MS treatment during puerperium and lactation

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- Who can stop DMT during pregnancy?
  - No relapse during last month
  - No activity in MRI
  - No sever disability
- Which treatment can be used in pregnancy?
  - IFN
  - GA
  - Natalizumab

- If a sever relapse occur during pregnancy :
  - IV methyl prednisolone can be used during pregnancy if a sever relapse occur.
- First trimester IVMP may induce cleft palate and cleft lip
- IVIG may be used safely throughout pregnancy and therefore may be preferable during the first trimester.
- If MP is not sufficiently effective, use of plasma exchange can be considered .

- **MRI safety in pregnancy**: no conclusive evidence of fetal harm for MRI scans up to 3T.
- **Gadolinium effect on fetus :**
  - ***avoided*** because gadolinium compounds cross the placenta .
  - If necessary : informed consent from the mother

- Women with a history of MS-related urinary tract involvement have increased risk of infection during pregnancy.
- Recommended routine monitoring for urinary tract infection and chronic antibiotic prophylaxis may be appropriate.
- If the woman has neurogenic bladder, increased frequency of intermittent catheterization may be needed during pregnancy to prevent incontinence.
- Avoiding excessive gestational weight gain, continuing with range of motion, and stretching exercises may improve ability for mobility during pregnancy.

Which type of delivery method?

- ***Acceptable:***
  - ***Any anesthetic choice***
  - ***Any delivery method*** regard to obstetric decisions.

- In disabled pregnant MS patient may consider assisted vaginal delivery or even cesarean section.

MRI activity in MS and completed pregnancy

Data from a tertiary academic center

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- 123 women (median EDSS 1.0) : prepartum and postpartum MRI scans.
- 54.4% had either new T2 or Gd+ lesions postpartum.
- 79% of subjects with postpartum relapse had new MRI activity compared with 37.1% without relapse ($p < 0.001$).
- 24.9% maintained no evidence of disease activity status postpartum.

- **There was a high level of *inflammatory radiographic disease activity* which was related to relapses in postpartum patients with MS.**
- **MRI provides a sensitive tool to assess disease activity postpartum.**

Predictors of early postpartum relapse?

- Higher ARR in year before pregnancy.
- Acute relapses during pregnancy.
- a higher EDSS score at conception .
- lack of prior DMT use 2 years preconception.

Disease activity before and during pregnancy is an important factor :

- MRI activity
- Clinical relapses

Which data is necessary to decide for beginning DMT?

- What was ARR before pregnancy?
- Was there any relapse during pregnancy?
- What is the EDSS?
- Which treatment did she receive before pregnancy?
- Did she receive DMT during pregnancy?
- Is there any activity based on clinical and paraclinic data?

E. Predictors and dynamics of postpartum relapses in women with multiple sclerosis. Mult Scler. 2014.
Multiple sclerosis in pregnancy. Continuum (Minneap Minn).

Breatfeeding and gadolinium contrast agents

- the excretion of the gadolinium contrast agents into breast milk is <1%.
- Peak excretion occurs at about 50 minutes.
- less than 1% of orally ingested contrast is absorbed by the infant.
- The use of gadolinium in the mother is considered safe during lactation without requiring interruption of breastfeeding.
- If the patient wishes to avoid any gadolinium ingestion at all by the infant, they should “pump and dump” the milk for 24 h after gadolinium contrast exposure.

American College of Radiology (ACR) guidelines :

- all IV iodinated contrast and **gadolinium** that administration to the mother is considered safe for both the baby and **nursing** mother.

Thomsen HS, Morcos SK, et al. The use of iodinated and gadolinium contrast media during pregnancy and lactation. Eur Radiol. 2005.

Safety of IV pulse methylprednisolone therapy during breastfeeding in patients with multiple sclerosis

Cavit Boz, Murat Terzi, Serap Zengin Karahan, more...

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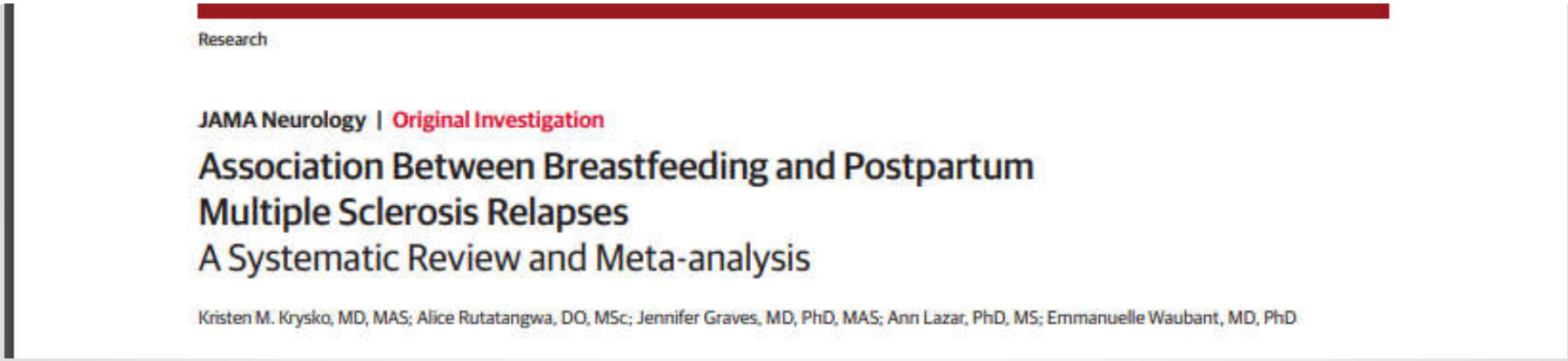
Methylprednisolone therapy:

