TNF INHIBITORS IN PREGNANCY: STOP, REDUCE OR CONTINUE? – OBSERVATIONS FROM A PREGNANCY OUTPATIENT CLINIC

Isabell Haase1, Susanna Spaehting-Mestekemper2, Matthias Schneider1, Rebecca Fischer-Betz1, Heinrich-Heine-University Düsseldorf, Polyclinic of Rheumatology and Hiller Research Unit, Düsseldorf, Germany; Rheumaparxis, Munich, Germany

Background: Women with active Rheumatoid Arthritis (RA) are more prone to relapses and complications during pregnancy. The potential risks of disease activation and treatment during gestation should be weighed in a shared decision prior to conception. An increasing number of women who wish to conceive are being treated with TNF inhibitors (TNFi). Some wish to discontinue or at least reduce therapy while pregnant and require information on opportunities and risks.

Objectives: To study the outcome of pregnancies in women with RA who either discontinued, reduced or maintained their TNFi treatment after conception.

Methods: Pregancies from an outpatient pregnancy clinic were evaluated before conception, during each trimester and postpartum. Clinical characteristics, disease activity (DAS28-CRP), medication use and pregnancy outcome were analysed. A flare was defined as increase in clinical activity leading to intensified treatment (new treatment with prednisolone or increase in dosage ≥5 mg/day and/or treatment with intraarticular glucocorticoids and/or (re-)treatment with DMARDs/TNFi). All women received extensive counselling before pregnancy based on current knowledge and subsequently decided to continue or stop TNFi at conception. If they stayed on TNFi and were in remission, women received the suggestion to stretch the therapy intervals in a disease activity guided manner. These real-world data will help to provide women with comprehensive advice on treatment options and risks regarding TNFi therapy at pregnancy counselling.

Results: After exclusion of one miscarriage, 56 completed pregnancies were enrolled and grouped according to their decision to stop (group 1) or continue (group 2) TNFi therapy during pregnancy. The latter were subdivided into those who could stretch the therapy intervals (group 2a) and those who could not (group 2b). Group 1 also contained seven women who received Tocilizumab or Rituximab until conception. Despite low disease activity (DAS ≤ 3.2) at conception in all groups, a higher flare rate during pregnancy and postpartum was observed after discontinuation of TNFi. In addition, a higher dose of oral prednisolone and more frequent intraarticular therapy was reported in group 1 (Table 1). Postpartum, 38.9% restarted TNFi therapy. About half of the women who chose to stay on therapy during gestation were able to stretch the injection interval of their TNFi, which was either Adalimumab (every 3.0 weeks), Certolizumab (median every 4.0 [min 4.0, max 5.0] weeks) or Etanercept (median every 3.0 [min 2.0, max 6.0] weeks) (Table 2). Relapse rate as well as prednisolone consumption was comparable between group 2a and group 2b.

Conclusion: Women with RA who discontinue TNFi at conception face a higher risk of flares during pregnancy and often have an increased demand for steroids to control disease activity. When in remission under ongoing TNFi therapy during pregnancy, it seems possible and safe for women to reduce the frequency of injections in a disease activity guided manner. These real-world data will help to provide women with comprehensive advice on treatment options and risks regarding TNFi therapy at pregnancy counselling.

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SUBCLINICAL THYROID DYSFUNCTION IS A CARDIOVASCULAR DISEASE RISK IN FEMALE RHEUMATOID ARTHRITIS

Suad Hannawi1, Haifa Hannawi2, Issa Al Saim2. 1Ministry of Health and Prevention, Rheumatology, Dubai, United Arab Emirates; 2Ministry of Health and Prevention, Dubai, United Arab Emirates; 3The Royal Hospital, Muscat, Oman

Background: Rheumatoid arthritis (RA) is a multisystem autoimmune disease that is associated with other autoimmune diseases particularly hypothyroidism. Subclinical hypothyroidism had been reported in RA. As well, RA patients are at double the risk of cardiovascular diseases (CVD). The increased risk of CVD is not fully explained by the
traditional and non-traditional CVD risk factors. In general population, hypothyroidism had been reported as a CVD risk factor.

Objectives: This study aimed for the first time to investigate the relationship between thyroid function parameters and the CVD risk as manifested by the carotid intima media thickness (cIMT) among RA patients.

Methods: All the RA patients were recruited through a specialized rheumatology clinic at the Ministry of Health and Prevention of UAE, from April 2016 to December 2018. Fasting Free thyroxine (FT4), Free triiodothyronine (FT3), and thyroid stimulating hormone (TSH) were assessed in all the participants within the same week of the cIMT measurement. Linear regression analysis used to look for the correlation of the thyroid function test (TSH, FT3, and T3) and the cIMT.

Results: A total of 154 female RA patients satisfying ACR/EULAR criteria for diagnosis of RA were recruited. None of the patients had history of thyroid, renal, or neurological disorders. None of the patients were pregnant. The mean age for the participants was 50 ±12 years (Min16 –Max 87). The mean FT4 was 15.7 ± 3.6 (NR: 12-22 pmol/L), mean FT3 was 4.54 ± 1.0 (NR: 4-8.6 pmol/L), and mean TSH was 2.60 ± 3.3 (NR:0.27-4.2 mIU/L). The mean cIMT was 0.57±0.11 mm. correlating TFF with cIMT showed that while there was no correlation between each of the FT3 and FT4with the cIMT (P value 0.46 and 0.19, respectively), there was a significant negative linear relationship between TSH value and the cIMT (P=0.03, β= -0.006).

