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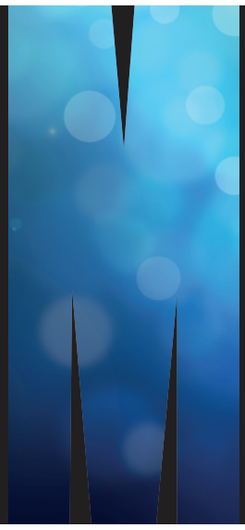

TREATMENT AND PREGNANCY IN MULTIPLE SCLEROSIS

Source: Yeh W, Widyastuti P, van der Walt A.....Jokubaitis V on behalf of the MSBase Study Group. Natalizumab, fingolimod and dimethyl fumarate use and pregnancy-related relapse and disability in women with multiple sclerosis. Neurology, 2021. n.neurology.org/lookup/doi/10.1212/WNL.0000000000012084

WHAT IS THIS RESEARCH ABOUT?

- Multiple sclerosis is an autoimmune disease of the central nervous system, which consists of the brain and spinal cord.
- Multiple sclerosis can cause different symptoms in people depending on which part of the brain or spinal cord is affected. These can include loss of vision/eyesight, bladder urgency, and difficulties with balance and walking. After a relapse (i.e. new period of experiencing symptoms), symptoms may start to improve. However, recovery is not always complete, which can lead to permanent disability.
- Multiple sclerosis affects more women than men. It is most often diagnosed when a person is aged between 20 - 40 years. This means that family planning is an important aspect of care for these individuals.
- Over the past 15 years, there has been an increase in the number of effective treatments for multiple sclerosis which reduce the risk of a further relapse and prevent disability progression.
- Past studies in women with MS have reported a fall in relapse rate during pregnancy that then increased following pregnancy both with no and mildly effective drug treatment.
- Pregnant women are excluded from randomized-controlled trials of disease-modifying therapies (DMT), and there is limited trial evidence to inform management through pregnancy and the postpartum period.
- It is unclear how modern treatments might affect the risk of relapse and disability progression in women with MS who become pregnant. We aimed to investigate this.

Written by Dr Wei Yeh, PhD Candidate, Dept. of Neuroscience, Central Clinical School, Monash University.

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WHAT DID THE RESEARCHERS DO?

- We used data from the MSBase Registry, the largest international Registry of clinical outcomes in people with multiple sclerosis.
- We included 1,619 women with multiple sclerosis who had 1,998 pregnancies conceived after 31 December 2010. We then compared this group to women with pregnancies conceived during 2005-2010 and also before 2005, looking at relapse rates before, during and after pregnancy with the introduction of modern drug treatments.
- We used statistical methods to determine any factors which predict or protect against relapse during and after pregnancy. We also looked at factors that predict or protect against accumulating disability after pregnancy.

WHAT DID THE RESEARCHERS FIND?

- The rates of relapse in the one-year before pregnancy were highest for women in the pre-2005 group and lowest in the 2010 onwards group.
- In the 2010 onwards group, relapse occurred in 12% of pregnancies and after delivery in 14% of women.
- Relapses were more common during pregnancy among women who stopped their pre-pregnancy treatments of natalizumab (Tysabri) or fingolimod (Gilenya), two highly effective treatments. These women also had a higher chance of relapse in the first three months after delivery compared to those on other treatments.
- Continuing treatment with natalizumab into pregnancy, and beyond the first pregnancy trimester, prevented any increase in relapse rate later in pregnancy.
- Predictors of relapse: Women with higher rates of relapse before pregnancy were at higher risk of relapse during and after pregnancy. Higher relapse rate during pregnancy and higher levels of disability before conception were also predictive of post-pregnancy relapse.
- Re-starting natalizumab (Tysabri) after delivery reduced the risk of relapse by 89%.
- Women who breastfed, whether they received treatment or not, were 39% less likely to relapse after delivery.
- Disability progression after delivery (both in treated and untreated) was uncommon, occurring in only 6% of women.

WHAT DO THESE FINDINGS MEAN?

- Our findings play an important role in informing discussions between neurologists and women with multiple sclerosis around family planning and management of their disease.
- Pregnancy is a time of low relapse activity in most, but not all women with MS. Relapse risk may be elevated in women who have more active disease before pregnancy, or who are treated with certain more effective treatments such as natalizumab (Tysabri) and fingolimod (Gilenya).
- The first few months after delivery remains a high risk period for relapse in women with MS.
- We show that continuing treatment with natalizumab (Tysabri) into pregnancy, and re-starting it after delivery, is an effective strategy at preventing relapses during and after pregnancy.
- Relapses are the key driver of accumulating disability after pregnancy.

WHAT YOU NEED TO KNOW

- Proactive planning and use of the right treatment to optimise disease control is important for all women with multiple sclerosis.
- Natalizumab (Tysabri) use during and after pregnancy is an effective strategy to consider in women deemed at high risk of relapse during these time periods.
- Breastfeeding is encouraged for its benefits for the mother and baby, and also potential protective effects against relapse.
- Uncertainties still exist around specific treatments and their use for women with multiple sclerosis around pregnancy and breastfeeding. The Australian Therapeutic Goods Association has categorised Natalizumab (Tysabri) as Category C and Fingolimod (Gilenya) as Category D. Discussions regarding the use of DMTs should take place with the treating neurologist prior to conception.

NEUROIMMUNOLOGY, GENOMICS AND PROGNOSTICS RESEARCH GROUP

Our goal is to improve the long-term outcomes for people with multiple sclerosis (MS) through evidence-based management, and treatment individualisation strategies. My group's particular focus is on the optimization of MS therapy use, and the interplay between therapy use and women's health.

MS is an autoimmune degenerative disease of the central nervous system. Globally MS affect about 2.8 million people, in Australia, MS prevalence is around 1 in 1,000, equating to about 25,600 Australians. MS represents a significant burden to Australian society with an estimated annual cost of >$1.7 billion AUD, due to lost productivity, and healthcare costs that increase markedly with disease-associated disability.

The long-term disability outcomes of people with Multiple Sclerosis (MS) vary greatly, ranging from little or no disease-associated disability, to severe disease that can render individuals wheelchair or bed-bound within a decade of onset. Further, MS disproportionately affects 3 times more women than men, and is usually diagnosed during a woman's reproductive years (20-40). My group's research focus sits at the intersection between biology and clinical outcomes research.

Our research falls under three broad umbrellas:

- Women's Health, Pregnancy and Neonatal Outcomes
  Identification of genetic and epigenetic signals associated with disease outcomes and treatment response
- Integration of biological (biomarker, genetic) and,
- Environmental data with clinical outcomes data to inform prognostic modelling.

Our research integrates biological data with clinical outcomes data with the aim of better understanding what drives disability outcomes in MS, and similar neuroimmunological conditions such as neuromyelitis optica spectrum disorder (NMOSD).

We collaborate nationally and internationally in order to be able to answer some of the big questions in MS. We have strong collaborative links with the MSBase Registry. Dr Jokubaitis is a member of the MSBase Scientific Leadership Group. She is the co-Chair and Scientific Leader of the MSBase Women's Health, Pregnancy and Neonatal Outcomes Registry.

We have a number of on-going projects that utilize genetic, genomic, biostatistic, and epidemiological methodologies to approach our research aims.

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