- for postpartum relapse to nine patients for three consecutive days
- seven patients received a daily infusion monthly.
- Breast milk samples were obtained before infusion and 1, 2, 4, 8, and 12 hours after completion of infusion.

- Corticosteroids appear to be minimally excreted into breast milk.
- The relative infant dose (RID)for methylprednisolone was lower than the generally accepted value.
- the doses of corticosteroids ingested from breast milk would add a negligible 10% to the infant's endogenous corticosteroids production

- As infant exposure would be very low if a mother choose to breastfeed 2-4 hours after infusion.
- if deemed necessary, breastfeeding can be suspended for 24–48 h after the infusion using a “pump and dump” approach in the interim.

- Cooper SD, Felkins K, Transfer of methylprednisolone into breast milk in a mother with multiple sclerosis. J Hum Lact. 2015
- Boz C, Terzi M, Zengin Karahan S, et al. Safety of IV pulse methylprednisolone therapy during breastfeeding in patients with multiple sclerosis. Mult Scler. 2018.


Research

JAMA Neurology | Original Investigation

Association Between Breastfeeding and Postpartum Multiple Sclerosis Relapses

A Systematic Review and Meta-analysis

Kristen M. Krysko, MD, MAS; Alice Rutatangwa, DO, MSc; Jennifer Graves, MD, PhD, MAS; Ann Lazar, PhD, MS; Emmanuelle Waubant, MD, PhD

- **The PRIMS study** :no difference in the first 3 months postpartum ARR between women who breastfeed or No breastfeeding.
- Some studies reported that exclusive breastfeeding for at least 2 months post-delivery may reduce 6 months postpartum relapse risk.
- **A meta-analysis** – indicate that breastfeeding, independent of its duration, might actually hav protective effect on the postpartum relapse rate and delay the timing of a relapse.
- **Other study(portaccio E):** the occurrence of a postpartum relapse relates only to preconcept and antenatal disease activity, but not to breastfeeding itself.

- Portaccio E. Breastfeeding is not related to postpartum relapses in multiple sclerosis. Neurology. 2011.
- Langer-Gould A. One can prevent post-partum MS relapses by exclusive breastfeeding: yes. Mult Scler. 2013.
- Pakpoor J.Breastfeeding and multiple sclerosis relapses: a meta-analysis. J Neurol.

- Despite reduction in postpartum relapses with breastfeeding, ARRs remained fairly high postpartum, highlighting the need to identify additional strategies to prevent postpartum relapses.

breastfeeding is protective against postpartum relapses in MS, although high-quality prospective studies to date are limited and well-designed observational studies that aim to emulate a randomized trial would be of benefit.

Should immediate restart of DMTs.(the potential increased risk of postpartum relapses) .

the optimal time of resuming treatment after delivery has not been defined yet.

conclusive data :the early reintroduction of DMTs reduces the postpartum

relapse risk are still lacking

in high risk patients with sever disease activity decision to start a DMT immediately after birth is reasonable.

in women with high preconception disease activity, treatment should not be postponed and early (during the first 10 days postpartum) reintroduction of DMTs may be recommended.

- In support of this, early administration of IFNb or GA (within 3 months postpartum) have proven to reduce the risk of reactivation by 50% and significantly reduce the risk of relapses postpartum and over a follow-up period of at least 1 year.
- Similarly, natalizumab started within 8 days of delivery prevented postpartum relapses in five of six highly active MS patients.

- None of the currently licensed DMTs interact with hormonal contraception.
- Treatment and usage of DMDs during pregnancy should be tailored toward the patient's needs.
- The use of most DMDs is contraindicated during breastfeeding

- Recently the EMA has updated the label of IFNb allowing, the use during pregnancy and lactation.
- due to high MW only small amounts (0.006% of maternal dose) of IFN b are excreted in breast milk.
- when given orally, IFNb has no systemic biological effect.
- women who intend to breastfeed may use IFN b without concerns that this might affect the newborn.

Breastfeeding under IFN b is considered safe

- No data are available on the excretion of GA in breast milk.
- the large MW of GA, crossing into breast milk is very unlikely and hence nursing is potentially safe
- There appears to be no adverse effect of maternal GA on breastfed babies.

If clinically required GA can be continued during the entire pregnancy.
Breastfeeding under GA is probably safe.

