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Abstract
Myasthenia gravis (MG) is an autoimmune disorder with bimodal age of presentation, occurring in young women of reproductive age and at an older age in men. Occasionally, MG is diagnosed during pregnancy. Management of MG includes symptomatic treatment with cholinesterase inhibitors and immunosuppressive therapy for controlling the disease activity. Treatment of MG in women of reproductive age, who may be contemplating pregnancy, requires discussion regarding the choice of medication as well as the understanding of risks/adverse effects involved with various treatments. During the peripartum period, it is essential to ensure careful monitoring of the disease state along with the well-being of the mother and fetus and to coordinate neonatal monitoring overseen by a multidisciplinary team comprising a high-risk maternal fetal medicine specialist, a neurologist familiar with these complex issues, and a neonatologist.

KEYWORDS
immunosuppressive medications, myasthenia gravis, neonatal, pregnancy, teratogenic

1 | INTRODUCTION

Myasthenia gravis (MG) is a chronic autoimmune disorder presenting with fatigable weakness of the skeletal muscles. The reported estimated prevalence of MG in the general population varies greatly, ranging from 15 to 179 per 1 000 000.1 The estimated incidence rates range from 1.7 to 21.3 per 1 000 000, with bimodal distribution, the first peak occurring in women in the third decade and then in men over 60 y of age.1 Early onset MG (prior to age 40 y) is three times more prevalent in women than men.2 This age of increased MG prevalence overlaps with the time for child bearing. When treating a patient in the child-bearing age range, who may over time contemplate getting pregnant, one must consider a medication that would not reduce fertility or harm the development of the fetus. Before initiating any such treatment in patients in this age range, pregnancy status should be elicited. Selection of the appropriate treatment option requires balancing the risk of exposure to the fetus vs the risk of MG worsening/crisis.

2 | IMPACT OF PREGNANCY ON MG

The clinical course of MG during pregnancy varies from one patient to another and even between pregnancies in the same patient. Different studies report varying effects of pregnancy on MG; 19%–50% will experience worsening, 30%–59% will remain stable, and about 20% will improve.3-5 A single observational study suggested possible predictors for the course of MG during pregnancy: the MG composite score (MGC), duration of MG prior to pregnancy, and results of repetitive nerve stimulation (RNS).3 In this study, worsening was seen in patients who had abnormal RNS results. Interestingly, a lower MGC score was associated with worsening and a higher MGC score with improvement during pregnancy. The group that remained stable had longer disease duration and normal RNS testing prior to pregnancy.3 However, no similar correlation between prior MG status and exacerbation during pregnancy was found by Batocchi and colleagues.6 Exacerbations of symptoms mostly occur in the first or second trimesters or after delivery.3,6

3 | IMPACT OF MG ON PREGNANCY

MG is not known to affect pregnancy significantly. Some studies have shown preterm premature rupture of membranes and increased...
incidence of cesarean section due to uterine inertia, whereas other studies did not show similar adverse effects on the course of pregnancy or mode of delivery.3,5,7-10 There are only 11 reported cases of MG with severe preeclampsia reported thus far in the literature.11 Although rare, this poses difficult management issues. Bone marrow suppression during pregnancy has been reported in an MG patient.12 Higher maternal mortality is associated with shorter disease duration prior to pregnancy,8 and this could be due to less than full optimization of MG treatment.

### 3.1 Pre-pregnancy counseling and medical care

In an ideal situation in planning a pregnancy, no medications other than prenatal vitamins should be taken; however, in MG patients continued symptomatic treatment and at times use of immunosuppressants is required.

Careful pregnancy planning is strongly recommended to optimize fetal health. Effective methods of contraception should be utilized when not considering pregnancy to minimize the chances of exposure of the fetus to potentially deleterious medication in case of an unplanned pregnancy. In addition to general nutritional advice and prenatal care, counseling includes evaluating medications for their effect on fertility and stopping or switching maintenance MG medications that may have adverse effects on the fetus. Since no set guidelines exist for optimum timing for discontinuing immunosuppressive medications prior to conception, pharmacokinetics of the drug are used to determine that interval.