Conclusion: Subclinical thyroid dysfunction might be an additional non-traditional CVD risk factors that can help in filling the gap of understanding the increased risk of CVD in RA. Further studies at a larger scale are needed to confirm the study findings. Also, there is a need to confirm if management of thyroid dysfunction in RA may help in overall improvement of this subset of population.

REFERENCES:

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THU0138

RHEUMATOLOGISTS’ ADHERENCE TO THE TREAT-TO-TARGET PRINCIPLE IN EARLY RA PATIENTS WITHIN THE PRAGMATIC CAREARA TRIAL: ROOM FOR IMPROVEMENT?

Veerle Stouten1, Diederik De Cock1, Sofia Pazmino2, Kristien Van der Elst1, Johan Joly1, Delphine Bertrand1,2, René Westhovens1,2, Patrick Verschueren1,2, On behalf of the CareRA study group.1 KU Leuven, Skeletal Biology and Engineering Research Center, Department of Development and Regeneration, Leuven, Belgium; 2University Hospitals Leuven, Rheumatology, Leuven, Belgium

Background: Treating to a predefined target is a principle adopted in guidelines to treat rheumatoid arthritis (RA). It is currently the most efficient strategy to control disease activity, but its implementation in daily clinical practice remains challenging.

Objectives: To evaluate rheumatologists’ adherence to a treat-to-target (T2T) approach at a threshold of low disease activity (DAS28CRP<3.2) in patients with early RA during the 2-year Care in early RA (CareRA) study.

Methods: CareRA is an investigator-initiated pragmatic multicentre trial, in which patients with early RA and naïve to conventional synthetic disease modifying anti-rheumatic drugs (csDMARD) were included (n=379). Participants were randomized to different remission induction schemes consisting of a csDMARD combination or methotrexate (MTX) monotherapy with and without a prednisone tapering down scheme. Following the T2T approach, specific treatment adaptations had to be performed in case of DAS28CRP>3.2 during the first study year, unless a predefined reason not to intensify treatment was provided. As first step, dose of MTX had to be increased from 15mg to 20mg weekly. As second step, dose of the other csDMARD was escalated in the combination arms and lefunomide was added in the MTX monotherapy arms. From week (w)52 onwards, further T2T was advised but type of treatment adaptation was left at the rheumatologists’ discretion. Adherence to this T2T approach was defined as performing a dose escalation or changing/adding DMARD medication in case of DAS28CRP>3.2 and was evaluated at every study visit during 2 years. Additionally, remission (DAS28CRP<2.6) rates at w104 were compared between patients in which T2T was applied at every visit and patients not always treated to target. Only data from patients for which DAS28-CRP scores were available were taken into account to evaluate the low disease activity state.

Results: The proportion of patients with DAS28CRP<3.2 was 26% (93/365) at w8, but decreased to a stable average of 16% on the following visits and further diminished to 10% (30/303) at w104. The frequency of T2T adherence in these patients varied from 59% (55/93) at w8 to 17% (5/30) at w104 (Figure 1). The most frequent reason not to intensify treatment during the first study year was that rheumatologists considered the disease already well-controlled. This reason was reported in 50% of non-adherent cases at w8, in 15% at w16, 14% at w28, and 24% at w40. The second most frequently given reason for non-adherence during the first study year was that giving glucocorticoids or NSAIDs temporarily was preferred over changing DMARDs, as reported in 3% of cases at w8, 15% at w16, 27% at w28, and 35% at w40. T2T was applied at all visits in 41 out of 110 (37%) patients needing at least 1 adaptation during the 2-year trial. Of these 41 patients, 36 (88%) were in remission at w104, while of the 69 patients not always treated to the T2T principle, 40 (58%) were in remission at the end of the 2-year trial (p=0.001).

Conclusion: This study shows the difficulty of applying T2T strictly, both with and without a fixed protocol to follow. In less than half of patients theoretically in need of a treatment adaptation, treatment was intensified at all visits during the first 2 years of treatment. In the majority of cases rheumatologists gave as reason for overruling the T2T guidance that they considered the disease already well-controlled. This reason was reported in 50% of non-adherent cases at w8, in 15% at w16, 14% at w28, and 24% at w40. Additionally, remission (DAS28CRP<2.6) rates at w104 were compared between patients in which T2T was applied at every visit and patients not always treated to target. Only data from patients for which DAS28-CRP scores were available were taken into account to evaluate the low disease activity state.

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THU0139

IS ADDING ANTI-CARP OR ANTI-PADI4 BENEFICIAL FOR DIAGNOSIS OF RHEUMATOID ARTHRITIS?

Bojdan Kolar1, Magdalena Drygalska1, Marek Ciesla1, Maria Majdan2

1University of Rzeszow, Faculty of Medicine, Rzeszow, Poland; 2Medical University of Lublin, Department of Rheumatology and Connective Tissue Diseases, Lublin, Poland

Background: Post-translatory modification (PTM), such as protein citrullination or homocitrullination (cambamylation) are key issues for the development of RA. There are known more than 300 PTMs. Some of them such as homocitrullination, are of chemical origin, but most of them (over 200) are of enzymatic origin. ACPR, anti-PADI4, anti-CarP and indirectly