The effect of disease modifying therapies for MS on fertility and pregnancy

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What am going to talk about

- MS
- MS treatment
- DMT’s and pregnancy
- Our study
Multiple Sclerosis (MS)

- Autoimmune disease of the central nervous system
- Chronic inflammation
- Demyelination
- Gliosis
- Neural loss

MS - MRI
MS - Epidemiology

- 350,000 patient in the US
- 2.5 millions patients worldwide
- 3:1 more common in women
- Age of onset between 20-40

- Israel – around 5,000 patient with MS
MS – Disease course

- **Relapsing-remitting MS (RRMS)** – 85% of the patients

- **Secondary Progressive MS (SPMS)** – for patients with RRMS the risk for developing SPMS is 2% each year.

- **Primary Progressive MS (PPMS)** – 15% of the patients
MS - Clinical manifestation

- Weakness of the limbs
- Spasticity
- Optic neuritis
- Diplopia
- Sensory symptoms
- Ataxia
- Bladder dysfunction
- Constipation
- Cognitive dysfunction
- Depression
- Fatigue
- Sexual dysfunction
- Vertigo

Treatments for MS

- Treatment of acute attacks (exacerbations)
  - Glucocorticoids

- Disease modifying therapies
  - INF β
  - Glatiramer Acetate
  - Natalizumab
  - Fingolimob
  - Dimethyl Fumarate
  - Teriflunomide
  - Mitoxantrone
  - Alemtuzumab
MS and Pregnancy

- Reduction in relapse frequency during pregnancy (especially on final trimester).
- Increase in relapse risk in the first 3 months postpartum.
- Some studies showed lower birth weight in babies born to MS patient.

The effect of DMTs on pregnancy outcomes

- DMT is usually discontinued during the pregnancy and breast feeding → limited information
- Teratogenic effect:
  - Fingolimod, Mitoxantrom, Teriflunomide
- INFβ – latest study showed not association with any risk
- Glatiramer Acetate & Natalizumab – not associated with any risk

- Thiel, S., et al., Interferon-beta exposure during first trimester is safe in women with multiple sclerosis-A prospective cohort study from the German Multiple Sclerosis and Pregnancy Registry. Mult Scler, 2016.
The effect of DMTs on Fertility

- Drugs that show no effect:
  - INF β, Glatiramer Acetate, Fingolimod, Teriflunomide
- Natalizumab – reduced fertility in animals (no information in humans)
- Mitoxantrome – amenorrhoea and azoospermia

The dilemma
The dilemma

- Should newly diagnose MS patient that are interesting in having kids should hold off treatment till after the pregnancy?
Our study
The aim of our study is to evaluate the association between DMTs and fertility, pregnancy and progression of the disease in patient with MS.
Methods

- Comparison between two groups:

  - RRMS Patients without pre-conception treatment
  - RRMS Patients with pre-conception treatment
Methods

- Multivariate analysis adjusted to age, disease severity, known fertility problems and previous pregnancy
- The information regarding the patients will be taken from Sheba MS Center’s data base
- Parameters for comparison
  - Pregnancy related
  - Disease related
What are we doing different?

- Bigger focus on time to conception and fertility
- Large data base
- Different drugs
- Study with clinical implication
160 births of RRMS Patients

- 55 – without pre-conception treatment
- 105 - with pre-conception treatment
Collecting the data

- We have collected the info regarding the disease
  - Relapses
  - Disease progression
  - DMT’s usage

- We still need to collect the info regarding the pregnancy
  - Time to conception
  - Artificial intervention
  - Pregnancy loss, fetal anomalies
  - Gestational week delivery, birth weight, mode of delivery, Apgar score
Results

- Initial process of the data shows **no difference in the disease progress** between the group.
- Too soon to tell if there is a different with the fertility, pregnancy and outcomes between the groups.
Down the road

- Complete collection of the info
- Statistical analysis
- Conclusions
Thanks!!