Pyridostigmine is completely safe during the time prior to conception and during pregnancy.8,12 Prednisone is considered relatively safe as it does not pose significant risk to the mother or the fetus. It has been inconsistently reported to be associated with increased risk of cleft lip/palate and use of lowest possible dose during pregnancy is recommended.8,14,15 Medications that may be used with caution include azathioprine (AZA) and anti-calcineurins. Use of AZA has not been associated with reduced fertility or increased risk of congenital malformations.16 Uterine growth retardation has been reported, although it cannot be solely attributed to the use of AZA. Its continued use should be weighed against the possibility of disease worsening and a negative outcome secondary to that. Anti-calcineurins, including cyclosporine and tacrolimus, can be continued with caution as no major malformations are reported with either drug.

The medications that should be discontinued prior to conception, due to the teratogenic effect on the fetus, include mycophenolate mofetil (MMF), methotrexate, and cyclophosphamide. MMF has a black box warning for use in women of child-bearing potential. It should be discontinued at least 6 wk prior to conception.17 Methotrexate can be detected in red cells for up to 10 wk and in liver for about 4 mo after discontinuation.18 It should be discontinued at least 3–4 mo prior to planned conception as it has teratogenic effect on the fetus. Cyclophosphamide use has been associated with increased rate of amenorrhea and infertility.16,19 It is recommended that patients wait for 3 mo after discontinuation of cyclophosphamide before conception.16

Lack of adequate human studies limits the ability to provide recommendations regarding use of rituximab or eculizumab when anticipating pregnancy. Animal studies in monkeys have not shown any evidence of teratogenicity with rituximab. B-cell lymphopenia has been reported in infants exposed in utero. Animal studies with mouse analogue of eculizumab (murine anti C5-antibody) showed an increased rate of fetal loss, although no effect on fertility was noted. Continued use of rituximab and eculizumab as a maintenance treatment in MG should only be considered if the potential benefits clearly outweigh the risks to the fetus.

### 3.2 Effect of medication on fertility

Of the maintenance medications for MG, pyridostigmine and corticosteroids do not have a negative impact on fertility.

AZA has not been shown to alter fertility in men or women. It is, however, linked to mutagenesis in sperm. Based on this, for treated males, it has been recommended that AZA be stopped 3 mo prior to conception (which is equivalent to one cycle of spermatogenesis); however, there are conflicting data that suggest it may be safe to continue AZA.16,20-22 If there is a question about starting AZA in the male partner of a couple contemplating pregnancy, referral to a geneticist and/or sperm cryopreservation should be considered. Furthermore, ultrasound survey of the fetus is recommended if conception is by a treated father.

No data are available on fertility in males treated with MMF. In pregnancies fathered by patients treated with MMF, the rate of prematurity and malformations are similar to those seen in general population.23 Female fertility has not been reported to be affected.

Cyclophosphamide has been shown to reduce ovarian reserve in a dose-dependent manner.25 Use of cyclosporine is not associated with reduction in female fertility. Doses higher than 2 mg/kg/day in men can cause asthenoteratospermia (malformed sperm with reduced motility); but no effect is reported in lower doses. Tacrolimus has not been reported to affect fertility. There is paucity of data on the effect of fertility with use of rituximab. Animal data suggest no effect on fertility with eculizumab.

### 3.3 Interaction with oral contraceptives

There are no reports linking MG medications to reduced efficacy of oral contraceptives. Estrogen based contraceptives can increase the levels of tacrolimus, thus increasing the chances of toxicity.26

### 3.4 Role of thymectomy

Thymectomy is a standard treatment offered to patients with acetylcholine receptor (AChR) antibody MG.27 Patients who have
undergone thymectomy are less likely to have MG exacerbations during pregnancy as compared with mothers who have not had thymectomy.28 Incidence of neonatal MG is also less in infants of mothers who have had thymectomy.8 Thymectomy should be considered in women prior to considering a future pregnancy.

3.5 | Medication use during pregnancy

The medications typically used in patients with MG include pyridostigmine, prednisone, as well as agents broadly classified as steroid sparing immunosuppressants such as AZA and MMF. Less commonly used immunosuppressive medications in the United States include methotrexate, tacrolimus, cyclosporine, cyclophosphamide, and rituximab. In the older system of drug classification by the Food and Drug Administration (FDA), most of the MG medications were categorized as either Class C or D, with the exception of methotrexate which was categorized as X. The old system, which assigned five letter risk categories—A, B, C, D, or X—established in 1979, was felt by clinicians to be overly simplistic and confusing. A new system, pregnancy and lactation labeling final rule (PLL R), was adopted in 2015 and provides information about the risk to the fetus, registry information, and safety during breast feeding as well as information about effect on fertility and birth control. Prescription drugs submitted for FDA approval after June 30, 2015 use the PLLR labeling format, while drugs approved on or after June 2001 are being phased in gradually to adopt the new format. Medications approved prior to 2001 are not subject to the PLLR rule, however, are required to remove the old pregnancy letter category. Table 1 includes recommendations for maintenance medications for MG patients regarding their effects on fertility and pregnancy.

