Family planning in patients with MS patients

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- ***common concerns before marriage***
  - *Sexual dysfunction ?*
  - *Disable after marriage?*
  - *Can MS patients use contraceptive?*
  - *Can a MS patient have a child?*
  - *Effect of pregnancy on disease course?*
    - *Is MS going to disable mother and put her in a wheelchair*
    - *Effect of Pregnancy on MS Relapses?*
  - *Effect of MS on pregnancy?*
  - *chance of inheritance of MS ?*

Q: What are common sexual dysfunction problems in MS

- Common problems related to sexual functioning in this population include:

- decreases in genital sensation
- decreases in libido
- vaginal lubrication
- Difficulties in orgasm
- erectile dysfunction.

Q: How prevalent is sexual dysfunction in adults with MS?

- **A:** Though research in this area is still fairly limited, studies indicate prevalence rates of 40 to 80% in women and from 50 to 90% in men.
- A survey of MS patients (n=5868) found that 67.2% of participants endorsed sexual dysfunction symptoms that were present always or almost always in the previous six months.
- Moreover, a clinical sample from the Mellen Center revealed that 60% of patients endorsed some form of sexual dysfunction (n=105).

Disable after marriage?

- According to available statistics, 66% _ 75% of people with MS maintain their ability to walk.

- The global scientific community hopes that the continuation of current will greatly improve the symptoms of MS.

Can a patient with MS become a mother?

- Most of MS are young women and like to be a mother.
- Most women with MS can be mother and have no limitations.
- Pregnancy should be planned.
- Some DMTs are teratogen and should be changed before pregnancy.
- Allowing a woman with MS to become pregnant depends on the activity and severity of the disease and the level of the mother's disability

- ***Does MS impair fertility?***
- Sexual dysfunction
- High grade endometriosis
- Autoimmune thyroid disease
- Diminished ovarian reserve

- ***Does MS impair fertility?***
- Overall, fertility does not impaired in women with MS.
- The relationship between infertility and MS is not fully understood.
- fertility does not seem to be impaired to a larger extent in women with MS.
- a clear relationship between infertility and MS has not been established.

- ***Does MS impair fertility?***
- There seems to exist a link between disease aggressiveness and progression with several processes that might impair fertility.
- The use of certain immunosuppressant agents such as mitoxantrone and cyclophosphamide, is associated with reduced fertility and reproductive toxicity.
- It is important to discuss and plan the ideal moment to start treatment and managing pregnancy and contraception aiming at better results.

Oral contraception

- *no positive proof of an effect of OCP on the lifetime risk of development MS .*
- Most contraceptive methods appear based on current evidence to be safe for women with MS.
- The only restriction is use of combined hormonal contraceptives among women with MS with prolonged immobility because of concerns about possible venous thromboembolism and change in bone mineral density.

Oral contraception

- . Disease-modifying therapies (DMTs) do not appear to decrease the effectiveness of hormonal contraception although formal drug–drug interaction studies are limited.
- Neurologists can help women with MS make contraceptive choices that factor their level of disability, immobility, and medication use.
- For women with MS taking potentially teratogenic medications, highly effective methods that are long-acting (e.g. intrauterine devices, implants) might be the best option.

Assisted reproduction technique (ART)

- Elevation in relapse rate during ART.
  - in the 3-month period following use of ART,
  - especially if gonadotropin-releasing hormone agonists were used and if the cycle was unsuccessful.

- Generally, not recommend to refrain from ART but inform about the increased risk and counsel to stay on MS treatment while undergoing ART.

Assisted reproduction technique (ART)

- ***Early preconception consultations are essential to individualising pregnancy management in women with MS, and an early, well-planned, spontaneous pregnancy should be the aim whenever possible.***

- ***The management of women with MS and the desire for motherhood by multidisciplinary units is warranted to ensure appropriate guidance through the entire pregnancy.***

Assisted reproduction technique (ART)

- *.. There is ample evidence from clinical observations that ART – independently of the type of hormonal treatment used – increases the relapse risk, the number of new or enlarging T2 lesions and gadolinium-enhancing lesions, particularly in the first 3 months after failing to conceive-*

- *Gonadotropin-releasing hormone (GnRH) agonists are known to stimulate immune cell proliferation; cytokine, chemokine and endothelial growth factor production; as well as estrogen levels.*
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Assisted reproduction technique (ART)

- The use of GnRH antagonists seems to carry less of a risk but this still needs to be confirmed in proper prospective studies.

- There is some evidence that maintaining the patient on GA or IFNβ during the procedure until conception, may help preventing relapse risk.

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Chance of MS disease in child

- MS patients worry that they *may pass their disease on to their children*.
- No single gene produces MS.
- Risk for MS in the general population is about 0.13%.
- When a parent has MS, risk to a child is about 2% to 4%.
- MS has been observed in 6%–12% children when both parents had MS.
- the risk is a little greater to develop MS when a sibling has the disease (2.7%) than when a parent does.
- Such data suggest the importance of environmental over genetic factors in MS.

