first psychiatric appointment after the labor took place on 13th February. The patient felt very muffled, she was afraid that she would not manage to take care of her baby. The doctor decided to reduce the dose of the medication to 50 mg/day, however, this solution was not successful.

The patient still suffered somnolence, thus the doctor decided to change the treatment to pernazine 7.5 mg/day and aripiprazole 7.5 mg/day. The patient did not show psychotic symptoms and because of the pharmacological treatment she did not breastfeed her baby.

Case 3

A woman aged 28, single, vocational education, on disability pension because of mental illness, treated psychiatrically because of schizophrenia and once hospitalized due to this illness. The patient was under the care of a self-help community center because of the fact that she lived alone and she needed help with her everyday responsibilities like shopping and expenditure planning. Medical history of obesity: height 158 cm, weight 104 kg, BMI – 41, morbid obesity. She kept psychiatric appointments regularly, however, always with the assistance of the nurse from the self-help community center. She was treated with aripiprazole in the dose of 15 mg/day and olanzapine in the form of ODT 10 mg/day. The patient was in remission of psychotic symptoms. Because the patient had sexual intercourses, at each appointment she was asked about the date of her last period. The patient gave the date of her last

period, and during the appointment the doctor paid attention to the reduction of her body weight. On 12th January, the doctor concluded (after performing a pregnancy test) that the patient was 7 months pregnant. Nevertheless the patient was gullible, she did not find anything wrong in the fact that she had not informed the doctor about her pregnancy and that she had been lying about her periods. Because of the advanced pregnancy, the doctor recommended urgent and necessary gynecological appointment in order to evaluate patient's and her baby's condition. At the same time, the psychiatrist reduced doses of medications: aripiprazole to 7.5 mg/day and olanzapine to 5 mg/day. A gynecologist confirmed advanced pregnancy – 30th week. The patient was referred to a gynecology ward on 3rd February (33rd week of pregnancy), with the diagnose “Preeclampsia, metabolic syndrome, obesity, condyloma acuminatum, premature delivery”. The labor, through C-section because of the somatic state of the patient, took place three days later. The patient gave birth to a male child – weight 1,700g, APGAR at 3 minutes – 8 points. During her stay on the ward, she had psychiatric consultation and was in touch with her psychiatrist. Just after the labor, during the psychiatric consultation in the maternity ward, she received the recommendations of pharmacological treatment – olanzapine 5mg/day. The patient was discharged in a good mental condition, she had the possibility of constant contact with her baby, who was still hospitalized because of prematurity. The patient received the recommendations of the necessity to continue the treatment in the Mental Health Unit. The patient visited the doctor two weeks after the delivery. She did not show productive symptoms. She was recommended to lose weight and the treatment was changed to aripiprazole 7.5 mg/day.

Discussion

The described stories of women prove that a pregnant patient suffering from schizophrenia is a challenge not only for a psychiatrist but also for a gynecologist. There are some general criteria concerning the treatment of pregnant women, however, there should be an individual approach to each patient. It is important to evaluate the risk associated with continuation and discontinuation of treatment during pregnancy. None of the presented patients planned pregnancy. Education of a patient and her partner, preparation to the pregnancy, proper diet, changes in lifestyle, elimination of stimulants, discouraging of planning a baby in the active phase of the illness – all of these are needed to lower the risk of relapse and the influence of drugs on a growing fetus.

Because of the early stage of pregnancy, two patients (case 1 and 2) were recommended to discontinue medications gradually and to remain under constant control of the psychiatrist. The risk associated with discontinuation of medications was evaluated on the basis of analysis of the medical history, earlier episodes and pregnancy. In the case of patient 3, whose pregnancy was confirmed in 7th month, the dose of the medications was reduced. Presented patients, at the moment of getting pregnant, were treated with second-generation medications – olanzapine, aripiprazole, quetiapine. Only one patient (case 2) used haloperidol injections. Two patients (case 1 and 2) were also treated with

mood stabilizers – valproate and carbamazepine. The most data concerning the use of anti-psychotic drugs during pregnancy concern the first-generation drugs, first of all because of their long term presence, the greatest clinical experience, and because they were considered relatively safe [14]. Possible teratogenic effects of mood stabilizers have long been known. According to FDA, carbamazepine is classified within group C (potential risk of congenital defects), while valproate is classified within group D (higher risk of congenital defects) [11]. This is why it is so important to discontinue the medication as soon as possible. Available research concerning second-generation medications show that there is no clear information concerning their teratogenic effect [3, 15–17], and most data concerning the safety of usage during pregnancy comes from case studies or retrospective research. The analysis of the available literature shows that the risk of congenital defects caused by the usage of drugs in the first trimester of pregnancy is: for olanzapine – 0.7–1.4, for quetiapine 0.6–1.7, aripiprazole – 0.5–3.1 [18]. Studies pay attention to the possible metabolic complications, which may have negative consequences for both, the mother and the child. They are mostly observed with reference to olanzapine and clozapine [19]. So far there is no confirmation that the use of quetiapine during pregnancy has an impact on congenital defects. However, this data come mostly from clinical case studies [20]. Similarly, there is no data on the use of aripiprazole concerning its teratogenic effect [21, 22].

