Impact of disease modifying drugs (DMD) on pregnancy outcomes in women with multiple sclerosis

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NEW SZÉCHENYI PLAN

1.BACKGROUND

Multiple sclerosis (MS) is most frequent chronic inflammatory demyelinating disorder among women of fertile age, so poses extra challenge of guiding these women regard to pregnancy. The prevalence of the disease varies with geography ranging between 2 and 150 per 100,000 [1–3] The appearance of the disease is determined by a combination of exogenous factors and genetic background.[4] In the majority of MS patients (80%), the disease begins with relapsing course (RRMS), characterized by relapses and remissions, and followed by a progressive phase (secondary progressive MS, SPMS). In smaller subset of patients, the relapsing phase is not observed and the disease progresses from the beginning (primary progressive form, PPMS)

1.2. MULTIPLE SCLEROSIS AND PREGNANCY

It is widely accepted that because of the immunological and hormonal changes during pregnancy, the gestational period has a protective effect regarding MS relapses. [5] Pregnancy does not seem to negatively influence the evolution of this disease. However some papers have shown a negative impact from MS on the newborn.[6–7] Immunmodulatory and immunsupressive drugs used at any stage of pregnancy may affect fetus formation and/or development. This is particularly important in relation to unplanned pregnancy, since a mother may have used immunmodulatory compounds for a few critical weeks during a fetal development. In Hungary there is no clinical trial will ever be evaluated on this population of patients.

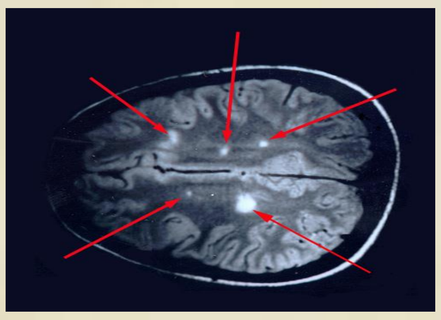
Table 1. Food and Drug Administration Guideline for teratogene effect of immunmodulatory drugs

CLASS B	glatiramer acetate, iv. immunglobulin
CLASS C	beta-interferon, mitoxantron, corticosteroid
Teratogen agents (CLASS X)	azathioprin,cyclophosphamide,methotrexate

Immunmodulatory recommendations for MS needs to be discountinued before conception because of the drugs are still under investigation.

Some physicians may, even when aware of the risks, consider it necessary to continue with some medications for their patients.

Figure 2. This MRI scanning presented by a tipical demyelinisation plaques of MS



2.OBJECTIVES

Our primary aim was to assess the pregnancy complications and delivery risk in our survey population compared to general (non-MS) patients. The secondary aim was to identify the risk exposure of immunmodulatory treatment during and after pregnancy.

3. MATERIAL AND METHODS

Our retrospective study was conducted in January 1998 in Department of Obstetrics and Gynecology, Department of Neurology, and County Hospital of Orosháza and Szentes. In this period in our multicenter retrospective study, all pregnancies beginning in patients with MS diagnosed according to McDonald criteria. Disability was measured by the Expanded Disability Status Scale (EDSS). Body mass index (BMI) was calculated as body weight (kg)/height (m). Control group consisted of 75 healthy volunteers matched for age, parity and gravidity. Multiparous and primiparous MS subgroups were also created. Statistical analysis was made by SPSS (Statistical Package for Social Sciences) 20.0 using Independent Sample T-test with the confidental interval (CI) of 95 % for a continous data and chi-scare test for categorical data. The relationships between different MS therapy and pregnancy outcomes were analyzed using the One-Way ANOVA. Results were considered significant when $p<0,05$. The study was approved by the Ethics Comittee of the University of Szeged. (No.

3.RESULTS

Table 2. Data on peripartum relapse among Hungarian MS mothers.*$p<0,05$

Relapse rate	
Before pregnancy	1,37±1,9
During pregnancy	0,29±0,6 *
Postpartum period	0,86±1,1

A summary of data on these patients and their pregnancies is presented in Table 3.

	Primiparous (n=30) n	%	Multiparous (n=45) n	%
Average age at childbirth (years)	29,15±5,13		25,18±3,88	
Average age at diagnosis of MS (years)	27,35±6		23,31±5,31	
EDSS score	1.38±1,4		1.53±4,6	
Spontaneous pregnancy	30	100	43	95,5
IVF/ICSI	2	2,6	2	4,4
BMI (kg/m2)	38,96±7		43,9±7,7	

Comparison of maternal and neonatal data in primipara and multipara MS patients (Table 4.)

