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Neonatal outcomes in pregnant women with untreated and treated panic disorder

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ABSTRACT

Objective: The objective of the present study was to compare neonatal outcomes including gestational age, birth weight and hospitalization of newborns of pregnant women with treated with antidepressants and untreated panic disorder.
Methods: The study sample included 146 pregnant women (44 patients with panic disorder treated with antidepressants, 52 patients with untreated panic disorder, and 50 healthy controls). Panic disorder was diagnosed by means of the Structured Clinical Interview for the Diagnostic and Statistical Manual of Mental Disorders, *Fourth Edition*.
Results: The highest proportions of preterm birth (28.8%), low birth weight (34.6%) and requirement of neonatal care (25.0%) were observed in infants of untreated patients. Pharmacotherapy group and control subjects had similar neonatal outcomes. Compared with infants of healthy subjects and the pharmacotherapy group, infants of untreated patients had significantly lower birth weight and gestational age at delivery. In addition, newborns of untreated patients had higher rate of hospitalization at the neonatal care unit.
Conclusion: Our results suggest that treatment with pharmacotherapy of panic disorder during pregnancy may have beneficial effects on the risk of negative neonatal outcomes due to maternal panic disorder in the infants.

1. Introduction

Although anxiety disorders are more frequently observed than depressive disorders in pregnant women [1,2], in contrast to depression, the number of investigations that have addressed the effects of anxiety disorders on pregnancy is very limited. Interest in anxiety disorders, however, has increased recently with large numbers of studies published in the last decade [3]. Prenatal stress and anxiety disorders are known to be potential risk factors for postpartum depression [3,4].

Panic disorder (PD) is a relatively frequent anxiety disorder, the onset or course of which may be affected by pregnancy [5–8]. Previous studies have suggested that the prevalence of PD in the pregnancy period varies from 0.2% to 5.2% [2,6–12]. A few available studies revealed no difference between pregnant and nonpregnant women with regard to the prevalence of PD [7,8]. PD may onset in the pregnancy period in up to 53.8% of patients, and the symptoms of preexisting PD may worsen, improve, or remain unchanged during pregnancy [3].

General stress or anxiety due to PD during pregnancy may negatively affect resistance of placental blood flow, birth outcomes, sleeping or feeding of the baby in the perinatal period, as well as hyperactivity/attention, cognitive-behavioral and emotional development of children [13–20]. In addition, limited data have suggested that untreated PD during pregnancy is specifically associated with a higher risk of cleft lip with or without cleft palate and multiple congenital abnormalities [21], shorter gestational age, high risks of preterm birth and small for gestational age babies [22,23]. Moreover, PD appeared to have more negative effects on birth weight compared to major depression and generalized anxiety disorder [24].

Intrauterine growth restriction and preterm birth are important health issues, because they are related to an increased risk of morbidity and mortality in the neonatal period and later years [25–28]. Various studies have also suggested that lower gestational age and lower birth weight (LBW) are associated with intraventricular hemorrhage and necrotizing enterocolitis [29–31]. It is unclear whether treatment of PD during pregnancy may prevent its negative effects on birth weight

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and gestational age of the infants. A population-based study has suggested that appropriate treatment of PD during pregnancy had a protective effect on risks including congenital abnormalities [21]. To our knowledge, there is no a similar published study about birth weight and gestational age.

The treatment options available for pregnant women with psychiatric diagnoses are important considerations in the clinical practice. Despite known effectivity of some psychotherapeutical methods especially cognitive-behavioral therapy, pharmacotherapy with antidepressants including selective serotonin reuptake inhibitors (SSRIs), tricyclic antidepressants (TCAs) such as imipramine and clomipramine, and venlafaxine is frequently used in the treatment of panic disorder [32,33]. In this present study, we aimed to examine and compare the effects of pharmacotherapy and untreated PD with regard to birth outcomes including gestational age, birth weight and requirement of neonatal care.

2. Methods

2.1. Sample

A total of 96 pregnant women with PD (44 patients in pharmacotherapy group and 52 patients in untreated group) examined at the Psychiatry Outpatient Clinic of Meram Faculty of Medicine of Necmettin Erbakan University in Konya, Turkey, and the Perinatal Mental Health Outpatient Clinic of Bakırkoy Research and Training Hospital in Istanbul, Turkey were included in the study and 50 control healthy pregnant women.

Inclusion criteria for the study were as follows: (1) maternal age of at least 18 years, (2) existence of at least 8-week follow-up period for pharmacotherapy group, (3) the first examination before the 27th gestational week (at the first or second trimesters), (4) the Clinical Global Impression-Improvement Scale (CGI-I) after the treatment (for pharmacotherapy group) should be 1 (very much improved) or 2 (much improved) after at least 8 weeks of treatment.

