CASE REPORT

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The Use of Clozapine During Pregnancy And Lactation: A Case Report

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Abstract

Antipsychotic medications are frequently used in clinical practice. Clozapine is considered to be the most effective antipsychotic treatment in patients with treatment-resistant schizophrenia. Although clozapine has been available in the market for a long time, safety data on its usage during the lactation period are very limited. The current report presents the short-term clinical outcome of infants exposed via breastfeeding to maternal clozapine at 75-mg/day.

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INTRODUCTION

Pregnancy and lactation are major challenges in the pharmacological treatment of women with clinically significant psychopathology during reproductive period. It is well known that discontinuation of pharmacological treatment during the perinatal period can cause recurrence of psychiatric disorders. Breast milk is an important source of nutrition for infants during the first two years of life, particularly in the first 6 months [1]. It has been reported that breastfeeding is associated with reduced morbidity, mortality and occurrence of illnesses throught the positive effects of breast milk on the immune, gastrointestinal and endocrine systems [2,3]. Therefore, breastfeeding has noteworthy lifetime biological and psychological benefits for the infants [4].

Antipsychotic drugs are frequently used in the treatment of major psychiatric disorders such as bipolar disorder, schizophrenia and related psychotic disorders. Clozapine, which is a SGA, is considered to be the most effective pharmacological agent in the treatment of patients with schizophrenia, second-generation antipsychotics (SGA), even when the patients are refractory to other antipsychotic medications [9]. Severe adverse events, especially agranulocytosis, restricts the usage of clozapine in general clinical practice, although its benefits are markedly greater compared to possible detrimental effects [6,7]. Limited available data suggest that the use of clozapine during pregnancy appears to be relatively safe [8,9]. Similar to other psychotropic drugs, all antipsychotics are excreted into the breast milk to varying degrees [10]. However, the available data suggest that adverse events associated with in breastfed infants either are either not observed or are minimal and transient [11]. Owing to limited data and the potential serious risk of agranulocytosis, there are concerns regarding the use of clozapine during lactation [11-13]. Additional scientific data are needed to definitively decide its usage during lactation. In this report, a female patient who used clozapine from pregnancy to lactation was presented.

CASE REPORT

A 34-year-old pregnant woman at the 8th-week of gestation was referred to the perinatal psychiatry outpatient clinic from another hospital. During the psychiatric interview, the patient was diagnosed with schizophrenia according to the Structured Clinical Interview for the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) (SCID-I)[14] for 9 years. The patient had a history of four times hospitalization due to active symptoms. The patient reported that in past, there was significant persistence of the symptoms despite the usage of binary antipsychotic combinations including olanzapine, quetiapine, risperidone, amisulpride, haloperidol, flupenthixol, zuclopenthixol, aripiprazole and paliperidone. During the

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last hospitalization 5 years previously, clozapine at 200 mg/day was administered to the patient. The dosage was gradually decreased due to remission in the symptoms following the initiation of clozapine. The patient was taking clozapine at 75 mg/day for 2 years.

The patient did not present with any symptoms of schizophrenia other than mild negative symptoms at the first assessment. After a discussion with the patient and her husband about the risks and benefits of continued and discontinued treatments, it was decided to continue prophylactic treatment with clozapine at 75 mg/day during the pregnancy and the postpartum period. Written informed consent was obtained from the patient and her husband. The baby was born with elective caesarian-section without any complications. The patient wanted to breastfeed her baby despite the possible risks of clozapine in the breastfed infant. For this reason, clozapine was continued at the same dosage. The patient did not report any adverse events in the baby in the follow-up period of 6-months. In addition, the baby was examined monthly by a pediatrician with regards to physical well-being. Hemogram tests were performed for every 2-weeks in the infant and no hematological side effects of clozapine were detected. After 6-months of the postpartum period, the patient did not consult with the the outpatient clinic for routine controls.

DISCUSSION

Similar to the present case, Imaz et al. [15] reported that clozapine had no acute toxicological effects such as agranulocytosis and seizure in the newborns. Previously, two case reports [16,17] and a case series [18] describing clinical outcomes in the infants of a total of 6 breastfeeding women prescribed with clozapine have been published in the literature. Mendhekar et al. [16] reported delayed speech development in a 5 year-old child exposed to clozapine at 100 mg/day for 1 year via breastfeeding. Barnas et al. [17] reported no psychomotor abnormalities up to 6 months of age (dose=100 mg/day). Dev and Krupp [18] examined adverse events in breastfed infants of 4 women who use clozapine and noted agranulocytosis in one infant and lethargy in one infant. Thereby, the authors reported adverse events in 50% of breastfed infants exposed to clozapine. In the current case, the patient used clozapine at 75 mg/day and no any psychomotor or hematological effects in the infant were observed during the 6-month follow-up period. The risk of agranulocytosis is approximately 1% and is highest in the first 20-weeks of consumption of clozapine in adults [6]. In addition, the risk of seizure that is known to be correlated with daily dose and the plasma levels of drug [19] is another potential serious effect of clozapine in adults. Therefore, although the relative infant dose of clozapine appears to be low, its usage during lactation can be associated with a number of potential complications, especially in high doses [12].

In this case, blood levels of clozapine in the mother and breastfed infant were not examined. Despite lack of such data indicating exposure degree in the infant, the current case report presents additional data on the maternal use of low-dose clozapine without any adverse events in newborns and the breastfed infants. The use of clozapine may be inevitable in schizophrenic patients who are resistant to other treatments and are remitted solely with this antipsychotic. In that case, the breastfed infant should be closely monitored. However, further case reports and especially studies are urgently need.

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