Multiple Sclerosis and Pregnancy

Riley Bove, MD, MMSC

Assistant Professor of Neurology, Harvard Medical School; Associate Neurologist, Brigham and Women's Hospital, Boston, Massachusetts, US

Abstract

For many women with multiple sclerosis (MS), bearing and breastfeeding a child can be undertaken safely with the management of an informed medical provider. In the past year, the need for a North American MS pregnancy registry has come into sharper focus; reports from a multicenter randomized estriol trial have been presented, and the scope of investigations has widened beyond mothers to include fathers with MS, as well as children of parents with MS. More data are anticipated regarding the effects of breastfeeding and fertility treatments on MS course, as well as ideal levels of vitamin D during pregnancy.

Keywords

Pregnancy, multiple sclerosis, registry, fatherhood, fertility, vitamin D

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Correspondence: Riley Bove, MD, MMSC, Assistant Professor of Neurology, Harvard Medical School; Associate Neurologist, Brigham and Women's Hospital, Boston, Massachusetts, US. E: rbove@bwh.harvard.edu

The importance of pregnancy management in multiple sclerosis (MS) is underscored by the fact that MS affects three times more women than men, with first symptoms typically during the peak reproductive years.

Childbearing—An Achievable Goal for Many Women with Multiple Sclerosis

While providers were cautious in prior decades, it is increasingly clear that most women with MS who wish to can safely become pregnant, carry a pregnancy, and breastfeed their newborn. There appear to be minimal effects of maternal MS on neonatal outcomes. Additionally, childbearing does not appear to adversely affect long-term MS outcomes and may even be protective, although data are patchy.¹ However, many questions remain about optimal MS management during this timeframe. To address these questions, there have been many recent important developments.

Helping Women with Multiple Sclerosis Achieve their Family Planning Goals

It is noteworthy that several reviews of pregnancy management in MS have been published, by teams of MS providers² as well as by multidisciplinary groups, such as MS Centers for Excellence in Reproduction and Child Health.¹² These publications reflect a need to synthesize evidence from a broadening field into consensus guidelines that can be used by neurologic and obstetric providers.

A Need for Multiple Sclerosis-specific Pregnancy Registries

Most MS providers recommend discontinuation of disease-modifying therapies (DMTs) prior to conception and during pregnancy.³ Typically, DMTs should be discontinued at last 5 maximal half lives prior to conception (with the exception being teriflunomide, where according to the manufacturer, conception should be tied to serum drug levels).

Despite these guidelines, there are many unknowns. For instance, many studies, including one by Dr Kerstin Hellwig and colleagues in Germany, have reported no increased risk for fetal malformations in pregnancies exposed to glatiramer acetate.⁴ On the other hand, instances of possible abnormal fetal development associated with fingolimod have been reported.⁵ To achieve broader comparative data across a range of DMTs, a North American MS pregnancy registry is essential.⁶ In response, the Autoimmune Diseases in Pregnancy Project created by the Organization of Teratology Information Specialists in 2012 has begun monitoring pregnancies in women with MS to evaluate the effect of the disease and its related treatments on the birth outcome.

Managing Women through Pregnancy— More Data Required

In addition to the critical information to be gleaned from MS drug registries, further studies are needed to guide women with MS and their providers in three important areas.

Breastfeeding

Additional evidence supporting the apparent protective effect of breastfeeding against postpartum relapses is required (including mechanistic studies). To date, several studies have reported that breastfeeding, particularly if exclusive (i.e. the infant receives no supplemental calories from formula or other source), is associated with a reduced risk for postpartum relapses. Since not enough is known about the safety of DMTs in breastmilk, mothers are usually advised to restart DMTs only after weaning. Therefore, further data are required to guide the safety of DMTs in breastfeeding as well as the optimal duration of breastfeeding off DMTs.¹

Vitamin D Levels

The ideal gestational blood levels and supplementation dosage of vitamin D as they relate to either protection against postpartum relapses in the mother, or long-term MS risk in the child, are unknown. Low vitamin D levels have been linked with a more aggressive MS course in general–but, at least in one study, gestational vitamin D levels were not tied to the risk for postpartum relapses. Low gestational vitamin D levels have also been implicated in the developing child's subsequent risk for developing MS. As a general recommendation, the American College of Obstetrics and Gynecology has advised that 1,000 IU daily is probably safe; it is not known whether higher levels are desirable and/or safe in women with MS.¹

Fertility Treatments

A possible increased risk for relapses associated with assisted reproductive technologies has been reported in five small case series.⁷ More information is needed in this area, to guide women with MS who are contemplating fertility treatments.

Reports from the Estriol Treatment Trial

There is a now well-established protective effect of pregnancy on the risk for relapses, as well as an increased risk for relapses postpartum (during which time one-third of women with MS will relapse). These observations

have brought to attention the possible role of pregnancy hormones, such as estriol (a form of estrogen that is markedly elevated during pregnancy). The preliminary findings from a multicenter, prospective study of estriol as an add-on therapy to glatiramer acetate (Principal Investigator: Dr Rhonda Voskuhl, University of California, Los Angeles) have over the past year been presented at two academic meetings (European Committee for Treatment and Research in Multiple Sclerosis and American Academy of Neurology 2014 presentations). From the preliminary results, it appears that there may be a benefit of estriol over the first treatment year. It is not yet clear whether at 2 years, estriol add-on therapy provided any significant protection from relapses compared with glatiramer acetate monotherapy.

Widening the Scope Beyond Mothers, to Include Fathers and Children

Finally, the field of MS has also begun to consider fertility and fatherhood in *men* with MS. In terms of fertility, studies have reported relative testicular hypofunction⁸ as well as low testosterone in men with MS.⁹ Reassuringly, no adverse birth outcomes have been reported in pregnancies fathered by men with MS,¹⁰ including by men exposed to first-line injectable DMTs.¹¹ Additionally, initial studies of the impact of parental MS on childhood development suggest that while children may exhibit a range of positive and negative responses to parental MS and disability, their development appears to be adversely affected by MS-associated mood disorders in a parent with MS.¹².

Conclusion

The field of pregnancy management in MS is rapidly expanding. More data are required to guide patients who come to us with the questions like:

- What role will childbearing have on my MS?
- What effect will my MS have on my newborn and their later development and how can I affect this?
- Should I, and when should I stop and restart my MS medication? ■

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