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Clinical follow-up of pregnancy in myasthenia gravis patients

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Abstract

This study aimed to analyze the outcome and impact of pregnancy in women with myasthenia gravis (MG). Obstetric and clinical data were retrospectively analyzed before, during and after pregnancy. Predictors of outcome were studied. We included 35 pregnancies from 21 MG patients. In the course of MG symptoms in 30 pregnancies with live births, 50% deteriorated (mainly during the second trimester, $p = 0.028$), 30% improved, and 20% remained unchanged. The deterioration group had more frequent abnormal repetitive nerve stimulation (RNS) ($p = 0.028$) and lower myasthenia gravis composite (MGC) scores ($p = 0.045$) before pregnancy. The improvement group was associated with higher MGC scores ($p = 0.012$) before pregnancy. The no-change group was associated with longer duration of MG ($p = 0.026$) and normal RNS ($p = 0.008$) before pregnancy. The course of MG in the second pregnancy was different from that in the previous pregnancy in 65.3% of cases. Obstetric complications were reported in 20 pregnancies; the most common was preterm premature rupture of membranes (PPROM) (25.8%), and the most severe were abortion (11.4%) and fetal death (2.9%). Most of the patients delivered via caesarean section (66.7%). Spinal anesthesia was performed in 73.3%. Transient neonatal myasthenia gravis occurred in 12.9% of live-born infants, and no predictors were found. In conclusion, severity and duration of MG, RNS and treatment influence MG and pregnancy. Pregnant MG patients have greater rates of PPROM and caesarean delivery. Our data suggest that duration of MG, MGC and RNS before pregnancy may be useful in helping to predict the course of MG during pregnancy.

Keywords: Myasthenia gravis; Pregnancy; Abortion; Caesarean; Treatment

1. Introduction

Myasthenia gravis (MG) is an acquired autoimmune disorder causing neuromuscular junction dysfunction [1–7]. It has its highest incidence in the second and third decades of a woman's life, a period overlapping with the childbearing years [3,7,8]. Therefore, it is not unusual for neurologists to evaluate pregnant patients during the course of disease. In addition, neurologists should be aware that the initial manifestation of MG can occur during pregnancy or postpartum periods [9].

Pregnancy does not worsen the long-term outcome of MG [10]. However, pregnancy and postpartum status have been reported as triggers for exacerbating or worsening the disease [2]. Consistent with this, the course of MG is highly variable and unpredictable during pregnancy. MG can also lead to increases in maternal mortality, morbidity, pregnancy wastage and premature labor [1–4,9].

To the best of our knowledge, there are few studies showing the relationship between pregnancy and MG and also correlating the characteristics of MG in different groups according to MG severity status. This study is also the first study addressing pregnancy in Brazilian MG patients. The aim of this study was to analyze the outcome and course of pregnancy in Brazilian MG patients as well as the impact of the pregnancy on the course of MG.

2. Material and methods

We retrospectively analyzed 69 women patients with MG who were followed in our neuromuscular outpatient clinics from 1990 to 2015. We included women who fulfilled the following criteria: (1) MG diagnosis based on clinical features compatible with MG associated with abnormal repetitive nerve stimulation (RNS) and/or the presence of anti-acetylcholine receptor antibody (anti-AChR antibody); (2) concomitance of MG during the pregnancy period; (3) neurological and obstetrical assessment follow-up in our hospital during the three-month periods before, during and after pregnancy (women were examined every 3 months); and (4) information about delivery and newborn outcome. We excluded patients without complete neurological

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or obstetrical data for calculation of MGFA or MGC scores as well as any incomplete data in the periods before, during and after pregnancy. Obstetrical assessment could include concomitant follow-up in local hospitals.

Relevant data, including age, clinical assessment, time to MG diagnosis, course of the disease during the pregnancy, effects of pregnancy on the mother, mode of delivery, gestational age, status of the mother and child after delivery, course of the pregnancy, mode of delivery, newborn outcome and MG management were recorded. For this study, MG severity was graded using a combination of the Myasthenia Gravis Foundation of America (MGFA) clinical classification [11], Myasthenia Gravis Composite (MGC) score [12], and changes in drug therapy during and after the pregnancy. The MGFA classification and MGC score were retrospectively calculated based on the neurological assessment.

The MG severity status was classified into three main groups: improvement (stable marked improvement of myasthenic signs with or without reduction in drug dosage); no change (no objective improvement in MG status); and deterioration (clinical worsening with same drug dosage, increased drug dosage or new drug was added) [3].

