MS/NMO management during pregnancy

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Pregnancy in MS and NMOSD

- Pre-pregnancy counselling
  - pregnancy planning,
  - fear of hereditary transmission of the disease
- Management of therapy: before pregnancy
- Management of therapy: during pregnancy
- Management of therapy: post-pregnancy

Pregnancy in MS

CASE I

• 29/F

• 1st attack 2016-06 BS attack (diplopia)

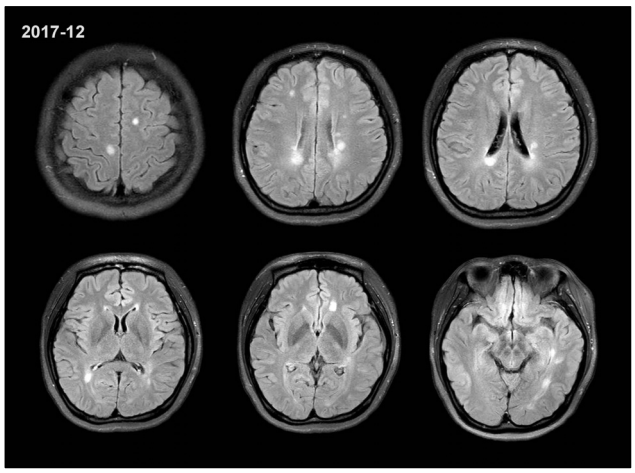
• 2nd attack 2017-04 partial myelitis

CSF OCB (+)-Type II

RRMS 진단 하에 teriflunomide 시작한지 6개월 째 본원 방문

◆치료 6개월동안 임상적 재발(-)

◆결혼한지 2년째, 임신 원하고 있음.



Pre-pregnancy counselling

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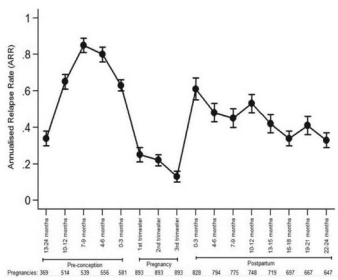
Pre-pregnancy counselling

ARR for the pre-conception, pregnancy and postpartum



Hughes Mult Scler 2014

Factors predictive of relapse occurring in the postpartum period

❖ **893 pregnancies in 674 females with MS**

Table 4. Factors predictive of relapse occurring in the first 3 months of the postpartum period. CI: confidence interval.

Variable	Unadjusted odds ratio (95% CI), p value	Adjusted odds ratio[a] (95% CI), p value
Age at onset of MS	1.00 (0.97, 1.04), 0.873	1.01 (0.96, 1.08), 0.594
Duration of MS at conception	1.00 (0.96, 1.04), 0.934	1.04 (0.98, 1.11), 0.199
ARR in 2 years pre-conception	13.39 (8.83, 20.32), <0.001	14.12 (9.09, 21.93), <0.001
ARR during pregnancy	1.71 (1.25, 2.34), 0.001	[b]
EDSS at conception		
<2.0	1.00	1.00
≥2.0	2.99 (1.75, 5.12), <0.001	1.10 (0.52, 2.33), 0.813
DMT use 2 years pre-conception		
No	1.00	1.00
Yes	0.55 (0.36, 0.84), 0.006	0.55 (0.32, 0.96), 0.034

[a]Hosmer and Lemeshow Goodness of Fit Test = 1.000.
[b]When ARR during pregnancy was included, the Hosmer and Lemeshow Goodness of Fit Test demonstrated a poor fit, and this covariate was therefore omitted from the model shown.

Hughes Mult Scler 2014

Pre-pregnancy counselling

Management of therapy: before pregnancy

Glatiramer acetate/interferon beta

◆The European labeling for branded glatiramer acetate was amended in December 2016 and the warning that the drug should not be used during pregnancy was removed.

◆It is preferable to avoid the use of glatiramer acetate during pregnancy unless the benefit to the mother outweighs the risk to the fetus.

◆Exposure to IFNβ during early pregnancy does not have adverse impact on pregnancy outcomes with no increase in abortive or teratogenic risk.

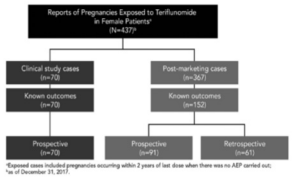
Amato MP. Neurology **2010**/ Lu E. Neurology 2012*Coyle PK. BMJ Open 2014/ Thiel S. Mult Scler 2016*

Safe to continue until conception

FDA-and EMA-approved DMT, with known suspected pregnancy risks

Name	Teratogenic in animal models	Signal for increased malformation in human pregnancies	Recommended washout period before conception attempt
Dimethyl fumarate	Yes	No	None
Fingolimod	Yes	Yes	2 months
Teriflunomide	Yes	Yes in precursor leflunomide	Until plasma levels are below 0.02ug/mL
Alemtuzumab	No	No	4 months
Natalizumab	No	No (transient hematologic abnormalities in exposed newborns observed)	1-2 menstrual cycles unless concern for disease reactivation in pregnancy