3.5.1 | Pyridostigmine

Pyridostigmine has not been shown to cause teratogenicity in animal models, and there are no adequate and well-controlled human studies. This provides symptomatic relief, same as in non-pregnant MG patients. Maximum recommended dose for pyridostigmine is less than 600 mg/day.13 Intravenous cholinesterase inhibitors should be avoided as they can cause premature labor.15

3.5.2 | Prednisone/prednisolone

Prednisone/prednisolone is often the sole immunosuppressant used through the course of pregnancy in patients with MG. Prednisone and prednisolone are inactivated by the placenta, reducing the exposure to the fetus.29 Premature rupture of membranes and intrauterine growth retardation may occur.14,15 Cleft lip and palate have been inconsistently associated with maternal use of corticosteroids during early pregnancy. Use of corticosteroids increases the risk for development of gestational diabetes and hypertension in the mother.16

3.5.3 | Azathioprine

AZA has been used for a number of years in pregnant patients with various systemic autoimmune disorders and after solid organ transplantation. AZA crosses the placenta, where it is metabolized to an inactive metabolite, thiouric acid. The old FDA pregnancy classification assigned to AZA was category D; however, it has been successfully used during pregnancy without significant issues. This older classification has now been replaced by the PLLR system as mentioned above. Sporadic malformations including cardiac septal defects have been reported, although a specific pattern of congenital malformations has not been seen.16 Increased risk of preterm delivery and low birth weight infants is seen in patients treated with AZA, although it remains unclear whether this is due to the drug or the primary autoimmune disease itself. Various other studies report of use of AZA during pregnancy for other autoimmune disorders without increased risk of congenital malformations.30,31

3.5.4 | MMF

MMF is a reversible inhibitor of inosine phosphate dehydrogenase. It readily crosses the placenta and is linked to an increased incidence of spontaneous abortions and congenital malformations. An embroyopathy associated with the use of MMF affecting the ear, mouth, fingers, and organs (termed EMFO tetrad) has been described. EMFO tetrad has demonstrated involvement in the following ways: ears, microtia and auditory canal atresia; mouth, cleft lip and palate; fingers and toes, brachydactyly fifth fingers and hypoplastic toenails; and organs, cardiac, renal, central nervous system (CNS), diaphragm, and eyes.32,33 Due to these teratogenic effects, the drug has a black box warning against its use in women of child-bearing potential.

3.5.5 | Cyclophosphamide

Cyclophosphamide has been shown to have a teratogenic effect on the developing fetus. It is absolutely contraindicated in early pregnancy and is associated with severe embryopathy, including craniofacial abnormalities, developmental delay, and distal limb defects.34 Use in the latter part of pregnancy is also associated with fetal harm and should be taken with extreme caution.