Chance of MS disease in child

- Lower vitamin D levels have been associated with a higher risk for MS,and MS risk is lower among women born to mothers with high vitamin D intake during pregnancy.
- Although safety of vitamin D supplementation in pregnancy is not established, supplementing vitamin D-deficient mothers might seem sensible,but the dose given should achieve and not exceed a normal serum concentration (25-hydroxy vitamin D range 50–125 nmol/l)

The effect of MS on pregnancy

- Pregnancy complications are not higher than healthy women.
  - such as spontaneous abortions (SA), placental abnormalities, ectopic pregnancy,…
- low birth weight is not increased in women with MS.
  - Some authors discuss a *reduced birth weight (but still in the normal range)* .
  - In NMO patients : increased risk of abortion, PRES & pre eclampsia.

Effect of pregnancy on MS disease activity

- Changes in circulating pregnancy hormones (estrogen, progesterone, prolactin and others) have effects on immune responses that underlie MS pathology.

- The number of acute MS relapses is approximately halved during pregnancy, especially in the third trimester, and approximately doubled during the three months postpartum.

- Pregnancy probably has no impact on long-term course or the likelihood of secondary progressive MS.

Effect of pregnancy on MS disease activity

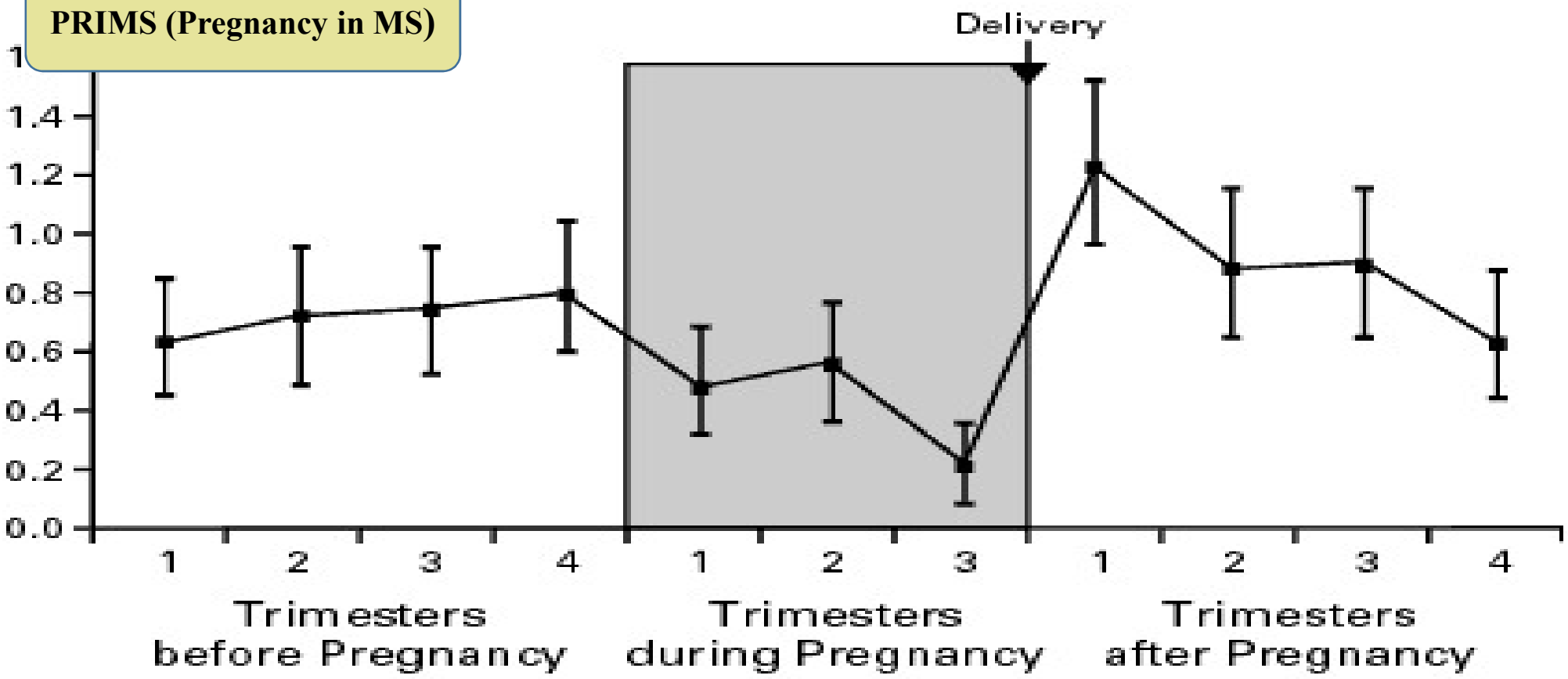
- In the past female with MS were counseled not to get pregnant .
- **PRISM study :**
  - 269 DMT –unexposed pregnancies in 254 women
  - the ARR during pregnancy was decreased significantly during pregnancy
  - Pregnancy did not contribute to a major change in disability progression
  - Predictors for postpartum relapses:
    - ***Number of relapse in the year before pregnancy***
    - ***Number of relapse during pregnancy***
    - ***A higher EDSS at the beginning of pregnancy***

