COMPARISON OF DOSE REDUCTION METHODS BETWEEN RAPIDLY AND GRADUALLY DE-ESCALATION IN PERSISTENT RHEUMATOID ARTHRITIS TREATED WITH BARICITINIB OVER 15 MONTHS

M. Yamasaki1, Shin-Yokohama Arthritis and Rheumatology Clinic, Rheumatology, Yokohama, Japan

Background: However tsDMARDs and treatment strategies have improved the outcomes of rheumatoid arthritis (RA), it is unknown who can taper or stop tsDMARDs and strategies for de-escalation.

Objectives: We analyze predictors of de-escalation in RA patients treated with baricitinib over 15 months in each group who start baricitinib with 4mg/day and 2mg/day.

This study will assess and compare (1) characteristic of patients who achieve remission (REM) or low disease activity (LDA) as who can taper baricitinib and (2) two de-escalation methods, rapidly and gradually de-escalation in patients who respond first-line therapy.

Methods: Cases were recruited to Shin-Yokohama Arthritis Register (SHARE) between 2015 and 2020 (n=3,961). Patients were diagnosed according to ACR/EULAR 2010 classification criteria and treated with baricitinib started with 4mg/day(n=42) or 2mg/day(n=108) over 15 months. 45 cases fulfilled EULAR definition for difficult-to-treat RA (D2T-RA). In 150 (Male25, Female125 cases, RA duration 12.5±5.9years) cases, Clinical Disease Activity Index (CDAI), Health Assessment Questionnaire-Disability Index (HAQ-DI), anti-CCP2 and clinical parameters were analyzed. Two de-escalation methods were compared in this study. In rapidly de-escalation methods, baricitinib were stopped in patients with stable REM/LDA with no swollen joint over 12 weeks. In gradually de-escalation methods, baricitinib were decreased to 50%, 42%, 28%, 14% in order with stable REM/LDA with no swollen joint over 12 weeks.

Results: (1)“Detect predictors who can achieve REM/LDA with no swollen joint as starting de-escalation baricitinib” In patients started with baricitinib 4mg/day group, 17 patients achieved REM/LDA with no swollen joint(40.5%), there were no differences in duration of RA, onset age of RA, biologics and/or JAK inhibitors naïve, anti-CCP2 titer and CDAI at the start baricitinib between REM/LDA and non-achieved cases. In patients started with baricitinib 2mg/day group, 59 patients achieved REM/LDA with no swollen joint (54.6%). In 2mg/day group, biologics and/or JAK inhibitors naïve was predictor for achieving REM/LDA with no swollen joint. In 2mg/day group, D2T-RA patients was negative predictor.

(2)“Comparison of sustained REM and/or LDA rate between rapidly and gradually de-escalation of baricitinib in rheumatoid arthritis” In whole patients, 15 patients were tapered baricitinib with rapidly de-escalation methods and 61 patients were with gradually de-escalation. Gradually de-escalation methods showed less relapse rate compared with rapidly de-escalation after tapered baricitinib (33.3% vs. 93.8%, p<0.0001). Particularly in 2mg/day group, 12 patients were tapered baricitinib with rapidly de-escalation methods and 47 patients were with gradually de-escalation. Gradually de-escalation methods showed less relapse rate compared with rapidly de-escalation after tapered baricitinib for 32.7 months (33.3% vs. 80.9%, p<0.0001). However 2cases in 4mg/day group and 8cases in 2mg/day showed increase of CDAI, all these cases regain LDA after increasing baricitinib.

Conclusion: Tapering baricitinib using gradually de-escalation methods may help to succeed deduction of baricitinib in RA patients with sustained clinical REM and/or LDA with no swollen joint in each group who start baricitinib with 4mg/day and 2mg/day.

REFERENCES:

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CAN NONSTEROIDAL ANTI-INFLAMMATORY DRUGS CONTROL THE SYMPTOMS OF MODERATE RHEUMATOID ARTHRITIS?

