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## Review article

# Treatment of psychosis during pregnancy – a case report and a mini-review

Nielsen RE. Treatment of psychosis during pregnancy – a case report and a mini-review.

**Objective:** Describe clinical problems in treating a patient with psychotic symptoms during pregnancy by presenting a case report, and review the current evidence on antipsychotic drugs during pregnancy.
**Methods:** The review consists of a non-systematic clinical review of current data on treatment with antipsychotics during pregnancy. The case, a 27 year old female initially diagnosed with posttraumatic stress disorder (PTSD) after a rape and emotionally unstable personality disorder, illustrates some of the common challenges a clinician meets. The patient initially discontinues all treatment as she is unsure if the drugs could have a teratogenic effect and is changed to a treatment that is regarded as safe during pregnancy.
**Results:** The current data supports treatment with chlorpromazine although there is a risk of side effects, e.g. extrapyramidal symptoms and hypotension, but also treatment with olanzapine and risperidone. If the patient is currently treated with clozapine, this treatment should be continued, due to clozapines unique efficacy profile. Blood monitoring for six months after birth is recommended when the newborn has been exposed to clozapine treatment.
**Conclusion:** Current evidence on treatment with antipsychotics during pregnancy is sparse, but not treating is associated with increased risks compared to treatment.

**René E. Nielsen**

Unit for Psychiatric Research, Aalborg Psychiatric Hospital, Aarhus University Hospital, Aalborg, Denmark

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René Ernst Nielsen,
Unit for Psychiatric Research, Aalborg Psychiatric Hospital, Aarhus University Hospital, Mølleparkvej 10, 9000 Aalborg, Denmark.
Tel: +45 28 72 29 62;
Fax: +45 72 13 72 35;
E-mail: ren@rn.dk

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### Summations

- Chlorpromazine is the safest antipsychotic drug to use during pregnancy.
- Risperidone and olanzapine can be used during pregnancy.
- In clozapine-treated patients, a switch in antipsychotic drug treatment is not recommended.

### Considerations

- The data quality on safety of antipsychotics during pregnancy is lower than that for other topics.
- The review is done as a clinical review, not as a systematic review.

### Introduction

Treatment with psychopharmacological drugs during pregnancy is often associated with great concern from the patient, her family and often also from the clinician. The level of evidence for psychopharmacological treatment during pregnancy is generally poor as randomised controlled clinical trials of safety and efficacy in pregnant women are not acceptable due to ethical reasons, e.g. putting an unborn child at risk by giving a potentially teratogenic drug (1,2). Our current knowledge primarily stems from registry studies, prospective

non-randomised trials, case reports and data gathered from reports submitted by clinicians to the pharmaceutical companies (3).

In this illustrative case report, we will show some of the clinical problems in treating a patient with psychotic symptoms during pregnancy, and we will also review the current evidence on antipsychotic drug treatment during pregnancy in general.

## Case report

The patient is a 27-year-old female initially diagnosed with post-traumatic stress disorder after a rape and emotionally unstable personality disorder. She is currently in a stable relationship and has a son with her current partner.

For the past 7 years, she has been followed in a community outreach team, currently in a team with the main focus on treatment of psychotic disorders. During this 7-year period, she has been admitted 10 times, of which several have been compulsory admissions. During these hospitalisations, she has initially been violent, both to nursing staff and also herself, and compulsory measures have been required. Her relapses are characterised by sudden onset of symptoms, with a fast deterioration to manifest psychosis.

Due to a general lack of energy and increased nausea, she consults her general practitioner who diagnoses a pregnancy. The patient initially discontinues all medication, consisting of aripiprazole 30 mg a day and escitalopram 10 mg a day. She is persuaded by her psychiatrist to initiate treatment with 4 mg of risperidone and 20 mg of citalopram. Routine scans are planned in collaboration with the obstetric department to check for malformations and to establish a more secure gestation age.

