New reports on the use of MS medications during pregnancy

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Most disease modifying therapies used to treat MS are not recommended for use during pregnancy or in those who are planning a pregnancy and clinical studies for pregnant women are generally not undertaken. As such, when pregnancies do occur in people under treatment for their MS, pregnancy outcomes for the baby and mother are of great interest to patients and their doctors to guide treatment decisions for future families. For this reason 'pregnancy registries' are often set up to record this data. Several recent papers have reported on pregnancy outcomes for interferon-beta 1b (Betaferon), teriflunomide (Aubagio) and natalizumab (Tysabri).

The first study published in the *Journal of Neurology, Neurosurgery and Psychiatry* examined pregnancies during treatment with interferon-beta 1b. The results covered 423 pregnancies as part of the Bayer Healthcare Pharmacovigilance database, which represents the largest collection of pregnancies in people taking interferon-beta 1b to date. The majority of the pregnancies recorded were normal, resulting in healthy babies. The rate of spontaneous abortion was consistent with the rate in the normal population. All major and minor complications and birth defects were also similar to the normal population. This included outcomes such as preterm delivery, babies which were small or large for gestational age and ectopic pregnancies, among others. No specific pattern of birth defects were seen, even when the mothers' age at the time of taking interferon-beta 1b was taken into account.

Another study reported on the safety of teriflunomide during pregnancy via a Global Pharmacovigilance database of Sanofi Pharmaceuticals. The report, from the medical journal *Neurology and Therapy*, looked at pregnancies that occurred unexpectedly during clinical trials of teriflunomide. 70 pregnancies occurred in women taking teriflunomide and 19 pregnancies in partners of men taking teriflunomide for MS. Of the 70 pregnancies in women taking teriflunomide, 26 went on to have healthy babies, with 13 spontaneous abortions and 29 induced abortions. The spontaneous abortion rate was the same as the general population and induced abortions were by choice not because there were any abnormalities seen.

When women taking teriflunomide are planning pregnancy or become aware they are pregnant, they have the option to stop taking the medication and use other medicines to rapidly clear the teriflunomide from their system. In the 26 successful pregnancies, ten stopped taking teriflunomide before becoming pregnant (with nine undergoing the procedure to clear the teriflunomide from their system). The other 16 women stopped taking teriflunomide after becoming pregnant (13 of which had the clearing procedure). These women stopped taking teriflunomide between a few days to 11 weeks into their pregnancies. The rapid elimination procedure quickly reduced levels of teriflunomide in the body to below the level predicted to be dangerous during pregnancy. All the babies who were exposed to teriflunomide either through the mother or father taking teriflunomide were born normal and healthy.

The final study examined the effect of taking natalizumab during the first trimester of pregnancy. The study was published in the *Multiple Sclerosis Journal*. Standard clinical practice is to stop natalizumab treatment three months prior to the start of pregnancy, however when some patients stop taking natalizumab they return to the level of disease they experienced prior to the treatment, so relapse risk must be weighed against the risk of treatment during pregnancy in individual cases.
The study compared 101 people with MS taking natalizumab to 78 people with MS who were not taking natalizumab for their MS (some untreated and some taking other medications) and 97 healthy controls. These pregnancies were successful in 77 people taking natalizumab, 69 people with MS not taking natalizumab and 92 healthy controls. Three quarters of the women taking natalizumab stopped the treatment before 10 weeks of pregnancy.

No differences were seen in the rates of low birth weight (defined as under 2.5kg), premature births or major malformations. People with MS in this study, irrespective of whether they were treated with natalizumab, had higher rates of miscarriage and lower average birth weights than healthy controls. The reason behind this difference is unclear but the authors discuss that this may be due to differences in inherent characteristics of the women in each group (such as age) rather than due to their MS or treatment choices. Further studies with more participants are needed to answer this question definitively. Overall, this small study found that treatment with natalizumab did not affect pregnancy outcomes in comparison to others with MS.

There are two pregnancy registries currently open for Australian MS patients taking fingolimod (Gilenya) and dimethyl fumarate (Tecfidera), which collect vital data on pregnancy outcomes in these patients.
Any person with MS who is considering becoming pregnant while undergoing treatment for their MS must discuss their options with their treating neurologist.