E. Pogozheva1, A. Karateev1, V. Amirzhanova1, E. Filatova1, I.V.A Nasonova Research Institute, Pain Management, Moscow, Russian Federation

Objectives: to evaluate the efficacy of long-term pain therapy with nonsteroidal anti-inflammatory drugs (NSAIDs) in patients with rheumatoid arthritis (RA) with an inadequate disease activity (DAS 28 >5.1)

Methods: the study included 404 RA patients, disease duration was more than 1 year, mean DAS 28 3.7±1.6, mean age 58.6±10.0 years, 69% women, 76.7% RF “+, 81.5% ACPA “+”91.2% of the patients received conventional DMARDs (methotrexate), 8.8% - biological agents. All patients received NSAIDs (acetylsalicylic acid) to control their symptoms. The follow-up period was 6 months. We evaluated the dynamics of the DAS 28 Index, the level of pain and patient global health on a 100- mm visual analog scale (VAS).

Results: the level of pain (VAS) decreased from 63.1 ± 15.4 to 46.3a 8.3 (p=0.001) by 3 months of follow-up and up to 39.5a 11.2 (p=0.001) by 6 months of follow-up. The patient global health (VAS) also improved from 58.2 ± 13.4 at baseline to 40.3 ± 11.2 (p=0.001) at 3 months and to 35.5 ± 9.7 (p=0.001) at 6 months of follow up. The mean DAS 28 remained within the moderate disease activity and decreased from 3.7±1.5 to 3.4 ±1.1 (p<0.01) after 3 months, and to 3.1a 0.9 (p<0.01) after 6 months.

Conclusion: long-term NSAID therapy allows to control the disease activity in patients with moderate RA. This should be taken into account when planning therapy, including deciding whether to “switch” DMARDs and prescribing biological agents.

Disclosure of Interests: None declared
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HYPERSENSITIVITY REACTIONS TO NON STEROIDAL ANTI-INFLAMMATORY DRUGS: A BOUT 87 CASES

K. Ksouda1, R. Sahounn1, R. Attheymen1, I. Bouaziz1, A. Hanène1, S. Haminni1, L. Chtourou2, Z. Khaled1, 1Medecine School of Sfax, Pharmacovigilance Department, Sfax, Tunisia; 2Hedi Chaker Hospital, Gastroenterology Department, Sfax, Tunisia

Background: Non-steroidal anti-inflammatory drugs (NSAIDs) are one of the leading causes of hypersensitivity reactions to drugs. The pathogenesis may be immunological mechanisms (allergic reactions) or non specific immunological reactions often inncriminated in cross reactivity independently of chemical structure of these molecules. Understanding of the underlying mechanism is necessary for prevention and choice of safe alternatives [1, 2].

Objectives: Analyze all cases of non-steroidal anti-inflammatory drugs cutaneous eruption reported to sfax pharmacovigilance service since January 2015 to December 2020 and evaluate the possibility of cross-reactions between different molecules in this class.

Methods: We conducted a retrospective study of all cases reported to sfax pharmacovigilance department. An enquiry of pharmacovigilance was performed in patients who presented side effects to ANS. The imputability study was carried out by the French method of Imputability. Medical history specifies if there is a re-administration to assess tolerance and cross-reactivity.

Results: Our study included 87 patients whose average age was 45, 8 years. The sex ratio (F/M) was 1:1. Lysine salicylate acetyl is the most incriminated (31%), then mefenamic acid (19.5%), diclofenac (19.5 %), ketoprofen in (9.2%), piroxicam in (6.9 %), ibuprofen in (5.4%), colchocin in (3.4%), tiaprofenic acid in (1.1%) and naproxen in 1.1% of cases. The most common skin injury was urticaria in 29 cases (33.3%). Fixed drug eruption was observed in 17 cases. Maculopapular rash was observed in 19 cases, anaphylaxis in 5 cases and 4 cases of photosensitivity were observed. In our study we found cross-reactivity between (NSAIDs) in 8 patients.

Conclusion: The diagnostic approach is often based on the controlled administration of the drug to assess tolerance and to identify safe alternatives. In cases of intolerance to COX 1 inhibitors, cross-reactions to selective COX 2 inhibitors are very rare [3].

REFERENCES:

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METHOTREXATE INTOLERANCE IN MOROCCAN RHEUMATOID ARTHRITIS PATIENTS

M. Mahroug1, H. Azzouzi2, H. Boutaib1, O. Lamkhanat1, A. Lnhla1, 1Mohammed VI University Hospital, Mohammed I University, Faculty of Medicine, Rheumatology, Oujda, Morocco

Background: Methotrexate intolerance is a principal reason for treatment discontinuation, hence the interest in a more in-depth study.

