Results: Fifty patients were reviewed, thirty eight (76%) were female and twelve (24%) were male with age ranging between 34 - 86 years (median 61.5 years). Switching to MTX injection was done within 2 yrs of diagnosis in 21 (42%) patients, between 2-5 yrs of diagnosis in 11 (22%) patients and more than 5 yrs after diagnosis in 18 (36%) patients. The main reasons of switching were either maximum MTX dose (25mg) or intolerance to oral MTX at any dose.

After switching methotrexate, review at 6 months showed 26 patients (52%) in remission (compared to 6 at baseline) and 3 (6%) patients avoided the need to go on biologic therapy. Five patient commenced on biologic therapy between 3 and 6 months.

Table 1. Disease activity compared at Baseline and at 6 months

<table>
<thead>
<tr>
<th>Disease Activity</th>
<th>Baseline</th>
<th>At 6 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Remission &lt;2.6</td>
<td>6</td>
<td>26 (p&lt;0.0001)</td>
</tr>
<tr>
<td>Mid (26-3.19)</td>
<td>11</td>
<td>10</td>
</tr>
<tr>
<td>Mod (3.2 - 5.09)</td>
<td>25</td>
<td>9 (p&lt;0.01)</td>
</tr>
<tr>
<td>Severe (&gt;5.1)</td>
<td>8</td>
<td>5</td>
</tr>
</tbody>
</table>

Conclusion: Switching to SC Methotrexate even in patients with long duration of disease results in significant number of patients achieving remission or lower disease activity (P<0.001). This may obviate the need of biologics therapy

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2212

The average concentration of 7-hydroxy MTX in RBC was inversely correlated with DAS28 of the disease (p=0.043).

Conclusion: The preliminary results indicate a positive correlation between the level of 7-hydroxy-MTX and MTXPGs in RBC and MO. In this regard, the concentration of 7-hydroxy-MTX can be used as a prognostic marker for MTX therapy in the absence of opportunities in clinical centers to measure the entire line of MTXPGs in RBC and MO. Since the data obtained are somewhat at odds with the few literary sources, it is necessary to conduct further research on this fact.

REFERENCES:

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2276

The prospective study included 65 patients aged 53±11 years, 50 women, 13 men, diagnosed with RA, according to the ACR/EULAR 2020 criteria.

Background: 7-hydroxy Methotrexate (7-hydroxy-MTX) is a phase I metabolite of MTX, which is converted by hepatic aldehyde dehydrogenases. It is known that 7-hydroxy MTX can reduce the effectiveness of methotrexate, which is associated with increased excretion of methotrexate due to a decrease in polyglutamation and binding to enzymes [1].

Objectives: To analyze the level of 7-hydroxy-MTX in peripheral blood cells in order to study the correlation of the level of this metabolite with the level of polyglutamates of methotrexate (MTXPGs).

Methods: The prospective study included 65 patients aged 53±11 years, 50 women, 13 men, diagnosed with RA, according to the ACR/EULAR 2020 criteria, methotrexate (MTX) naive. The duration of the disease was 7.5±24 months. All patients were administrated MTX subcutaneously at a dose of 10-15mg/m2. The visits were carried out at weeks 0, 4, 12, 24 and 36, at all visits samples were taken for the content of MTXPGs with 1,2,3 and 4 glutamate residues and 7-hydroxy MTX separately in red blood cells mass (RBC) and mononuclear cells (MO). The mononuclear fraction was isolated by layering on verogrfalin-ficoll. All patients received folic acid at a standard dose of 5mg 24 hours after parenteral MTX administration. Samples were collected no earlier than 36 hours after MTX administration. All patients had normal renal function. Disease activity was assessed using the DAS28 index calculated by C-reactive protein.

Results: The average concentration of 7-hydroxy MTX is shown in Table 1.

