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Short Communication

Multiple sclerosis in pregnancy: meeting the challenges

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ABSTRACT

Multiple sclerosis being a chronic, autoimmune inflammatory disease of central nervous system with its common and uncommon semiology has a predilection for women of child bearing age. The stressful period of pregnancy is further complicated with presence of multiple sclerosis. Overall multiple sclerosis has stabilising effect on pregnancy especially in its second and third trimester but adversely affects the post-partum period with increasing relapse rate. This is related with intense immune response triggered by marked changes in levels of circulating hormones. A better understanding of anti-natal, natal and post-partum effect of multiple sclerosis helps us to decide for institution or continuation of disease modifying drugs which are generally associated with favourable outcome.

Keywords: Disease modifying drugs, Labour, Multiple sclerosis, Pregnancy, Relapse

INTRODUCTION

Multiple sclerosis (MS) is a chronic inflammatory autoimmune disease affecting the myelin sheath of axons in brain and spinal cord with resultant demyelination and scarring due to neuronal loss. Lesions of MS can occur at different times and in different central nervous system locations (disseminated in time and place).

The course can be relapsing-remitting or progressive. About 80% of people between age of 20-45 are diagnosed with M.S and in adults the female to male ratio is 2.5:1. It is most commonly diagnosed in young women especially of child bearing age. Specific management concerns surround the pregnancy and postpartum periods.

The issue has been more complicated with the availability of multiple treatment options and by the fact that treatment of MS has entered in new era especially with the availability of a good number of disease-modifying drugs.

Potential impact of MS

Multiple sclerosis has a predilection amongst the female of child bearing age group and raises some potential impact.

Effect on fertility

Most studies have shown that MS does not have any noticeable effect on fertility. In rare cases there may be a decrease in fertility level.¹

Effect on pregnancy

So far there has been no evidence to show that MS can lead to complications during pregnancy or delivery such as ectopic pregnancy, pre-eclampsia, prolong labour or miscarriage as compared to women in general.² There is a slightly higher risk of lower weight babies and caesarean deliveries in women with MS as compared to diabetics and women with epilepsy. MS patients need not to be

monitored more closely than other women. However, if the pregnancy occurs when the women is still taking DMT's then more frequent ultrasounds are needed to keep a closer watch on the development of the baby.

Potential impact of pregnancy on MS

Often the concern is mainly about the effect of MS on the pregnancy, but it is also important to think about how pregnancy will impact MS. Otherwise pregnancy is typically stabilizing period in the clinical course of MS like other immune related disorders such as rheumatoid arthritis.³ However, there are some issues that get exacerbated during pregnancy.

- Fatigue- energy levels are already low due to MS, added to these are the nutritional demands of the growing baby.
- During pregnancy most women have sleep problems and once again for MS patients they become a greater issue.
- The baby puts extra pressure on back and bladder and walking problems also get aggravated during pregnancy. Mobility can also become a challenge but these issues resolve themselves once the baby is born.

Long-term effect on neurological status

Some studies, though they are not conclusive do suggest that having children is beneficial for MS patients in the long run. This is not to say that they should have many children, but just to say there are no ill-effects on MS from pregnancy, rather there may be some benefits. The relapse rate of MS is typically reduced during late pregnancy but increases in the post-partum period because during pregnancy the placenta derived estrogen hormonal levels increase significantly. These hormones have a dampening effect on the immune system. This refers to the immunotolerance adaptation characterized by implementation the T-helper cells (Th1) dominance to the Th-2 cells. Due to this reason some studies have found that the relapse rate drops by almost 70%, especially during the last three months or the third trimester. So, the hormonal changes do have an impact, but in a positive way. Similarly the abrupt fall in levels of estrogen following delivery is related with an increase in inflammatory activity with resultant increase in relapse rate and associated with increase lesion on neuro imaging.⁴ However, it is important to remember that starting a family and later looking after a young family can lead to greater stress and strain in a women's life and in more so if she has MS.⁵

Obstetric management in MS

The following few practical tips which are of clinical help for women with MS are:

- Presence of MS does not affect the mode of delivery and should have an individualized approach.

