Pregnancy outcomes in partners of DMARD exposed men with juvenile idiopathic arthritis - an observational study

Drechsel P[1], Klotsche J[1,2], Niewerth M[1], Horneff G[3], Minden K[1,2]

[1]DRFZ Berlin, [2] Charité University Medicine Berlin, [3] Asklepios Kinderklinik St. Augustin GmbH, all Germany

ACR 2018 1436

Conclusions

Men with JIA who are still treated in young adulthood often beget children under DMARD exposure. Adverse pregnancy outcomes do not appear to be more frequent with peri-conceptual paternal DMARD exposure than without. However, the patient number is too small to draw reliable conclusions; more data are needed to quantify the risk of DMARD exposure to pregnancy and to provide men with more certainty.

Background

Men account for about one third of all cases of juvenile idiopathic arthritis (JIA). During the disease course and often into adulthood, they are exposed to various disease-modifying antirheumatic drugs (DMARDs). If men with JIA wish to have a child, they have to weigh the risk of a disease relapse when discontinuing medication against a not yet clearly defined impact of drugs on birth outcomes.

Objectives

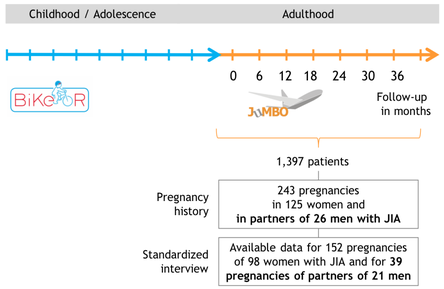
- To investigate outcomes of pregnancies in partners of male JIA patients who were exposed to DMARDs.

Patients & Methods

Patients with JIA who were enrolled in BiKeR, subsequently transferred to JuMBO (Juvenile arthritis MTX/Biologics long-term Observation) and reported at least one pregnancy in JuMBO between 2004 and 2018 were considered for this study.

Standardized interviews were conducted with the patients and their partners, the outcome of pregnancy was inquired.

In addition, prospectively collected physician-reported data on treatment and disease activity of JIA patients were considered in the analysis.

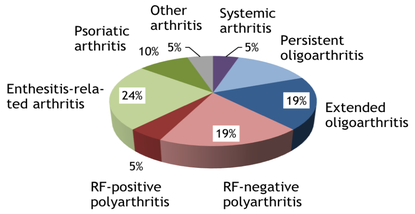


Disclosure: BiKeR: Supported by an unconditional grant from Pfizer, Abbvie, Roche/Chugai, and MSD; JuMBO: Supported by an unconditional grant from Pfizer, Abbvie and Roche.

Results

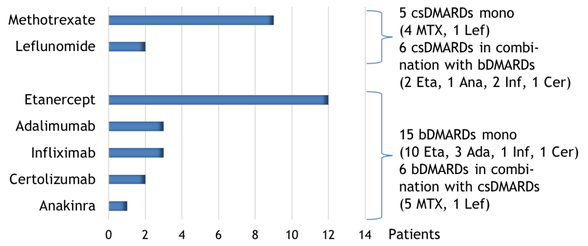
Patient characteristics

Until February 2018, detailed information was available for 39 pregnancies of partners of 21 men with JIA. At first pregnancy, the mean paternal age was 24.0±4.7 years, and the patients´ mean disease activity according to cJADAS-10 was 4.8±4.5.



Patient characteristics at 1st pregnancy outcome	Total sample n = 119	Males n = 21 (17.6%)
Disease duration, mean ± SD (n=116)	13.8 ± 5.9	13.3 ± 6.0
Age at JIA onset, mean ± SD, years (n=116)	9.7 ± 4.8	10.3 ± 4.9
Biologic drug exposure ever, %	89.1	90.5
Patient global (NRS 0-10), mean ± SD	3.1 ± 2.4	2.4 ± 2.0
Physician global (NRS), mean ± SD	2.3 ± 2.2	2.1 ± 2.2
Inactive disease (cJADAS-10 ≤1), %	10.9	22.2
Functional status by HAQ (0-3), mean ± SD	0.4 ± 0.6	0.3 ± 0.6
Patients with endoprostheses	8 (6.7)	0

All men had been exposed to 3.6±1.6 DMARDs for a mean of 10.2±5.5 years until the 1st pregnancy. Of the 39 pregnancies, there were 26 (66.7%) with peri-conception paternal DMARD exposure. In the remaining 13 pregnancies, DMARDs were stopped on average 3.4±2.3 years before conception. Eighteen of the 39 pregnancies in total and 11 of the 21 pregnancies under bDMARD exposure were planned pregnancies. Two patients had previously changed therapy due to the desire to have children.



The following maternal characteristics, which may be related to the pregnancy outcome, were additionally recorded: smoking 35.9%, alcohol consumption 2.6%, age at conception 24.0±4.3 years, body mass index before pregnancy 25.5±3.9.

Pregnancy outcomes

Pregnancy outcomes	Paternal DMARD exposure at conception (n=26)	No paternal DMARD exposure at conception (n=13)
Elective termination, n (%)	1 (3.8)	1 (7.7)
Spontaneous abortion, n (%)	2 (7.7)	2 (15.4)
Life birth, n (%)	22 (84.6)	10 (76.9)
Stillbirth, n (%)	1 (3.8)	0

The spontaneous abortion rates in pregnancies with and without paternal DMARD exposure were in the expected range of 9-17%, assumed for the German population aged 20-30 years[1]. Of the 9 pregnancies with paternal MTX exposure, 6 (66.7%) pregnancies resulted in a live birth, one (11.1%) was terminated electively, and 2 (22.2%) resulted in an early miscarriage.

Neonatal outcomes

Adverse neonatal outcomes were reported in 28% of the cases (in exposed pregnancies in 27%, in unexposed pregnancies in 30%).

Neonatal outcomes of life births (n=32)	Paternal DMARD exposure at conception (n=22)	No paternal DMARD exposure at conception (n=10)
Birth weight in g, median (range)	3292 (1610-4480)	3069 (1439-4125)
Preterm born (≤37 weeks), n (%)	3 (13.6)	3 (30.0)
SGA (small for gestational age, birth weight <10th percentile), n (%)	0	0
APGAR <7 at 5 min	0	0
Neonatal hospitalization, n (%)	5 (22.7)	3 (30.0)
Neonatal death (0-7 days)	0	0
Congenital anomaly	2 (9.1)	0

Two children had major congenital anomalies according to the EUROCAT classification[2]: one had clubfeet and one had an agenesis of the corpus callosum, both fathers were DMARD exposed at conception (to leflunomide, corticosteroids, NSAIDs and to MTX, certolizumab, corticosteroids, NSAIDs).

References: 1 - http://www.kinderwunsch-uni-bonn.de/Haeufigkeit-von-Fehlgeburten; 2 - European Surveillance of Congenital Anomalies, EUROCAT Guide 1.3, chapter 3.3: Coding of EUROCAT subgroups of congenital anomalies. Available from: www.eurocat-network.eu. Accessed 28 May 2018.

We would like to thank all rheumatologists who enrolled patients, in particular: E Seipelt, Berlin; S Tatsis, Hamburg / E Bärlin, Ludwigsburg / P Aries, Hamburg / F Striesow, Bonn / Fliedner, Osnabrück / B Wodtke, Bremen / M Aringer, Dresden
In addition, we are grateful to all patients for their participation in JuMBO.

minden@drfz.de