During week 6–8 of gestation, the patient develops increasingly frequent disaster thoughts, e.g. husband struck down by lightning. She also develops depressive symptoms, e.g. decreased mood, increased tiredness, decreased social activity, lack of interest, anhedonia and suicidal ideations. In an attempt to stabilise the patient, citalopram is increased to 40 mg per day, and symptoms decrease slightly with regards to suicidal ideations and anhedonia, but other symptoms like decreased mood and increased tiredness persist. The persisting symptoms could have been caused by the pregnancy or by residual symptoms from her depressive episode (4).

During the 27th week of gestation, the patient is admitted to the gynecological department due to pelvic joint pain. The patient's state worsens, probably as a result of the increased stress of the pregnancy, the constant psychical pain and decreased mobility, and she experiences several shorter episodes of psychotic symptoms, e.g. she relives the rape vividly, suffering increasingly due to bothersome auditory hallucinations. The patient's antipsychotic drug treatment is increased with risperidone 0.5 mg as needed in combination with her 4 mg of risperidone. As this does not stabilise the patient, treatment is intensified with a dose increment of 2 mg of risperidone to a total of 6 mg of risperidone in combination with diazepam as needed.

During week 38 of gestation, the patient delivers a healthy child by caesarean section. The child experiences shivering, irritability and crying during the initial days after birth. This is monitored, but not treated, and is probably a result of the selective serotonin reuptake inhibitor treatment (5).

## Discussion

This case illustrates some of the common problems in treatment during pregnancy. From the clinician's perspective, the choice to use pharmacological treatment for psychosis during pregnancy depends on an assessment of risks associated with the treatment and an evaluation of the risks associated with not initiating pharmacological treatment, e.g. worsening the patient's symptoms and general state. The patient and her immediate family are often concerned with the risks associated with continuation of medication, e.g. risks involved with the foetus exposure to medication, and has very little focus on the risk associated with discontinuation. To avoid sudden discontinuation of treatment in patients already treated, it is helpful for the clinician beforehand to discuss the possibility of pregnancy with female patients of fertile age. The risk of unplanned pregnancies is increased in females with psychosis disorders, and up to 60% of females with a psychosis disorder becomes a mother (6–8). The prevalence of psychotic symptoms during pregnancy is unknown unlike as for e.g. depressive symptoms during pregnancy (9). However, there is an increased risk of relapse, as high as 65% in pregnant patients with schizophrenia if treatment with an antipsychotic drug is discontinued (10). The clinician should explain the risks of treatment associated with the current medication if the patient gets pregnant; discuss possible other, safer, medications; and give explanations as to why sudden discontinuation of drug treatment poses a risk to the unborn child, e.g. increased risk of self-neglect, nutritional deficiencies, decreased antenatal care visits and increased use of substances (11). Information concerning the baseline risk of 1–3% of malformations in all pregnancies should be provided for the patient (6). If a pregnancy wish already exists, a thorough plan should be made initially in collaboration with the patient's own general practitioner and the psychiatrist. Anticonception should be discussed



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with the patient to ensure effective anticonception until necessary changes to the patient's pharmacological treatment has been made and a period has past to ensure that the patient does not relapse.

In patients already pregnant, collaboration among the general practitioner, the psychiatrist and the obstetric department should be established.

When treatment needs to be initiated in patients already pregnant, knowledge of effect or side effects from previous treatment attempts could guide the clinician in choice of treatment. If there is no treatment history, the clinician should be guided by the recommendations in the clinical overview below.

The patient's family should be included in the preparations and planning of the treatment and follow-up before, during and after pregnancy. A strong cooperation with the family will most often minimise concern and stress in the patient and her family, probably reducing the risk of relapse.

Besides optimizing the pharmacological treatment of the patient, focus on social support after birth is also crucial (1). A whole new lifestyle with increased expectations and demands, from the patient, the family and the newborn, can increase the patient's stress and make the patient more vulnerable to a relapse of psychotic symptoms.

In the paragraphs below, specific issues concerning antipsychotic drug treatment will be evaluated and clinical recommendations will be given.

### Atypical antipsychotic drugs

The patient was initially treated with aripiprazole, but the current data consists of only four case reports (12–15) not showing increased risk of adverse events during pregnancy. The data is still inconclusive, and the patient was switched to another drug.

