An Update
Myasthenia Gravis and Pregnancy

Johanna Hamel, MD[a,*], Emma Ciafaloni, MD[b]

KEYWORDS

• Pregnancy • Myasthenia gravis • Neonatal myasthenia gravis • Arthrogryposis

KEY POINTS

- Women with myasthenia gravis considering pregnancy should meet with their neurologist to review the role of thymectomy, maximize clinical improvement, and minimize the use of immunomodulating medications before conception.
- Treatment goal is minimal disease activity in the mother with minimal risk for harm to the fetus.
- The treatment team should include the neurologist, the obstetrician, and the anesthesiologist to support the patient during pregnancy and postpartum period, and to plan optimal mode of delivery.
- Newborns of mothers with myasthenia are at risk of transient neonatal myasthenia gravis and should be monitored for symptoms of myasthenia.
- Pregnancy outcome is generally favorable in women with myasthenia gravis who receive treatment.

INTRODUCTION: CONCEPTS OF TREATING WOMEN WITH MYASTHENIA GRAVIS IN THE CHILDBEARING AGE AND DURING PREGNANCY

Although myasthenia gravis (MG) can affect men and women at any age, female incidence peaks in the second and third decade, and therefore coincides with family planning and fertility. The first step when establishing care with a patient with MG is to confirm the diagnosis, either by detecting antibodies against the nicotinic acetylcholine receptor (AchR-Ab) or other postsynaptic antigens, such as muscle-specific tyrosine kinase (MuSK-Ab) and low-density lipoprotein receptor-related protein 4. In seronegative patients repetitive nerve stimulation testing or single-fiber electromyography is diagnostic by confirming dysfunction of the neuromuscular junction. Issues related to the

Disclosure Statement: The authors have nothing to disclose.
[a] Department of Neurology, Neuromuscular Division, University of Rochester Medical Center, University of Rochester, 601 Elmwood Avenue, Rochester, NY 14642, USA; [b] University of Rochester Medical Center, University of Rochester, 601 Elmwood Avenue, PO Box 673, Rochester, NY 14642, USA
* Corresponding author.
E-mail address: Johanna_hamel@urmc.rochester.edu

Neurol Clin 36 (2018) 355–365
https://doi.org/10.1016/j.ncl.2018.01.005
0733-8619/18/

care of patients with MG in the childbearing age may include questions about fertility, pregnancy planning, drug safety, and treatment optimization preceding conception. Disease severity varies between patients but also within an individual over time. Symptoms can vary throughout pregnancy, thus patients need to be aware of how to monitor and react to changes in their symptoms because treatment adjustments may become necessary. An individualized treatment plan is important, taking into account the patient's disease manifestations, comorbidities, and treatment goals. The pregnancy can affect the course of myasthenia, and the myasthenia can affect the pregnancy outcome and cause transient neonatal myasthenia and in rare circumstances arthrogryposis in the newborn. Although myasthenia does not affect smooth muscle, labor and delivery relies on striated muscle in the later stages, which can be prolonged. Certain medications, such as anesthetics, can worsen symptoms of MG. Lastly, symptoms can vary in puerperium and drug safety during lactation needs to be discussed.

TREATMENT AND DRUG SAFETY BEFORE PREGNANCY

Although MG itself does not affect fertility, immunosuppressive medications commonly used in MG do. Conversations between a woman with MG and her neurologist about fertility and pregnancy planning should begin early, such as when choosing an immunosuppressive therapy. Methotrexate (MTX) and mycophenolate mofetil (MMF) are contraindicated in women who try to conceive and should be discontinued 3 months (MTX) and 6 weeks (MMF) before conception.[1] Azathioprine and corticosteroids are continued because they do not seem to affect fertility.[2] Women treated with rituximab (RTX) are advised to use contraception 12 months after the last treatment. Effects of RTX on fertility beyond the 12-month period are not well known. However, a case series described two uncomplicated pregnancies in two patients previously treated with RTX.[3] Thymectomy improves clinical outcomes, reduces use of immunosuppressive agents, and is recommended for patients younger than age 65.[4] If a patient is planning to become pregnant, but has not yet had thymectomy, it should be considered to optimize disease control.[5] Patients who had undergone thymectomy seemed to have a lower likelihood of neonatal myasthenia in the infant.[6,7] However, thymectomy did not affect severity of symptoms, use of medication, and complications with delivery.[7]

TREATMENT AND DRUG SAFETY DURING PREGNANCY

Ideally a patient and the treating neurologist discuss treatment goals and options before becoming pregnant. Optimizing treatment before and during pregnancy with best possible safety profile for the patient and the fetus is of key importance. Depending on the patient's duration and type of symptoms (eg, ocular vs bulbar) and symptom severity, discontinuation of immunosuppressive therapy might be considered before conception. However, if a patient is already pregnant, discontinuation of therapy with the risk of worsening of myasthenic symptoms or of triggering myasthenic crisis often outweighs the risk of the unwanted medication effects on the fetus. Most recommendations related to drug safety are based on retrospective analysis, observational or animal studies, or stem from experiences with immunosuppressive medications when used in other diseases.

Treatment of MG includes symptomatic and immunosuppressive/immunomodulatory treatment. Treatment of choice during pregnancy is pyridostigmine and corticosteroids. It is not recommend starting other immunosuppressive agents because the effect of treatment can be delayed by many months and would not benefit the disease course during pregnancy itself, while increasing the risk