Table 1. Level of 7-hydroxy MTX in erythrocytes and mononuclear cells, mmol/L, Median [25; 75 quartiles]

<table>
<thead>
<tr>
<th>7-hydroxy MTX level in:</th>
<th>4 weeks</th>
<th>12 weeks</th>
<th>24 weeks</th>
<th>36 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>RBC</td>
<td>18.5(3.1;6.1)</td>
<td>10.2(3.6;5.08)</td>
<td>10.3(1.7;36.8)</td>
<td>7.0(1.25.3)</td>
</tr>
<tr>
<td>MO</td>
<td>0.4(0.1;1.5)</td>
<td>4.0(1.4;2.2)</td>
<td>3.5(1.8;1)</td>
<td>0.4(0.1;8.8)</td>
</tr>
</tbody>
</table>

The level of 7-hydroxy-MTX directly correlated with the level of MTXPGs 1-4, and summary MTXPG in both RBC and MO. Analysis of pairwise correlations according to Pearson showed that: after 4, 12 and 36 weeks, the level of 7-hydroxy-MTX did not correlate with the value of DAS28. After 24 weeks of therapy, the level of 7-hydroxy-MTX in RBC was inversely correlated with DAS28 of the disease (p=0.043).

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2628

The preliminary results indicate a positive correlation between the level of 7-hydroxy-MTX and MTXPGs in RBC and MO. In this regard, the concentration of 7-hydroxy-MTX can be used as a prognostic marker for MTX therapy in the absence of opportunities in clinical centers to measure the entire line of MTXPGs in RBC and MO. Since the data obtained are somewhat at odds with the few literary sources, it is necessary to conduct further research on this fact.

REFERENCES:
Disclosure of Interests: Sara Marsal Speakers bureau: BMS, Pfizer, UCB, Celgene, Roche, Sanofi, Consultant of: Pfizer, Abbvie, Roche, Celgene, Galapagos, MSD, UCB, BMS, Sanofi, Grant/research support from: Pfizer, Abbvie, Roche, Celgene, MSD, UCB, BMS, Novartis, Janssen, Sanofi, Héctor Corominas: None declared, Juan Jose de Agustin: None declared, Carolina Perez-Garcia: None declared, Maria Lopez Lasanta: None declared, Helena Borrell Paños: None declared, D Reina-Sanz: None declared, Raimon Sanmartí: None declared, J. Narváez: None declared, Clara Franco-Jarava: None declared, Charles Peterly Speakers bureau: Novartis, Bristol Myers Squibb, Amgen, Consultant of: Multiple companies on behalf of Spire Sciences Inc., Jose Antonio Narvaez: None declared, Vivek Sharma Shareholder of: Nēsos Corp, Employee of: Nēsos Corp, Konstantinos Alataris Shareholder of: Nēsos Corp, Employee of: Nēsos Corp, Mark C. Genovese Shareholder of: Gilead Sciences, Nēsos Corp, Employee of: Gilead Sciences, Matthew Baker Shareholder of: Nēsos Corp, Consultant of: Nēsos Corp.

OPIOIDS AND ANALGESIC USE IN EARLY RHEUMATOID ARTHRITIS: A LONGITUDINAL ANALYSIS OF LINKED REAL-WORLD PRESCRIPTION DATA

M. H. Derakhshan1, F. Morton1, G. E. Fraguolī2, C. Paterson1, J. Dale3, N. Basu1, I. Mcinnes1, D. Porter4, S. Siebert1 on behalf of Scottish Early Rheumatoid Arthritis (SERA) Investigators. 1University of Glasgow; Institute of Infection, Immunity and Inflammation, Glasgow, United Kingdom; 2University of Athens, Laiko General Hospital, Athens, Greece; 3NHS Lanarkshire, University Hospital Hairmyres, Glasgow, United Kingdom; 4NHS Greater Glasgow and Clyde, Gartnavel General Hospital, Glasgow, United Kingdom

Background: Large numbers of patients with rheumatoid arthritis (RA) receive regular opioids despite significant toxicity and a lack of evidence supporting their use in non-cancer pain. In order to address this situation, we need to understand when opioids are started in early RA where this has not been studied.