Treatment with risperidone is better described, and data regarding several hundred pregnancies have been published (1,16). In these cases, malformations have been reported but most often in cases where the patients were treated with concomitant medication with a known teratogenic side effect (1). No specific pattern of malformation, which could have pointed towards a specific teratogenic effect of risperidone, has been described (1).

Data concerning the use of olanzapine during pregnancy consists of more than 400 cases (1). No general increase in malformations is seen, except for a vague signal concerning increased risk of neural tube defects (17).

Clozapine and quetiapine have both been used, and more than 200 cases on each have been reported (1). No specific pattern of malformations has been shown, and no increase above the baseline malformation rate has been described (1,18). Clozapine has a potential toxic effect on the bone marrow. Monitoring of the white blood panel is recommended as described in current guidelines for the mother, but monitoring of the white blood panel for 6 months after birth has also been recommended for the exposed child (19).

Several have described an increased risk of preterm birth in patients treated with antipsychotic drugs, but it is unknown if this is a specific effect of the treatment or an effect of the psychotic disorders itself (20,21). The increased risk of preterm birth is not a uniform finding (22).

Other atypical antipsychotic drugs, amisulpride, asenapine, paliperidone, iloperidone, ziprasidone and sertindole, have not been used adequately to meaningfully discuss risks of treatment during pregnancy (1,6).

The risk of metabolic complications in the foetus has been discussed and investigated, and current data are inconsistent, with both increases and decreases in birth weight of the child being described, when the mother is treated with second generation antipsychotic drugs during pregnancy (20,23,24). An increased risk of hypoglycaemia in the newborn is seen, when the mother has been treated with second generation antipsychotic drugs during pregnancy (23,24). The metabolic side effects of second generation antipsychotic drugs are well known (25,26), and thorough monitoring of the mother is needed, as the risk of gestational diabetes is increased (1).

### Typical antipsychotic drugs

Typical antipsychotic drugs have been used for a longer time, and data concerning their safety is more abundant, although data predominately is on low dose treatment as used to control hyperemesis gravidarum (1).

The typical high-potency antipsychotic drug haloperidol has been tested in a recent multicentre study showing no increased risk of malformations (27), however, on a small sample. Previous data has showed some signals on increased risk of limb defects (1).

Middle-dose typical antipsychotics, especially perphenazine, are used increasingly as effectiveness has been shown to be similar to atypical antipsychotic drugs (26). Previously, perphenazine has been described as a safe drug during pregnancy, but data on perphenazine alone is limited (1), although phentiazines as a group is pretty well documented (18).

Several studies have been conducted concerning the safety of chlorpromazine during pregnancy (1,22,28–30). A signal pointing towards increased risk of cardiac malformations was seen but



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was not statistically different from baseline risk (1). The main problem with chlorpromazine treatment is hypotension and extrapyramidal symptoms in the mother and the newborn (18,31–33).

Prochlorperazine, trifluoperazine and fluphenazine have been used routinely in pregnant females but most often in low dose treatment to control hyperemesis gravidarum (1).

Data on the remaining typical antipsychotic drugs is not sufficient to discuss risks concerning treatment of pregnant women in a meaningful way.

So far, data on neurodevelopmental status of children exposed to antipsychotic drugs during foetal life is limited (1,6,34). Typical antipsychotic drugs have been investigated, and no neurodevelopmental problems have been described (35,36), although these data are not conclusive (34).

## Conclusions

In patients not previously treated with antipsychotic drugs, data suggests treatment with chlorpromazine as first choice as data on this drug is most abundant. Treatment with risperidone or olanzapine is also considered safe, although risk of metabolic complications in the mother and child should be taken into account and monitored.

In patients already in treatment with antipsychotic drugs, consideration to the risk involved in a medication change should be taken. As described previously, data is most abundant for chlorpromazine, but current available data has not shown increased risk when treating with risperidone or olanzapine. Circumstances, e.g. previous treatment trials with risperidone and olanzapine lacking efficacy, could necessitate continued treatment with the already instituted antipsychotic drug under close monitoring.

In patients already in treatment with clozapine, treatment should be continued because of its unique efficacy and the currently available data showing no increased risk of malformations. Weekly monitoring of the white blood panel for the first 6 months after birth is recommended.

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