Pregnancy-related issues in women with multiple sclerosis: an evidence-based review with practical recommendations

Beatriz Canibaño , Dirk Deleu , Boulenouar Mesraoua , Gayane Melikyan , Faiza Ibrahim & Yolande Hanssens

30% experience one during first 3 months delivery

PRIMS (Pregnancy in MS)



gnancy and multiple sclerosis (the PRIMS study): clinical predictors of post-partum relapse. Brain

Hutchinson M, Hours MM, et al. Rate of pregnancy related relapse in multiple sclerosis. Pregnancy in multiple sclerosis group. N Engl J Med. 1998;

Is It Safe to Withdraw a Disease-Modifying Therapy during Pregnancy?

- **potential risks of stopping a beneficial DMT during pregnancy?**
  - insufficient evidence to quantify either the risk of DMT therapy to the fetus or the risk arising from a temporary suspension of DMT therapy (a“drug holiday”).
- **How long after stopping DMT does pregnancy occur?**
  - Acute relapse
  - rebound in disease activity
    - increased clinical and MRI activity mote than before treatment on stopping treatment,
      - **Natalizumab**
      - **Fingolimod.**

Table 1
Summary of effects of disease-modifying therapies on multiple sclerosis

Immunomodulating Agents	Drug Half-Life	Fetal and Maternal Risks
Interferon β-1-b and β-1-a	10 h	Spontaneous abortions in animals; not seen in humans
Glatiramer acetate	6.76 h	None reported
Intravenous immunoglobulin	25–32 d	Probably safe in pregnancy
Fingolimod	6–9 d	Teratogenicity seen in animals and humans; no specific pattern observed
Dimethyl fumarate	1 h	Increased spontaneous abortion in animals; not reported in humans
Teriflunomide	18–19 d	Teratogenicity seen in animals; precursor leflunomide is a known human teratogen; no malformations in humans observed thus far
Natalizumab	7–15 d	Reduce neonatal survival at supratherapeutic doses in primates; transient hematologic abnormalities in late pregnancy exposure in humans
Alemtuzumab	12 d	Increased rates of fetal loss, decreased B and T lymphocytes in offspring in animals; no human malformations seen, but thyroid monitoring necessary for mother throughout pregnancy; no evidence for spontaneous abortion or birth defects
Rituximab/ Ocrelizumab	22 days/26 d	No human malformations seen; transient B-cell depletion in human neonates and animals following

- ***IFN-B :***
  - the pharmacologically plausible safety of IFN-β exposure in ***early pregnancy.***
  - ***In case of high disease activity, can be maintained during entire pregnancy. (EMA approval)***
- ***GA :***
  - ***early pregnancy exposure to GLAT appears safe .***
  - ***In case of high disease activity, can be maintained during entire pregnancy.***
- ***DMF(* Difosel.teczyfuma,zadiva)**
  - Low birth weight, delayed ossification and a higher risk for SA : at very high dose .
  - due to the very short half-life and the minimal tissue accumulation, DMF is rapidly eliminated
  - In case of an accidental exposure DMF should be stopped after positive pregnancy testing and an organ screening ultrasound might be considered.

- ***Teriflunamid:***
  - ***It is Teratogen***
  - ***It can detected in semen***
  - ***After stopping ,up to 11 months has serum level***
  - ***Wash out or use of contraception*** as long as the plasma drug level remains above 0.2mg/ L; an accelerated elimination procedure is needed if pregnancy occurs on treatment.

➢ ***Natalizumab:***

  ➢ ***In cases of high disease activity : continue NTZ during pregnancy with extend infusion intervals of 6 weeks and stop NTZ before gestational week 30 (active approach).***

➢ ***Fingolimod:***

- Absolute contraindication for fingolimod in pregnancy .
- Maintenance of contraception for up to two months following cessation of fingolimod.
- Rebound????
- Bridging with other DMTs might be an option, data do not exist.

- ***Alemtazumab:***
  - not to get pregnant for four months after the course of alemtuzumab
  - if pregnancy occurred after the first course, the second course of alemtuzumab should be postponed till delivery.
  - Due to a half life time of 4-5 days, alemtuzumab is completely eliminated afte 30 days

- ***Mitoxantron:***
  - ***Contraception at least 6 months***
- ***Rituximab :(zytux,rituxiver)***
  - Animal study: no teratogenic effects but a peripheral B-cell depletion and immunosuppression in the offspring.
- **Ocrelizumab(Xacrel)**

Rituximab

- estimated half-life is 18-22 days.
- Human data include 153 pregnancies after rituximab with known outcome and revealed no increased frequency of CA (2.3%).
- SA were reported in 21.6% .
- (12.1%) hematological abnormalities in newborn
- 2 (1.5%) exposure before the last menstrual period,
  - one (100%) with exposure in the first trimester,
  - 2 (22.2%) with exposure in the second trimester,
  - 6 (60%) with exposure in the third trimester of pregnancy.

•THANKS FOR YOUR ATTENTION.