- Triflunamid has small molecule
- is likely excreted into breast milk
- contraindicated during lactation

- DMF is a small molecule (144 Da)and half-life of 1 h.
- no data with regard to excretion of DMF or its metabolite in breast milk.
- Administration during lactation should be avoided.

- Fingolimod :excrete in human breast milk.
- the treatment should not be resumed if the mother intends to breastfeed.

Monoclonal antibody treatment during pregnancy and/or lactation in women with MS or neuromyelitis optica spectrum disorder

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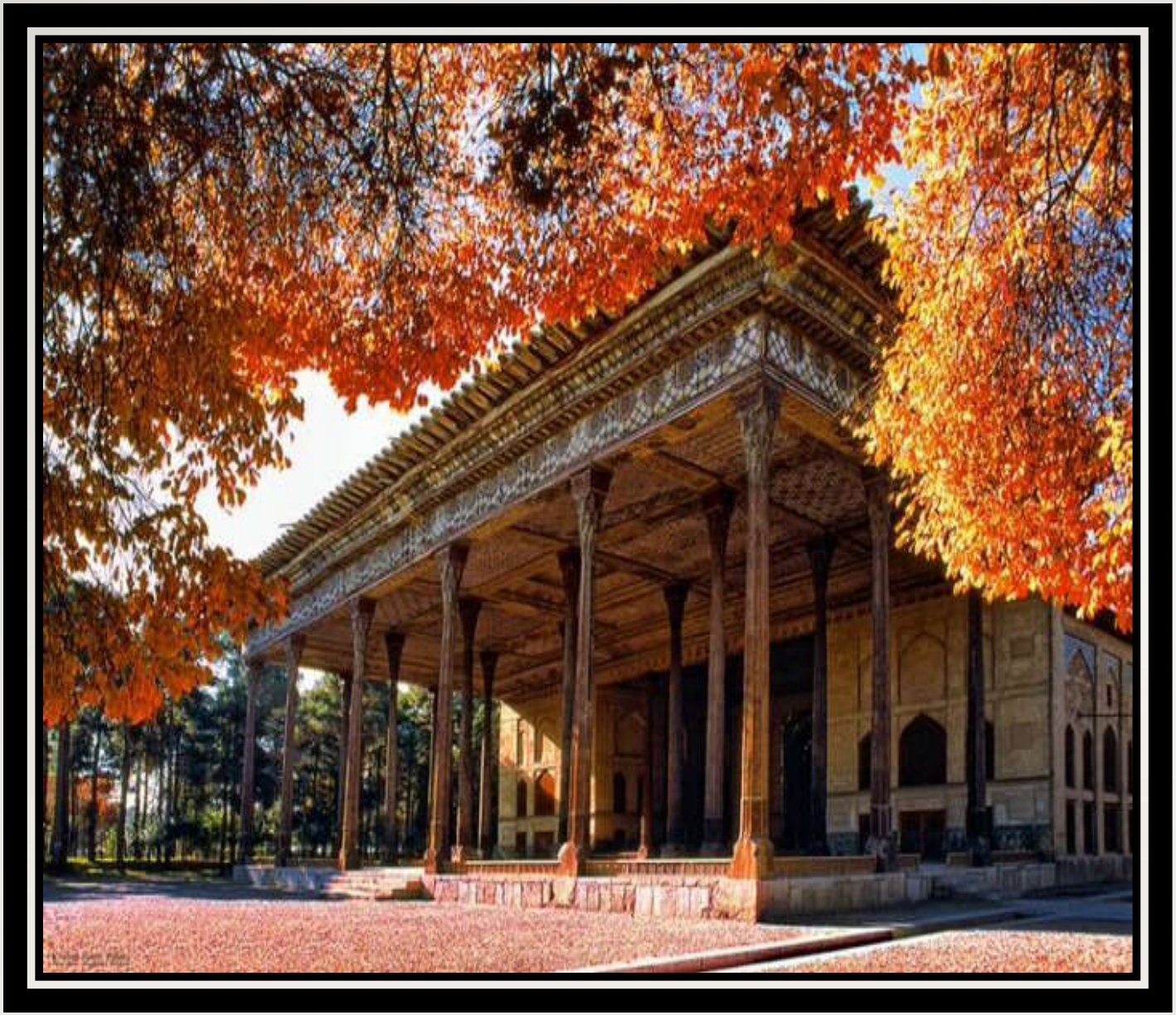
- 23 patients received MAbs (17 natalizumab and 6 anti-CD20) during lactation.
- Data were obtained at 1, 3, 6, and 12 months postpartum.
- No negative impact on infant health and development attributable to breast milk exposure after a median follow-up of 1 year.
- The concentration of natalizumab in breast milk and serum of infants was low.
- B cells normal in infants breastfed under anti-CD20.
- treatment with natalizumab, ocrelizumab, or rituximab during lactation might be safe for breastfed infants, but more data on the effect of Mab exposure during pregnancy are needed.



Thanks for your attent