Teriflunomide



- **Risk of major birth defects**
  3.6% (1/28) clinical trials
  0% (0/51) in post-marketing reports
  *** general population 2-4%*

=> Current human data do not indicate a teratogenic signal in teriflunomide-exposed pregnancies

Vukusic S. Mult Scler 2019

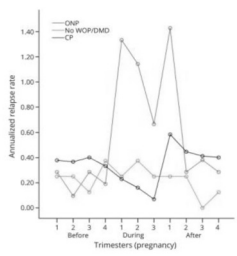
Pregnancy decision-making in women with MS treated with natalizumab

I. Fetal risks

-natalizumab exposure to up 12 weeks increased risk of spontaneous abortion (17%) than control pregnancies although within the limits expected in general population

-major congenital anomaly (3.7%)

II. Maternal risks



ONP other natalizumab pregnancies
No WOP/DMD no washout and early resumption of DMT
CP control pregnancies

Portaccio E. Neurol 2019

Pre-pregnancy counselling

Management of therapy: during pregnancy

Original Investigation

Vitamin D Status During Pregnancy and Risk of Multiple Sclerosis in Offspring of Women in the Finnish Maternity Cohort

Kassandra L. Munger, ScD; Julia Åivo, MD; Kira Hongell, MD; Merja Soilu-Hänninen, MD; Heljä-Marja Surcel, PhD; Alberto Ascherio, MD, DrPH

- Maternal vitamin D deficiency (25[OH]D levels <12.02ng/mL) during early pregnancy was associated with a nearly 2-fold increased risk of MS in the offspring (relative risk 1.90; 95% CI, 1.20-3.01) compared with women who did not have deficient 25 (OH)D levels.

Munger KL. JAMA Neurol 2016;73:515-519

◆ 임신 28주째 갑작스런 어지럼증 및 복시 호소

JAMA | Original Investigation

Association Between MRI Exposure During Pregnancy and Fetal and Childhood Outcomes

Joel G. Ray, MD, MSc, FRCPC; Marian J. Vermeulen, BScN, MHSc; Aditya Bharatha, MD, FRCPC; Walter J. Montanera, MD, FRCPC; Alison L. Park, MSc

- Exposure to MRI during the first trimester of pregnancy has not been associated with risk of harm to the fetus or in early childhood.
- Gadolinium based contrast agent use at any time during pregnancy was associated with an increased risk of a broad set of rheumatological, inflammatory, or infiltrative skin conditions and for stillbirth or neonatal death.

Rey JAMA 2016;316:952-961

◆ Non-contrast MRI상 pons에 새로운 병변

◆지속되는 어지럼증, 복시 있어 고용량 스테로이드 치료 권고

If relapse occurs, corticosteroids can be given during pregnancy and while breastfeeding.

Dobson R. Pract Neurol 2019;19:106-114

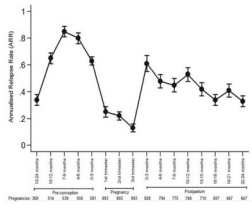
Management of therapy: post- pregnancy

- 39주 3일째, 질식분만, 3.2kg 여아
- 출산 10일째 병원 방문함.

Pregnancy in NMOSD

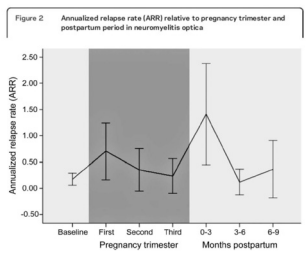
NMOSD remains active during pregnancy and the relapse rate increase postpartum

MS



Hughes Mult Scler 2014

NMOSD



Klawiter EC, Neurol 2017

Pregnancy-related attack in NMOSD

❖Of the NMOSD patients with pregnancy with or without immunosuppressive treatments (AZA, PD, or tacrolimus),

46%-83% had a pregnancy-related attack.

❖EDSS worsening 1 year after pregnancy => increase range from mean 0.5 to 2.1 point

❖Risk factors for pregnancy-related attack in NMOSD

- **Relapse in the previous year**
- **No immunosuppressive treatment during pregnancy**

Fragoso YD, 2013/ Shimizu Y, 2015/ Shi B, 2017/ Huang Y, 2017

Immunosuppressive treatments FDA pregnancy category

FDA pregnancy category	Drugs
FDA class C	Rituximab, Tacrolimus, Steroids
FDA class D	Azathioprine, Mycophenolate mofetil, Mitoxantrone, Steroids in first trimester
FDA Class X	Methotrexate
FDA Class Not Assigned	Tocilizumab, Eculizumab