- For patients having spinal cord involvement and especially those with diminished sensation below T11 should be especially trained to be aware of onset of labour. They should be taught to understand the other symptoms of onset of labour like increasing spasticity, back pain, gastrointestinal upsets etc.⁶
- At times troublesome spasticity during labour may be tailored by epidural anesthesia or benzodiazepines like diazepam.⁷

Management of postpartum period

Women with MS are not different than others hence breast feeding is allowed rather encouraged. Even it should be continued if methyl prednisolone is required to manage a postpartum relapse.⁸ Amongst all the available treatment options both glatiramer acetate and interferon beta are considered safe with breast feeding. There is no evidence to support that regular methyl prednisolone or immunoglobulins could be of help in preventing the postpartum relapse. There is evidence of increased risk of postpartum depression both in mothers and fathers which should be managed like a non-MS condition.

Treatment of MS: issue of disease modifying drugs

A therapeutic dilemma exists regarding the use of disease-modifying drugs in pregnancy as the majority of medications used in MS are FDA category C for use in pregnancy with limited data on safety profiles to the developing foetus.⁹

An exception being Glatiramer Acetate (GA), which is FDA category B (no risk demonstrated in controlled studies in pregnant women).¹⁰ Despite the availability of few clinical trials of disease modifying drugs in MS, a vast clinical experience exist with women who have been exposed to these disease modifying drug treatment during pregnancy. Thus, a better understanding of pharmacology of these drugs, enables us to draw some conclusions about safety.

However, opinion regarding a washout period are becoming more relaxed because many experts now recommend cessation of DMT at the time when patient realizes that she is pregnant. The new guidelines by the experts are expected to reduce uncertainty about treatments that are considered to be safe and appropriate for this particular MS population. In general, the panel of experts suggest that first-line injectable MS treatments, such as glatiramer acetate and beta interferon formulations, can be safely used during pregnancy.¹¹

However, a narrow therapeutic benefit exists between disease-modifying therapies (DMTs) and pregnancy. This has led to many women affected by MS to delay beginning treatment until after they had completed their families, which may significantly increase the chances of a poorer outcome.¹² "There are increasing data that delaying starting disease-modifying drugs and/or routinely stopping

all disease-modifying drugs pre-pregnancy or immediately post-conception is associated with increase relapse rate during pregnancy, with a long-term negative effect in women with MS.”

The recommended guidelines regarding the use of currently approved DMT's including natalizumab, fingolimod, dimethyl fumarate, teriflunomide, ocrelizumab, alemtuzumab, cladribine are:

Pregnancy should not be recommended for 4- and 6-months following treatment with alemtuzumab and cladribine.

Treatment with teriflunomide is contra indicated in pregnancy and dimethyl fumarate and fingolimod should be avoided when possible.¹³

It is also been suggested that couples should not try to conceive for 12 months after receiving ocrelizumab

DISCUSSION

A bidirectional relationship exists between pregnancy and multiple sclerosis. The stressful period of pregnancy is complicated by multiple sclerosis likewise multiple sclerosis affects the outcome of pregnancy in the form of low birth weight babies and relative higher incidence of caesarean deliveries etc. The relapse rate in RRMS variant of multiple sclerosis typically reduces (even up to 70%) in last trimester of pregnancy with resurgence in post-partum period both clinically and radiologically.¹⁴

During a relapse or an acute attack of multiple sclerosis in pregnancy, intravenous methyl prednisolone can be used safely. The other safe drugs to be used in pregnancy are glatiramer acetate and beta interferon. The disease modifying drugs can also be used early in the course of management to prevent the long-term disability. In post-partum period breast-feeding is not only allowed but encouraged. A better understanding of pharmacokinetics, pharmacodynamics and teratogenic potential of these disease-modifying drugs by large multicentric trials will help us to deal with multiple sclerosis in pregnancy in a better way.

