Pregnancies in Patients with Long-Standing Rheumatoid Arthritis and Biologic DMARD Treatment: Course of Disease during Pregnancy and Pregnancy Outcomes

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Background & Objectives

The assumption of spontaneous remission among pregnant women with rheumatoid arthritis (RA) is common. Nevertheless, prospectively collected data describing the course of disease activity during pregnancies in women with long-standing severe RA are rare. Further, observational data suggest that biologic disease modifying anti-rheumatic drugs (bDMARDs) can be safely used until conception but the impact of bDMARD treatment during pregnancy is unclear.

We aimed to study pregnancy outcomes and courses of disease activity in women with bDMARD use prior to conception.

Patients & Methods

We descriptively analyzed all pregnancies and their outcomes that were reported to the German biologics register RABBIT until end of 2014 (N=106). In a subgroup of patients with pregnancies reported until 2011 (N=64), additional telephone interviews with a focus on the course of pregnancy, disease activity and treatment during pregnancy were conducted.

Table 1: Patient characteristics at conception stratified by treatment exposure.

	bDMARD naïve	bDMARD stopped before	bDMARD exposure
No. of pregnancies	11	38	57
Age in yrs	32.0 (4.1)	31.7 (4.6)	33.0 (4.1)
Disease duration in yrs	5.8 (3.0)	9.9 (5.1)	10.1 (6.3)
DAS28	2.9 (1.5)	3.4 (1.7)	3.5 (1.4)
CRP in mg/l	7.3 (6.3)	7.5 (15.4)	11.8 (19.0)
ESR in mm/h	12.4 (10.1)	15.6 (12.6)	22.0 (20.2)

Values are means (sd).

Exposure of patients, who stopped bDMARD before conception

13 RTX | 12 ETA | 9 ADA | 2 INF | 2 TOC

Exposure of patients, who where bDMARD-treated at conception

29 ETA | 11 ADA | 5 TOC | 4 CZP | 3 RTX | 3 ABA | 1 INF | 1 GOL

Results

Disease activity during pregnancy

Before conception, 23 patients were in remission, and 10 of them (43%) remained in remission during pregnancy. Of the 49 patients not in remission before conception, only 7 (14%) reached remission during pregnancy.

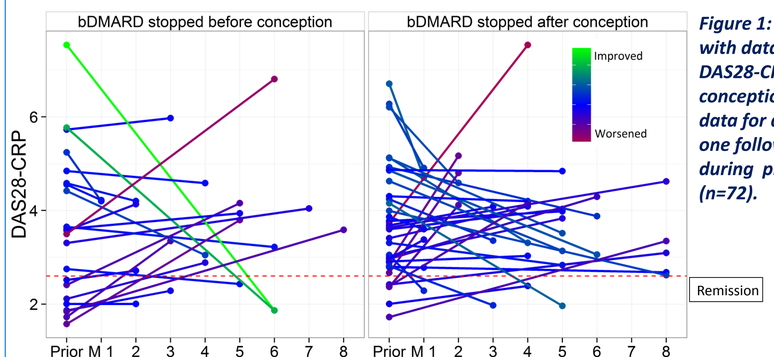

Figure 1: Patients with data on DAS28-CRP before conception and data for at least one follow-up during pregnancy (n=72).

Pregnancy outcomes

Table 2: Pregnancy outcomes stratified by treatment exposure.

	bDMARD naïve	bDMARD stopped before	bDMARD exposure
No. of pregnancies	11	38	57
Induced abortions	0	3 (8)	1 (2)
Spontaneous abortions	0	5 (13)	11 (19)
Live births	11 (100)	30 (79)	45 (79)

Values are numbers of cases (%).

Reported malformations and anomalies in the three treatment groups:

*bDMARD-naïve: no malformations or anomalies

*bDMARD stopped: **Anal atresia** (LI ADA = 4 weeks)
Congenital Nystagmus (after preterm birth; LI ADA >6 months)
Trisomia 21 (induced abortion; maternal age: 38; LI RTX >8 months)
Spina bifida (LI ETA >9 months)

*bDMARD exposure: **Talipes** (ADA, mother has talipes)

(LI: time between last infusion/injection and conception)

Higher disease activity in women with premature birth

In the subsample of patients with telephone interviews we compared disease activity during pregnancy in patients who gave birth at term vs. those with preterm babies.

Table 3: Disease activity in women with mature vs. preterm birth

	Mature births	Preterm singleton births (w/o twins)
No. of pregnancies	55	8
DAS28	3.6 (1.3)	4.3 (1.2)
Patient reported global health *	3.6 (2.1)	5.4 (1.8)
CRP in mg/l	13.0 (15.8)	39.2 (35.4)
Glucocorticoids in mg/d	5.9 (5.0)	10.8 (5.8)

*Values are means (sd). *Range of patients' global: 0 (good) – 10 (very poor).*

Conclusion

We observed that, in patients with long-standing rheumatic disease, remission during pregnancy is rarely reached. In contrast, disease activity increased during pregnancy in a considerable proportion of patients.

We found no significantly increased risk of malformations or other harmful consequences in patients exposed to bDMARD before or at conception. Within this limited sample of pregnancies a remaining risk cannot be ruled out entirely.

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