	Primipara (n=30) n	%	Multipara (n=45) n	%	p-value
Average birth weight (mean±SD) (g)	2765±861,8		3215,8±591,85		0,058
Prematurity (<37.week; <2500 g)	4	13,33	7	15,56	0,56
Spontaneous abortion	5	16,7	19	42,2	0,049*
Induced abortion	5	16,7	21	46,7	0,026*
Post-term birth	1	3	5	11,11	0,22
Macrosomia (>4500 g)	0	0	2	4,4	0,5
Intrauterin exits	6	20	0	0	0,003*
Congenital anomalies	0	0	0	0	-

4.CONCLUSIONS

1. Our results confirm that, in contrast with international data, the relapse rate did not significantly decrease during pregnancy and increase after delivery. [5]

2. The significantly increased risk of spontaneous abortion and intrauterine exits could be considered independent of beta-interferon use. [8–9]

Figure 3. Pregnancy outcomes in the MS and int the control group ($p>0,05$)

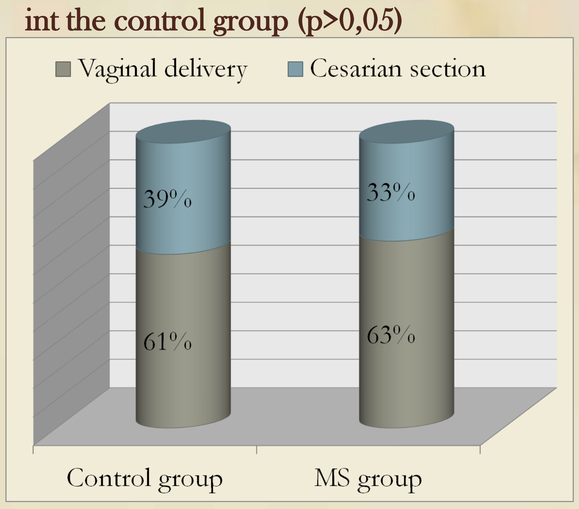


Figure 4. Prevalence of drug using during pregnancy (Early exposure to MS drugs: 9 ± 6 weeks)

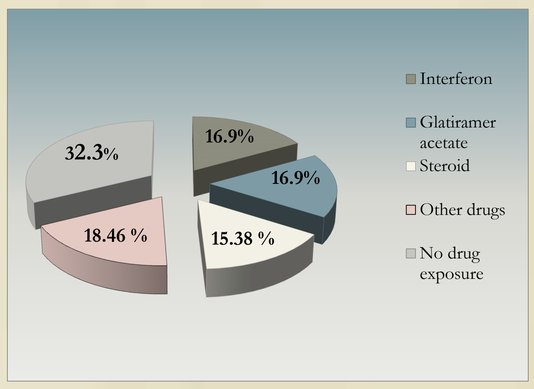
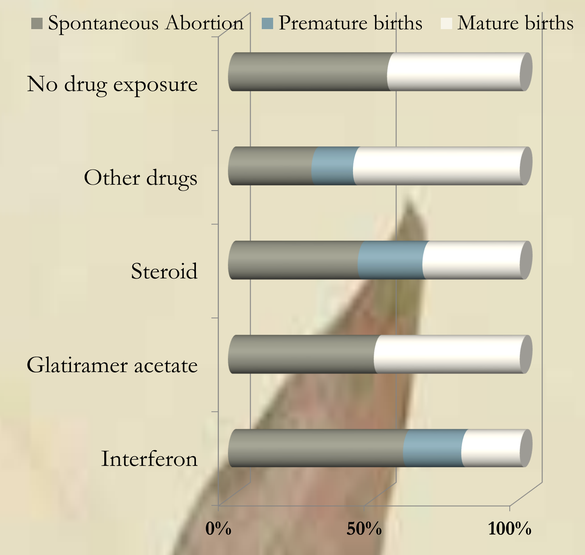


Figure 5. The relationship between immunmodulatory treatment and pregnancy outcomes



3. One-Way ANOVA did not reveal a significant correlation between any MS drug exposure and an unfavourable obstetric outcome.

4. Prevalence of obstetric, neonatal, perinatal complications in our patients and their offspring was low in comparison previous studies. [6–7]

5. >5 day hospitalisation was more prevalent in MS women compared to general population.($p<0,05$)

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