Objectives: To examine the temporal trend of opioid prescriptions before and after RA symptom onset and to compare this with DMARD and NSAID prescriptions.

Methods: RA participants (cases) were recruited as part of the Scottish Early Rheumatoid Arthritis (SERA) inception cohort. Controls without RA (five per case), matched for sex, age and post code over the same time period, were obtained through routine data linkage. Prescription data between Jan 2009 to Nov 2019 of cases and matched controls were compared using date of RA symptom onset as reference point. The Prescriptions Per Participant (PPP) for each three-month block was estimated by dividing the number of prescribed drugs in that selected drug classes (assigned using the British National Formulary) in that time block by the number of participants in each group. The differences between mean PPP of the RA cases and controls in each time block were tested by t-test for independent groups and subsequent adjustment for multiple testing.

Results: 1,720,335 prescriptions were available for analysis with 421,961 items for 421,961 items for 421,961 items for 4,558 matched controls. As expected, DMARD prescriptions in the SERA cases increased after the symptom onset period and were then sustained (Figure 1: top left panel). NSAID prescriptions in RA peaked during the 3 months after symptom onset and then reduced progressively (top right panel). Opioid analgesic prescriptions for the RA cases increased two-fold during the reference period and then reduced 6-9 months post-symptom onset. However, unlike NSAIDs, after this there was no further significant reduction in opioid prescriptions in the RA cases, which remained stable and significantly higher than in the controls for the remaining study period. The non-opioid analgesic mean PPP increased sharply at the time of symptom onset, with a steady gradual upward trend over time (lower right panel).

Conclusion: Opioid prescriptions increase significantly at the time of RA symptoms onset. Despite rapid introduction of DMARDs and resultant reductions in NSAIDs, analgesic use remains significantly higher than in controls. Further research is required to identify the factors associated with persistent opioid use in early RA with interventions aimed at the first 6 months.

REFERENCES:


ACKNOWLEDGEMENTS: The work was supported by Health Data Research UK which receives its funding from HDR UK Ltd funded by the UKRI MRC, EPSRC, Economic and Social Research Council, Department of Health and Social Care (England), Chief Scientists Office of the Scottish Government Health and Social Care Directorates, Health and Social Care Research and Development Division (Welsh Government), Public Health Agency (Northern Ireland), British Heart Foundation (BHF) and the Wellcome Trust. The SERA study was jointly funded by the Chief Scientists Office Scotland and Pfizer Ltd.

Disclosure of Interests: None declared DOI: 10.1136/annrheumdis-2021-eular.2628

METHOTREXATE AND CARDIOVASCULAR RISK IN RHEUMATOID DISEASES: A COMPREHENSIVE REVIEW

F. Verheoven1,2, C. Pratí1, M. Chouk1, C. Demougeot2, D. Wendling1,2,3. 1CHRU Besançon, Rheumatology, Besançon, France; 2Université de Bourgogne - Franche Comté, ÉA 4267 PEPITE, Besançon, France; 3Université de Bourgogne - Franche Comté, ÉA 4266 EPILAB, Besançon, France

Background: The management of inflammatory rheumatic disease has evolved in the last decade with the importance of the management of comorbidities. Methotrexate is the cornerstone of inflammatory rheumatic disease management, but its cardiovascular effects are still poorly understood.

Objectives: To assess the cardiovascular impact of methotrexate in inflammatory rheumatic disease.

Methods: A systematic review of the literature, following the prisma recommendations, was performed on the PubMed and Embase databases with the following keywords: ("Methotrexate") AND ("cardiovascular"). We included papers written in English and including patients older than 18 years.

Results: 570 references were identified and, 36 articles were kept for analysis. The mechanism of action of methotrexate lies mainly on the antagonism of purines. It reduces systemic inflammation, oxidative stress. In Rheumatoid arthritis, the use of methotrexate was associated with a decreased incidence of high blood pressure, an improvement of the lipid profile and of the insulin resistance. Major adverse cardiovascular events were decreased with methotrexate. The effects of methotrexate on the endothelial...