3.5.6 | Methotrexate

Methotrexate is contraindicated during pregnancy and lactation. In high doses, methotrexate works as an abortifacient. Its use at lower doses is also associated with significant fetal loss and fetal malformations.35 Aminopterin syndrome can occur, which is characterized by CNS malformations, skull defects, facial and limb deformities, and cardiovascular abnormalities.36
<table>
<thead>
<tr>
<th>Medication recommendation</th>
<th>Old FDA pregnancy classification</th>
<th>Effect on fertility</th>
<th>Impact on fetus</th>
<th>Impact on pregnancy/delivery</th>
<th>Lactation</th>
<th>Management decision</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pyridostigmine</td>
<td>C</td>
<td>None in men or women</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>Continue throughout pregnancy and later</td>
</tr>
<tr>
<td>Prednisone</td>
<td>C</td>
<td>Men: High doses can cause mild suppression of hypothalamic–pituitary–gonadal axis. Women: No effect</td>
<td>Associated with increased risk of cleft lip or palate if used in first trimester; increased risk of metabolic syndrome in adulthood</td>
<td>Increased risk of gestational diabetes, hypertension, and fluid retention</td>
<td>None</td>
<td>Maintain at the lowest effective dose</td>
</tr>
<tr>
<td>Azathioprine</td>
<td>D</td>
<td>No effect on fertility, although has mutagenic effect on sperm</td>
<td>Low birth weight, sporadic malformations such as cardiac septal defects</td>
<td>Increased risk of preterm delivery</td>
<td>May be continued</td>
<td>Men: Stop 3 mo prior to planned conception by a treated father. Women: May be continued with caution, if needed</td>
</tr>
<tr>
<td>Mycophenolate</td>
<td>D</td>
<td>No effect on fertility in men or women</td>
<td>Teratogenic: Black box warning for use in pregnancy, Embryopathy (termed EMFO tetrad) has been described</td>
<td>Contraindicated in pregnancy</td>
<td>Not recommended due to lack of data</td>
<td>Stop at least 6 wk before planned conception</td>
</tr>
<tr>
<td>Cyclosporine/tacrolimus</td>
<td>C</td>
<td>Cyclosporine: Doses &gt;2 mg/kg/d can cause asthenoteratospermia, no effect on fertility in women. Tacrolimus: No effect in men or women</td>
<td>Low birth weight, transient neonatal hyperkalemia, and renal impairment—Resolve spontaneously</td>
<td>May increase risk of preterm labor</td>
<td>May be continued</td>
<td>May be used with caution and continued monitoring</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>X</td>
<td>Men: Possible effect on spermatogenesis, known to have mutagenic effect in sperm. Women: No effect</td>
<td>Teratogenic: Causes CNS, skull, facial, and limb abnormalities</td>
<td>Contraindicated</td>
<td>Contraindicated</td>
<td>Stop at least 3 mo prior to planned conception for both men and women</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>D</td>
<td>Reduces ovarian reserve in women which is dose dependent</td>
<td>Teratogenic: Severe embryopathy including craniofacial abnormalities, developmental delay, and distal limb defects</td>
<td>Contraindicated</td>
<td>Contraindicated</td>
<td>Stop prior to pregnancy, wait at least 1 ovulation cycle before planned conception</td>
</tr>
<tr>
<td>Rituximab</td>
<td>C</td>
<td>No data available on effect on fertility</td>
<td>B-cell lymphocytopenia may occur, typically recovering within 6 mo of birth</td>
<td>Limited data – although no adverse effects reported</td>
<td>Not recommended due to lack of data</td>
<td>May be used with caution, if benefits outweigh risks and with continued monitoring</td>
</tr>
</tbody>
</table>
3.5.7  |  Anti-calcineurins: Cyclosporine and tacrolimus

The use of cyclosporine is associated with preterm labor and low birth weight infants. No specific congenital malformations have been reported. Tacrolimus use during pregnancy has been studied in transplant recipient population. Although it readily crosses the placenta, no major congenital malformations are reported. Preterm labor and low birth weight infants are the commonly seen adverse effects of exposure to tacrolimus prior to and during pregnancy. Transient neonatal hyperkalemia and renal impairment can occur, with spontaneous resolution. Renal function and potassium levels should be monitored in such neonates.

3.5.8  |  Rituximab

Rituximab is reserved for use in patients with severe myasthenic weakness requiring frequent use of rescue treatments with either intravenous immunoglobulin (IVIg) or plasma exchange (PE). There is limited data available regarding its use in pregnancy. It is generally accepted that, due to the long half-life of the medication, pregnancy should be avoided for 1 year after treatment, as hematological abnormalities can be seen in the fetus. No malformations have been reported.

3.5.9  |  Eculizumab

This is used in AChR antibody-positive MG patients with aggressive disease requiring repeated use of IVIg or PE. There are no reports of use of eculizumab in pregnant MG patients. Improved fetal and maternal survival has been reported in hemolytic-uremic syndrome or paroxysmal nocturnal hemoglobinuria patients treated with eculizumab during pregnancy; however, this may not be extrapolated to the MG patient population as these other diagnoses carry a high maternal (8%–20%) and fetal (4%–9%) mortality. Animal studies show increased fetal loss and developmental anomalies. The drug has been shown to cross placenta and has the potential theoretic risk of causing complement inhibition in the newborn.