Described patients on several occasions received information concerning their mental conditions and recommendations of pharmacological treatment for gynecologists. Pregnancy occurred to be the period of remission of psychotic symptoms, they did not need hospital treatment. First anxiety symptoms and sleep disorders appeared just before the labor (case 1 and 2). In the conducted research, 12% of patients needed hospitalization during pregnancy, 16% of patients needed emergency intervention straight after the labor, 19% needed consultation within the first year after the labor [23]. C-section was performed in all cases. The reasons of interventions were as follows: lack of progress in labor, poor somatic condition of the mother, and psychotic symptoms and conduct disorders. Clinical recommendations state that effective C-section may be a method of choice under the assumption that the risk of possible perinatal complications during natural labor may increase the risk of the development of psychosis in children in the future. There is also no clear data concerning the influence of oxytocin used during the perinatal period on possible puerperal aggravation of psychosis among parturients [24]. Moreover, violent behaviors during the labor may lead to complications [25].

Conducted observations show that schizophrenia is associated with the increased factor of preeclampsia, preterm delivery and low birth weight [4]. Thus, poorer functioning of pregnant women suffering from schizophrenia and paying less attention to their health condition [26] and to gynecological care (case 3) is of some importance here. It was noticed in the research that important factors influencing the newborn's health condition are: age, marital status, compliance to the psychiatrist's recommendations, previous miscarriages, but the patient's mental condition at the time of getting pregnant occurred to be the most important factor [27].

Presented stories of pregnant patients draw attention to the need of constant and early coordinated psychiatric and gynecological care. When there was a dialogue

between the psychiatrist and the gynecologist, there was no need of hospitalization after the delivery. In the case of the first patient, the information from the psychiatrist was unfortunately ignored. Moreover, denial of mental illness by the medical staff and striving for natural delivery had an impact on further hospitalization. One should remember that every hospitalization is a huge stress for a patient. Hospitalization straight after delivery, separation with the baby, may be associated with deterioration of maternal mental state. This is why the information flow, multimonitoring of a patient, would significantly influence safety during the pregnancy period and delivery in schizophrenic patients. The literature lacks research concerning interdisciplinary cooperation for a woman suffering from mental disorder during her pregnancy. Attention is only drawn to the fact that there is a need of such care [28, 29].

Cooperation between doctors of various specialties seems to be obvious, however, our experiences show that in a number of cases such a cooperation does not exist. Pregnant patients suffering from schizophrenia who get into the maternity ward often do not have psychiatric consultations that monitor their mental condition in the perinatal period. It also happens that there is nothing about schizophrenia in their hospital records, and the lack of breastfeeding is described using a formula “on mother’s request”, without a notice of the need of pharmacological treatment due to mental illness.

It would be important to take steps in order to develop new recommendations in the treatment of pregnant women suffering from mental disorders, based on gynecology-obstetrics and psychiatric care at the same time. There is also a lack of specialist care programs for pregnant women who are mentally ill. Recommendations should include data important for both sides, which would influence better monitoring of medical condition of both the mother and the child, and should be included in medical documentation (gynecological and psychiatric one).

Information for a gynecologist (from a psychiatrist) should concern:

- (1) the former course of the illness, necessity of hospitalization, cooperation or the lack of cooperation in patient’s treatment;
- (2) mental condition during former pregnancies and the patient’s actual well-being;
- (3) the possibility of the cessation of medications at least in the first trimester, or the exact data on the necessary pharmacotherapy;
- (4) mental condition around the 36th week of pregnancy in order to plan the labor (natural delivery, c-section);
- (5) the necessity of psychiatric consultation before and after the labor whatever is the patient’s mental condition.

Information for a psychiatrist (from a gynecologist) should include:

- (1) gynecological assessment at the beginning of pregnancy;
- (2) the assessment of conducted tests;
- (3) the assessment of embryo development;
- (4) coexistence of other diseases (hypertension, gestational diabetes, impairment of thyroid functions) which may influence mental condition;
- (5) planning the date and the mode of delivery.

Conclusions

Care for a patient treated for schizophrenia and being pregnant is still a huge challenge. The disorder itself influences the quality of preparation to pregnancy, results in the lower consciousness concerning healthy lifestyle and the need to control general health condition. Lack of possibility, in most cases, of planning pregnancy is associated with further complications concerning its further development. Moreover, treatment with antipsychotic medications is always associated with the risk concerning fetus' well-being, whereas treatment discontinuation may result in relapse. New-generation neuroleptics, which are most commonly used by young patients in reproductive period, are still not entirely tested, and the choice of the medication is made on the basis of lack of data concerning possible threats for a fetus rather than by its confirmed safety. This is why there is a need to decrease the potential threats associated with the patient's mental condition, and the influence of medication on pregnancy. It is only possible owing to a constant cooperation between doctors who take of the patient, both psychiatrists and gynecologists-obstetricians. This is when we may talk about providing full assistance to such a specific patient like a pregnant woman suffering from schizophrenia.

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