Objectives: We aimed to study the prevalence of methotrexate gastrointestinal intolerance and determine its associated factors in rheumatoid arthritis (RA) patients.

Methods: We designed a cross-sectional study on our RA patients recruited in January 2021 at our rheumatology department. Methotrexate Intolerance Severity Score (MISS) [1], previously validated in juvenile idiopathic arthritis
patients, was used to determine methotrexate (MTX) intolerance prevalence in RA patients. The MISS consisted of four domains: abdominal pain, nausea, vomiting, and behavioral symptoms, occurring before (anticipatory), after, and when thinking of MTX (associative). MTX intolerance was defined as six or more points on the MISS. Our statistical analysis was based on a descriptive study and logistic regression with SPSS20.

Results: We included 102 RA patients with a mean age of 51.60 ± 14.33 years. Women were predominant (93.1%). The mean disease duration was 14.86 ± 9.78 years, with a mean methotrexate use duration of 7.42 ± 6.44 years. The mean dose of methotrexate was 12.13 ± 9.06 mg per week. The prevalence of methotrexate intolerance was 55.9%, and seventy-six patients (74.5 %) experienced at least one gastrointestinal symptom during MTX treatment. After MTX administration, the most prevalent gastrointestinal symptom was nausea (93% of the intolerant patient), whereas abdominal pain occurred in 73.7 % and vomiting in 57.9%. These symptoms were also prevalent before and when thinking of MTX. Anticipatory nausea was reported in 45.6% and associative nausea in 54.5% of the cases, abdominal pain occurred anticipatory in 22.8% and associative in 42.1%, anticipatory vomiting was the least prevalent, affecting 8.8%. Behavioral symptoms affected 87.7% of intolerant patients, with restlessness being the most prominent symptom in 71.9% of them. Among the intolerant patients, 45 patients (79%) took parenteral MTX, and 12 (21.1%) took methotrexate orally. In comparison, young patients (49.11 ± 14.96 years) were more intolerant to MTX than old (54.76 ± 13 years, p = 0.048) ones. However, in univariate logistic regression analysis, we did not find any significant association between methotrexate administration route, dose, duration, and digestive intolerance.

Conclusion: Methotrexate intolerance was highly prevalent in our RA population. These results strengthen the idea that early detection of MTX intolerance may avoid effective treatment discontinuation, especially in younger patients.

REFERENCES:

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2021-eular.3315

Table 1. Regression analysis (risk of response of the disease at 6 and 12 months of treatment with Tofacitinib)

<table>
<thead>
<tr>
<th>Factor</th>
<th>Response at Month 6</th>
<th>OR</th>
<th>IC95%</th>
<th>P value</th>
<th>Response at Month 12*</th>
<th>OR</th>
<th>IC95%</th>
<th>P value</th>
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<tr>
<td>Age</td>
<td>1.00 0.97-1.03 0.788</td>
<td>1.02 0.98-1.06 0.211</td>
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<tr>
<td>Male</td>
<td>1.82 0.65-5.08 0.251</td>
<td>0.81 0.27-3.28 0.709</td>
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<tr>
<td>Positive Rheumatoid Factor</td>
<td>0.99 0.94-1.04 0.908</td>
<td>0.10 0.06-1.08 0.444</td>
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<tr>
<td>Positive Anti-CCP</td>
<td>0.91 0.026-2.56 0.730</td>
<td>0.63 0.17-2.26 0.485</td>
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<tr>
<td>Initial DAS28</td>
<td>1.61 1.04-2.49 0.033</td>
<td>1.19 1.13-3.05 0.018</td>
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<td>Dose</td>
<td>0.44 0.19-1.01 0.504</td>
<td>1.47 0.56-3.83 0.423</td>
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<tr>
<td>Treatment period</td>
<td>1.12 0.80-1.55 0.492</td>
<td>1.1 0.75-1.61 0.697</td>
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*Positive Anti-CCP at month 12 was omitted because of collinearity

Conclusion: Tofacitinib is an effective treatment option for patients with RA after conventional DMARDs and in patients after biologic therapy failure, but maybe is better used as it a T1 first-line of treatment. Further studies are required to determine the real role of tofacitinib in different lines of RA treatment.

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