3.6  |  Crisis during pregnancy

Worsening of MG symptoms and MG crisis can occur during the course of pregnancy necessitating use of rescue treatments. There are no data available regarding the incidence of MG crisis specifically during pregnancy. A single review of 37 pregnancies in myasthenic patients reported four crises (two during pregnancy and two occurring in the postpartum period). In general, MG exacerbations occur during pregnancy and the postpartum period in 19%–50% of women with MG. The diagnostic evaluation for MG crisis is the same as in non-pregnant patients—to evaluate for underlying infection and
introduction of new medications, especially the use of magnesium for pre-eclampsia/eclampsia. Recognition and timely treatment for exacerbation and crisis is important as they can impact the fetus negatively. Although there are no studies or reports about the effects of MG crisis on the fetus, acute respiratory failure in the mother carries a high risk of maternal morbidity and mortality.\textsuperscript{56,67} The treatment for MG crisis in a pregnant patient is the same as in a non-pregnant patient, with stabilization of airway and cardiac parameters as well as consideration of either IV Ig or PE. Both treatments, along with monitoring for usual adverse events, can be safely performed during pregnancy. Monitoring for hypercoagulability, flu-like symptoms, fluid overload, and renal impairment should be done when using IV Ig as the treatment option. With PE, monitoring for hypotension, infection, and fluid shift is recommended. No increase in adverse effects is seen with either procedure during pregnancy.\textsuperscript{38-51}

3.7 | Labor and delivery

For women who develop pre-eclampsia, monitoring of blood pressure and appropriate treatment is very important. Monitoring for seizures should be undertaken as well. Typically, in non-MG patients, IV magnesium is the first line of treatment. Use of magnesium can result in worsening of MG symptoms.\textsuperscript{52-55} Magnesium should be used judiciously, with the clear understanding that it may precipitate crisis. Preferred treatment includes phenytoin or diazepam/lorazepam for seizure prophylaxis.\textsuperscript{56,57} Control of hypertension can be achieved with use of hydralazine. In refractory cases, labetalol may be used with close monitoring of the MG.

Vaginal delivery is recommended for women with MG. The first stage of active labor involves uterine smooth muscle contractions. This stage is not affected by MG as smooth muscles have muscarinic AChRs and are not affected by the MG antibodies. The second stage of labor is characterized by a completely dilated cervix with further descent of the fetal head, with it beginning to touch the pelvic floor. During this time, uterine contractions continue; however, further movement of the baby in the birth canal is aided by voluntary contraction of the pelvic floor muscles. These muscles can get fatigued if the labor is prolonged, requiring assistance in vaginal delivery with vacuum suction extraction or forceps, or surgical intervention with a cesarean section. In a population-based cohort study over 30 years, Hoff and colleagues reported increased use of elective cesarean section in patients with MG over time and reduced use of forceps and vacuum.\textsuperscript{7}

MG, in itself, is not an indication for performing a cesarean section. It should be performed only for obstetrical indications. However, MG severity, including respiratory status, may need to be taken into account when determining the mode of delivery.

Evaluation of the status of pulmonary function prior to delivery should be considered. Careful monitoring of respiratory distress and bulbar and muscular weakness during labor and puerperium is warranted to expeditiously diagnose and treat an impending myasthenic crisis.

3.8 | Anesthetic management

As MG can affect the second stage of labor, adequate pain control may have a positive effect on muscle fatigue, and this potentially could reduce cesarean section rates. No studies have evaluated the impact of pain control on the mode of delivery; however, it is plausible that reducing muscle fatigue and stress of delivery could positively impact the outcome. Vaginal delivery with regional anesthesia is a preferred method for well-controlled patients or those with mild-to-moderate disease severity. Of the regional anesthetics, epidural is preferred over spinal anesthesia.\textsuperscript{5,8,58,59} Epidural analgesia can be safely used during labor and delivery.\textsuperscript{58} Amide local anesthetics are better with regard to safety as concomitant use of anticholinesterase inhibitors does not impact their metabolism. Ester type anesthetics, which are often used during labor, are rapidly hydrolyzed by plasma cholinesterase, and in patients on cholinesterase inhibitors, maternal and fetal toxicity may be enhanced.\textsuperscript{59} Ropivacaine has been used more recently as it is less likely to produce a motor block.\textsuperscript{58}

If cesarean section is warranted, epidural block may still be used. The presence of pre-existing respiratory impairment and the superimposed effect of high spinal motor block needs to be considered. Patients with mild MG without respiratory compromise or purely ocular MG may be best suited for spinal or epidural anesthesia. MG is not an indication for cesarean section by itself; however, the severity of symptoms, especially the bulbar and respiratory muscle weakness, needs to be considered along with obstetrical indications. Patients with severe bulbar and respiratory weakness should have cesarean section performed under general anesthesia.\textsuperscript{59} Induction and maintenance of anesthesia with inhalational agents (isoflurane, sevoflurane) or IV propofol and fentanyl should be considered.\textsuperscript{60-63} Use of neuromuscular blockers should be avoided unless absolutely necessary. Sugammadex has been used successfully to reverse neuromuscular blockade if neuromuscular blocking agents are used.\textsuperscript{64}