CONCLUSION

Along with relative efficacy of Beta interferon and glatiramer acetate, the use of disease-modifying drugs with their limited safety profile in pregnancy, led many pregnant women to defer the use of disease-modifying drugs until after they have completed their families. In some cases, particularly those for whom conception takes longer than anticipated, this has the potential to lead to a significant delay in starting treatment. Despite this fact the early use of disease modifying drugs in pregnancy has shown to delay or reduce the overall long-term disability. Thus, the use of high efficacy disease-modifying drugs to

control MS in pregnancy outweighs its benefit and suggest an early institution of these drugs in pregnancy.

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REFERENCES

1. Goodin DS. The epidemiology of multiple sclerosis: insights to a causal cascade. *Handb Clin Neurol.* 2016;138:173-206.
2. Buraga I, Popovici RE. Multiple sclerosis and pregnancy: current considerations. *Sci World J.* 2014;2014:513160.
3. Hellwig K, Haghikia A, Rockhoff M, Gold R. Multiple Sclerosis and pregnancy: experience from a nationwide database in Germany. *Ther Adv Neuro Disord.* 2012;5:247-53.
4. Confavreux C, Hutchinson M, Hours MM, Cortinvis-Tourniaire P, Moreau T. Rate of pregnancy-related relapse in multiple sclerosis. *Pregnancy in Multiple Sclerosis. Group. N Engl J Med.* 1988;339:285-9.
5. Dahl J, Myhr KM, Daltveit AK, Hoff JM, Gilhus NE. Pregnancy, delivery, and birth outcome in women with multiple sclerosis. *Neurol.* 2005;65(12):1961-3.
6. Kelly VM, Nelson LM, Chakravarty EF. Obstetric outcomes in women with multiple sclerosis and epilepsy. *Neurol.* 2009;73:1831-6.
7. Pasto L, Portaccio E, Ghezzi A, Hakiki B, Giannini M, Razzoloni L, et al. Epidural analgesia and caesarean delivery in multiple sclerosis post-partum relapses: the Italian cohort study. *BMC Neurol.* 2012;12:165.
8. Langer-Gould A, Huang SM, Gupta R, Leimpeter AD, Greenwood E, Albers KB, et al. Exclusive breastfeeding and the risk of postpartum relapses in women with multiple sclerosis. *Arch Neurol.* 2009;66:958-63.
9. Lu E, Dahlgren L, Sadovnick A, Sayao A, Synne A, Tremlett H. Perinatal outcomes in women with multiple sclerosis exposed to disease-modifying drugs. *Mult Scler.* 2012;18:460-7.
10. Alroughani R, Altintas A, Al Jumah M, Sahraia M, Alsharoqi I, AITahan A et al. Pregnancy and the use of disease-modifying therapies in patients with multiple sclerosis: benefits versus risks. *Mult Scler Int.* 2016;2016:1034912.
11. Salminen HJ, Leggett H, Boggild M. Glatiramer acetate exposure in pregnancy: preliminary safety and childbirth outcomes. *J Neurol.* 2010;257:2020-3.
12. Amato MP, Portaccio E. Fertility, pregnancy and childbirth in patients with multiple sclerosis: impact of disease-modifying drugs. *CNS Drugs.* 2015;29:207-20.
13. Lu E, Wang BW, Guimond C, Synnes A, Sadovnick D, Tremlett H. Disease-modifying drugs for multiple sclerosis in pregnancy: a systematic review. *Neurol.* 2012;79:1130-5.

14. Achiron A, Chambers C, Fox EJ, Mc Combe P, Otero S, Margolin DH, et al. Pregnancy outcomes in patients with active RRMS who received alemtuzumab in the clinical development program. *Multi Scleros J.* 2015;21:581-2.

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