Exclusion criteria for the study were as follows: (1) a history of a medical illnesses (e.g., endocrine abnormalities, cardiovascular and pulmonary system diseases, neurological disease, and metabolic disease) or pregnancy related complications (e.g., gestational hypertension, imminent abortion, placenta previa and other placental abnormalities, vaginal bleeding, and gestational diabetes) (2) any fetal malformation, (3) existence of maternal infection which can negatively affect fetal growth (e.g., toxoplasma, rubella, cytomegalovirus, herpes simplex, mycoplasma, chlamydia), (4) a history of bipolar affective disorder, schizophrenia or related psychotic disorders, (5) the existence of depression or anxiety disorders comorbid with PD (6) reported smoking or alcohol consumption, (6) mental retardation, (7) usage of any psychotropic medication other than antidepressants and low-dose benzodiazepines for a short time (1 week or less) for the pharmacotherapy group, (8) exposure to any psychotropic medication for the untreated and control groups, (9) receiving alternative treatments to pharmacotherapy such as cognitive-behavioral therapy for three study groups and (10) the existence of any psychiatric disorders for the control group.

2.2. Assessments

A semistructured form developed by the authors was used to assess sociodemographic features and medical history. PD was determined by means of the Structured Clinical Interview for the Diagnostic and Statistical Manual of Mental Disorders, *Fourth Edition* (DSM-IV) (SCID-I) [34]. The gestational age at delivery was calculated on the basis of the date of last menstruation. Birth weight and hospitalization of the infants in the neonatology care unit were obtained from the hospital records and from reports from the mother. Preterm birth was defined as birth that occurred at less than 37 gestational weeks. The term of LBW referred to infants born weighing less than 2500 g [35]. The efficacy of pharmacotherapy in the treated group was measured by CGI-I [36]. CGI-I was not performed in untreated group.

2.3. Procedures

The study procedure was approved by the ethics committee of Necmettin Erbakan University, Faculty of Medicine. The study was based on naturalistic observational clinical data screened from records of the outpatient clinics. Sociodemographic characteristics and obstetrical features were recorded during psychiatric evaluations. Psychiatric examinations and treatments were conducted by psychiatrists with at least 4 years of experience in psychiatric disorders, and diagnostic instruments. The study did not lead to any interference in the treatments of the patients. The treatment was decided with consent of the patients, their relatives and the psychiatrist. The follow-up visits in the treated groups ranged from 1 week to 4 weeks according to the patient's psychiatric status.

2.4. Statistical analyses

The data were analyzed using the Statistical Package for the Social Sciences (SPSS), version 16.0, for Windows (SPSS Inc., Chicago, IL). Categorical variables among the study groups were compared using the chi-square (χ^2) test and Fisher's exact test. For comparisons of continuous variables among the study groups, one-way analysis of variance (ANOVA) was performed. Tukey's honestly significant difference (HSD) test was used for post hoc multiple comparisons. All significant levels were 2-tailed and set at the level of 0.05.

3. Results

The mean age of the sample (n = 146) was 29.61 ± 5.33 years. Of the participants, 99.3% (n = 145) were married, 52.1% (n = 76) had completed primary school and 82.9% (n = 121) were unemployed. The proportion of primigravidae and history of abortion in the total sample were 27.4% (n = 40) and 28.8% (n = 42), respectively. The mean number of children was 1.44 ± 1.15 and 67 (45.9%) of the infants were of females. The delivery type was surgical in 99 (67.8%) women. The antidepressants prescribed in the pharmacotherapy group included imipramine in 13 (29.5%) patients, sertraline in 13 (29.5%) patients, citalopram in 11 (25.0%) patients, escitalopram in 2 (4.5%) patients, mirtazapine, venlafaxine, fluoxetine, sertraline plus mirtazapine and citalopram plus mirtazapine in 1 patient (2.3%). The doses of antidepressants were 20 mg/d for citalopram, 10 mg/d for escitalopram, 50 mg/d for sertraline, 15–30 mg/d for mirtazapine alone, 7.5–15 mg/d for mirtazapine together with sertraline and citalopram, 75 mg/d for venlafaxine, and 25–50 mg/d for imipramine. Eleven of 44 patients received low-dose additional lorazepam at 0.5–1.5 mg/day. The mean duration of lorazepam treatment was 4.54 days. In the treatment groups (total n = 44), the mean gestational age at the first evaluation was 15.34 ± 5.51 weeks (range = 5–26), and the mean follow-up period was 16.72 ± 5.70 weeks (range = 8–29).

There were no significant differences among the three study groups with regard to age, educational level, employment status, economic level, history of abortion, gender of baby, number of children, type of delivery or proportion of primigravidae (Table 1). Table 2 shows the mean gestational age, the mean birth weight, the rate of preterm birth, LBW and hospitalization at the neonatal care unit in the groups. Statistical analyses indicated that the study groups had statistically significant differences for these parameters. The most high rates of preterm birth (28.8%), LBW (34.6%) and hospitalization at the neonatal care unit (25.0%) were exist in infants of untreated women. Similarly, untreated women had infants with shortest gestational age (37.52 ± 1.79 weeks) and lowest birth weight (2809 ± 498 g).

Compared to the control group, newborns of untreated patients had significantly higher rate of preterm birth (P = 0.000), LBW (P = 0.00)