4 | POSTPARTUM CARE FOR MOTHER AND CHILD

4.1 | Transient neonatal MG

Weakness in sucking and swallowing resulting in feeding difficulty, weak cry, and poor muscle tone as well as respiratory difficulty can be seen in up to 20% of infants born to mothers with MG. This is thought to be caused by passive transfer of AChR or muscle specific kinase antibodies through the placenta.\textsuperscript{65,66} Symptoms present within 3 days of birth and may last for a few months. Diagnosis is suggested by history and confirmed by electrodiagnostic testing with abnormal RNS and detection of pathogenic antibodies in the neonate. AChR antibody epitope specificity has been proposed as one of explanations for the relative paucity of neonatal MG. A disproportionate ratio of antibodies against embryonic vs adult AChRs may influence the development of neonatal MG.\textsuperscript{67} Neither severity of disease in the mother nor antibody titers correlate or predict the occurrence of neonatal MG. Thymectomy
TABLE 2  General guidelines in managing male and female MG patients with child bearing potential

1. Assess disease activity and severity to determine the need for continued immunosuppression.
2. Check for status of pregnancy, confirmed by laboratory testing.
3. Strongly recommend effective contraceptive measures when initiating treatment with immunosuppressants, even in patients who are not considering pregnancy.
4. Strongly consider thymectomy, if clinically indicated.
5. Choose medications that would not impact fertility if the patient is considering future pregnancy.
6. Review treatment options if the patient would already be on immunosuppressive therapy and consider switching to medications with no or minimal effect on fertility, all while continuing contraceptive measures.
7. Discontinue any medications with potential for teratogenicity prior to pregnancy for at least the recommended time duration for that particular agent.
8. Counsel patients about regular follow up with the multidisciplinary team during pregnancy for monitoring of the disease activity and impact on the fetus.
9. Aggressively manage worsening disease activity with either intravenous immunoglobulin or plasma exchange to reduce risk to the fetus.
10. Monitor the progression of labor and consider instrumentation during the second stage of labor or escalate to cesarean section.
11. Conduct neonatal monitoring for the development of transient neonatal MG.

has a favorable influence in lowering the risk of neonatal MG in the subsequent pregnancies. The symptoms respond well to the use of cholinesterase inhibitors and resolve spontaneously.

The transplacental influx of antibodies into fetal circulation may result in decreased fetal movements, sometimes leading to congenital arthrogryposis multiplex. There is no association of this rare complication to the severity of the MG in the mother. There is a higher risk of recurrence of arthrogryposis multiplex in subsequent pregnancies and in siblings.

4.2 | Lactation

Traditionally, use of immunosuppressive medications while breast feeding has been felt to be associated with theoretical increased risk of immunosuppression in the neonate. However, this may be more dependent on the amount of excreted drug in the breast milk. AZA metabolites are present in very low quantities in breast milk. Infants ingesting such breast milk have not been reported to have any adverse effects. Based on available data, use of AZA is not contraindicated during lactation. No data are available for excretion of MMF in breast milk or its effect on infants. Given the lack of available data, breast feeding is not recommended in patients treated with MMF. Patients should not be started on MMF until weaning has been achieved. Lactation is contraindicated with concurrent use of cyclophosphamide. Cyclosporine is excreted in breast milk but is absorbed in minimal amounts by infants after consumption. No nephrotoxicity has been reported in a case series. Methotrexate is excreted in very small amounts in breast milk. The effect on infants exposed to the methotrexate in breast milk is unknown; however, breast feeding is not recommended until more data are available. Tacrolimus is excreted in low quantity in breast milk. Per the available data, breast feeding is not contraindicated in women on tacrolimus. Use of rituximab is not recommended due to lack of data. In small case series, eculizumab was not detected in breast milk; however, no recommendations can be made based on the case series.

Table 2 lists general guidelines for managing both men and women MG patients of child-bearing potential.

DISCLOSURES

The authors have no conflict of interests to disclose.

ETHICAL PUBLICATION STATEMENT

We confirm that we have read the Journal’s position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

REFERENCES


75. Eculizumab: https://www.accessdata.fda.gov/drugsatfda_docs/label/2011/125166s172lbl.pdf

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