Transient neonatal myasthenia gravis (TNMG) was diagnosed based on transient clinical signs of generalized hypotonia, sucking disturbances, weak cry and respiratory difficulties [3].

The data were analyzed using descriptive statistical methods. Statistical significance was assessed using either Student's t-test or the Mann–Whitney test for continuous variables and using the χ^2 test or Fisher's exact test for categorical variables. Statistical significance was set at $p < 0.05$ with a 95% confidence interval (CI).

3. Results

Twenty-one women were included. Thirty-five women were excluded because they did not have at least one pregnancy during their MG treatment, and another 13 women were excluded due to absence of neurological or obstetrical assessment before, during or after the pregnancy.

Our cohort therefore included 35 pregnancies from 21 patients whose ages during pregnancy ranged from 17 to 37 years (mean 26.2 ± 5.1 years, median 25 years). Ten patients had one child each; five patients had two children; one patient had three children; one patient had one child and had had one stillbirth; one patient had three children and had had one abortion; one patient had four children (2 of whom were twins) and one abortion; one patient had had an ectopic pregnancy; and one patient had had one abortion. Four pregnancies resulted in abortion (11.4%), three were spontaneous and one was an ectopic pregnancy. All abortions had occurred in the first trimester, and MG worsened after abortion only in one patient. Spontaneous abortion was statistically associated with the use of azathioprine in the first trimester ($p = 0.045$). One pregnancy resulted in fetal death.

Seven pregnancies in six women were concomitantly monitored by obstetricians in local hospitals, and the others were monitored by the Obstetric and Neuromuscular Service of the Federal University of Parana (Curitiba, Brazil).

Myasthenia gravis was diagnosed before pregnancy in 34 pregnancies (mean time between MG diagnosis and pregnancy was 6.8 ± 4.9 years) and during pregnancy in one woman.

Serum anti-AChR antibody (binding type) was analyzed in 15 patients and detected in 13. Eighteen pregnancies occurred in serum-positive women, and 15 of these resulted in live births. Table 1 shows the differences between the groups for pregnancies with live births.

RNS was performed in 20 women at the time of MG diagnosis, before the pregnancy in 19 women and during in one (because MG was diagnosed during her pregnancy). The mean time between RNS and pregnancy in the deterioration, improvement and no-change groups was 5.1 ± 5.6 years (3.86 ± 5.4, 4.0 ± 5.07 and 10.0 ± 5.05 years, respectively). RNS was abnormal in 17 women (28 pregnancies, 23 pregnancies resulting in live birth) and normal in the remaining 3 women (6 pregnancies, all resulting in live births). RNS was not repeated during the pregnancy, and, as only RNS performed at moment of MG diagnosis was analyzed, the mean time between RNS and pregnancy was based on "disease duration" as shown in Table 1. Table 1 also presents the distribution of abnormal RNS in the different groups in pregnancies resulting in live births.

Table 1
Ch aracteristics of patients with MG in 30 pregnancies with live births.

Characteristics	All pregnancies (n = 30)	Improvement group (n = 9)	Deterioration group (n = 15)	No-change group (n = 6)
Maternal ages, years (mean ± SD)	25.8 ± 5.2	26.1 ± 5.5 (p > 0.05)	24.33 ± 4.4 (p > 0.05)	26.2 ± 8 (p > 0.05)
Disease duration since diagnosis of MG, years (mean ± SD)	6.6 ± 5.1	5.4 ± 4.9 (p = NS)	5.5 ± 4.8 (p = NS)	11 ± 4.8 (p = 0.026)
MGC before pregnancy (mean ± SD; range)	3.43 ± 4.88 (0–25)	6.66 ± 7.19 (3–25) (p = 0.012)	1.8 ± 2.5 (0–7) (p = 0.045)	2.66 ± 3.01 (0–7) (p = NS)
Positive anti-AChR antibody*	15/19	4/6 (p = NS)	9/10 (p = NS)	2/3 (p = NS)
Abnormal RNS*	23/29	7/9 (p = NS)	14/14 (p = 0.028)	2/6 (p = 0.008)
Previous thymectomy	8	4 (p = NS)	2 (p = NS)	2 (p = NS)

NS, not significant.
* Data are shown as the number of abnormal tests/number of tests performed per pregnancy.