Effect of intravenous immunoglobulin treatment on pregnancy and postpartum-related relapses in multiple sclerosis

Abstract

Acute exacerbations may complicate the course of pregnancy and the postpartum period in patients with relapsing-remitting multiple sclerosis (RRMS). To evaluate relapse rate and the effect of immunomodulatory treatment with intravenous immunoglobulin (IVIg) during pregnancy and the postpartum period we retrospectively analysed the data of 108 pregnant RRMS patients. Group I patients were not treated, Group II patients were treated with IVIg 0.4 g/kg body weight/day for 5 consecutive days within the first week after delivery with additional booster doses of 0.4 g/kg body weight/day at 6 and 12 weeks postpartum (defined as 12 weeks after labor), and Group III patients were treated continuously with IVIg during gestation and the postpartum period (0.4 g/kg body weight/day for 5 consecutive days within the 6–8 weeks of gestation with additional booster doses of 0.4 g/kg body weight/day once every 6 weeks until 12 weeks postpartum). All patients underwent antenatal care and fetal ultrasonographic surveillance examinations. Relapse rate per woman per year during the pregnancy and the postpartum period as well as neonatal outcome data and IVIg related adverse events were analysed.

Relapse rate per woman per year for patients treated with IVIg for the whole pregnancy and postpartum period (Group III, N = 28) compared with the untreated Group I patients (N = 39) were as follows: first trimester 0.43 vs. 0.72, second trimester 0.15 vs. 0.61, third trimester 0.0 vs. 0.41, and postpartum period 0.28 vs. 1.33 (p < 0.05). Patients treated with IVIg only during the postpartum period (Group II, N = 41) also showed a decrease in relapse rate compared with untreated Group I patients, 0.58 vs. 1.33 (p = 0.012). The mean maternal age, disease duration, gestational age at delivery and fetal delivery weight did not significantly differ between the three groups. Mode of delivery, obstetrical complications, the use of epidural analgesia and breast-feeding, did not affect postpartum relapse rate. No severe adverse events were associated with IVIg treatment either during the pregnancy or postpartum period for the patients and newborns.

We conclude that in RRMS patients IVIg treatment could be considered as an optional treatment to reduce the incidence of pregnancy and postpartum-related relapses. Further randomized double-blind studies are needed to confirm our findings.

Key words multiple sclerosis · pregnancy · postpartum period · intravenous immunoglobulin
Introduction

Multiple sclerosis (MS) is more prevalent among women and frequently occurs during the childbearing years. In 85% of patients the disease is characterized by a relapsing-remitting course during which new neurological symptoms appear or existing symptoms worsen for a period of 2–8 weeks, and thereafter partial or complete recovery occurs [12]. It is well established that with each additional relapse, the probability of complete clinical remission decreases, and neurological disability and handicap are liable to develop [6, 8, 17]. The rate of relapse has been thought to decrease during pregnancy and increase in the postpartum period. The Pregnancy in Multiple Sclerosis (PRIMS) study, recently published [5], was the first large-scale prospective study that evaluated the effect of pregnancy and the postpartum period on the course of the disease in 254 women with MS. The results demonstrated that the rate of relapse declines during pregnancy, especially in the third trimester, and increases during the first three months postpartum before returning to the pre-pregnancy rate. The increased relapse rate during the postpartum period and the sustained pre-pregnancy year relapse rate during the first and second trimesters of pregnancy prompt serious consideration as to the need for MS patients to be treated during the pregnancy and postpartum period.

We have previously reported our experience in the treatment of MS patients during the pregnancy or postpartum period with intravenous IgG immunoglobulin (IVIg) [2, 13]. In the current study we retrospectively evaluated relapse rate/woman/year during the pregnancy and the postpartum period and the efficacy and safety of IVIg treatment in pregnant RRMS patients.

Methods

Patients

We retrospectively evaluated the data of pregnant RRMS female patients (N = 108), followed at the Multiple Sclerosis Center, Sheba Medical Center, Tel-Hashomer, Israel. Eligible subjects for analysis were patients with definite MS according to Poser criteria [15], a relapsing-remitting disease course, a positive β-HCG test and a first trimester ultrasound scan confirming the date of gestation. Gestational period was defined as 52 weeks from the last menstrual period composed of 40 weeks of gestation and 12 weeks of postpartum period. Immunomodulatory treatments were discontinued for at least three months prior to gestation. It should be noted, however, that when the decision to become pregnant was made and treatment was discontinued, the period till patients became pregnant varied and further increased the time that patients were without treatment. The mean time patients were free from immunomodulatory treatment was 8.2 months. This could suggest that discontinuation of immunomodulatory treatment prior to gestation may increase the relapse rate in the pre-pregnancy year as patients are not treated at least during part of this year. Data concerning the gestational period, fetal ultrasound examinations, delivery and neonatal outcome were obtained from the medical discharge reports. Demographic, neurological and laboratory data were obtained from the MS Center computerized database. A relapse was defined as the onset of new or worsening of preexisting neurological symptoms persisting for at least 48 hours, in the absence of fever and immediately preceded by a relatively stable or improving neurological state of at least 30 days. The Pregnancy and Postpartum Status Scale (EDSS) score [11], EDSS. Laboratory tests included blood count, chemistry and urine analysis.

Study design

The study population included three groups of pregnant RRMS patients analysed as follows: Group I patients who were not treated during the pregnancy or postpartum period; Group II patients who received IVIg (0.4 g/kg body weight/day for 5 consecutive days within the first week after delivery with additional booster doses of 0.4 g/kg body weight/day at 6 and 12 weeks postpartum), and Group III patients who were treated continuously with IVIg during gestation and the postpartum period (0.4 g/kg body weight/day for 5 consecutive days within the 6–8 weeks of gestation with additional booster doses of 0.4 g/kg body weight/day once every 6 weeks until 12 weeks postpartum). The decision to treat patients with IVIg was based on the willingness of the health insurance provider to supply the treatment. The study was approved by the Institution Review Board. All patients gave written informed consent to IVIg treatment.

Statistical Analysis

Demographic and clinical data are presented as mean ± SD. Relapse rates per woman per year during each trimester of pregnancy and the postpartum period were compared with the relapse rates during the pre-pregnancy year by the paired t-test, and p value <0.05 was considered statistically significant. Data were analyzed using the SAS software (SAS Institute, Cary North Carolina).

Results

Patients characteristics

A total of 108 pregnant women (mean age 28 ± 3.3 years; range 26–38) with RR MS were included in the analysis. There were 39 patients in Group I, 41 in Group II and 28 in Group III. Singleton pregnancies occurred in 107 patients and one patient had a twin gestation. Three patients (2.7%) developed gestational diabetes and seven (6.4%) had pregnancy induced hypertension. All patients delivered live births, no early or late abortions were observed. One hundred and four women had term pregnancies. Mean delivery age was 38 ± 3 weeks; four patients (3.7%) had a premature labor that occurred after less than 36 weeks of gestation. Ninety-three patients had normal vaginal delivery while fifteen (13.7%) had a cesarean section. Epidural analgesia was administered to 79.6% of the patients.

The clinical and demographic data of the three study groups are presented in Table 1. There were no significant differences between maternal age, parity, delivery age, birth weight and disease duration between these