AB0425 TREATMENT OF PATIENTS WITH RHEUMATOID ARTHRITIS IN POLAND - ESTIMATE THE FREQUENCY OF USE OF METHOTREXATE DURING A RANDOM APPOINTMENT WITH A RHEUMATOLOGIST

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Background: In accordance with the EULAR/ACR recommendations disease-modifying antirheumatic drugs (DMARDs), particularly methotrexate (Mtx) should be applied after diagnosis of rheumatoid arthritis (RA). The goal of the treatment is to get remission/low disease activity

Objectives: The aim of this study was evaluation of the RA treatment, the frequency of use of Mtx and its dose application during control visits to rheumatologist in Poland. The disease activity was evaluated by using disease activity 28 joint score (DAS-28).

Results: There were analysed 301 case records of patients diagnosed with RA on the basis of the ACR 1997 and/or ACR/EULAR 2010 criteria. Patients recently diagnosed were excluded from analysis. In the examined group were 226 women and 75 men, median age 58.0, disease duration 5.0. Patients were divided in groups depending on the type of applied therapy 215 (71%) patients were treated with Mtx monotherapy or combined with other DMARDs. 161 patients (53%) took glucocorticosteroids simultaneously. Average DAS28 – 5.09, disease duration 6.2. At 18 patients (6%) contraindications against the Mtx were stated. 127 patients (59%) took high dosage of Mtx (20–30 mg/week), 84 (39%) low dosage (7.5–15 mg /week) 31 patients (10%) were treated other than Mtx DMARDs in monotherapy or in combined therapy 14 (45%) took glucocorticosteroids simultaneously, average DAS 28 – 4.82, disease duration 5.0. 55 (18%) patients didn't undergo treatment of DMARDs in the moment of analysis, 11 (20%) patients underwent treatment with glucocorticosteroids. Duration of disease 2.1 average DAS 28 5.43.

Conclusions: In patients treated with DMARDs in it also with Mtx a remission and/or a low activity of illness weren't being observed what is indicating for the ineffective treatment with RA.

Mtx wasn't applied in recommended doses in spite of the moderate or high activity of illness

There were patients who never had been treated with DMARDs. Causes of this occurrence require further research

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6773

AB0426 THE EFFICACY OF THE TRIPLE COMBINATION THERAPY WITH METHOTREXATE, LEFLUNOMIDE AND METHYLPREDNISOLONE IN RHEUMATOID ARTHRITIS

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Background: The RA modern treatment approaches are based on "aggressive therapy", which aims at suppressing autoimmune inflammation and prevent joint destructions at the early stages of the disease.

Objectives: To evaluate the effectiveness and tolerability of the triple combination therapy with methotrexate, leflunomide and methylprednisolone in patients with rheumatoid arthritis.

Methods: The study included 150 patients with rheumatoid arthritis. As a result of randomization, 50 patients received triple combination therapy (methotrexate +methylprednisolone+leflunomide), 50 patients with monotherapy with methotrexate, leflunomide 50 others. As a result all patient groups were comparable after all clinical and demographic indices.

Results: Our results showed that triple therapy is very effective in treating patients with RA. A significant improvement on the criteria of the AAR (ACR>50) at the end of the study was observed in most patients receiving methotrexate, leflunomide and methylprednisolone. This is confirmed statistically and clinically positive dynamics significantly in almost all indicators used of efficacy (pain, stiffness, number of tender and swollen joints, the activity of AR, the value VSH index functional HAQ). In addition, the use of triple therapy decreased average dose simultaneous use of glucocorticosteroids daily (from 5.0 to 2.5 mg) and 76% of patients canceled anti-inflammatory non-steroid drugs.

Conclusions: After randomized trial data lasting 24 months based triple therapy (methotrexate, leflunomide and methylprednisolone) was highly effective in patients with high RA activity. A significant improvement according to the criteria of ACR (ACR>50) was obtained in 31 of 39 patients (79.48%), including the nine patients (23.07%) had developed clinical remission.

Administration of the basic triple therapy was characterized by a significant clinical effect ACR stability of >50. It was maintained during not less than 15 months of research in 28 (90.32%) of patients who received this treatment and only 3 of 11 (27.27%) patients who received methotrexate alone group and 8 in 10 (80%) who administered LF (p=0.039). Evidence recovery (ACR>50), as well as clinical remission was kept stable in all 28 patients that triple therapy was extended after the ending of basic research.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6317

AB0427 EFFICACY OF HYPNOTIC ANALGESIA FOR THE REDUCTION OF PAIN AND NEGATIVE EMOTIONAL STATES IN PATIENTS WITH RHEUMATOID ARTHRITIS OF THE "HOSPITAL CIVIL DE GUADALAJARA "FRAY ANTONIO ALCALDE"

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Background: Rheumatoid arthritis is a autoimmune and multisystemic disease. However, the negative emotions of anxiety and depression are the ones that have been most addressed, and there is a close relationship between pain associated with pain. Hypnosis is one of the best documented behavioral interventions in the management of acute and chronic pain in adults.

Objectives: To evaluate the efficacy of hypnotic analgesia for pain reduction and negative emotional states in patients with Rheumatoid Arthritis of the Guadalajara Civil Hospital Fray Antonio Alcalde

Methods: The method was developed through a quasi-experimental study, in which had two groups: a control group (CG) of 11 patients and an experimental group (EG) of 17, the women's age group were developed between 18 and 65 years old diagnosed with arthritis. The meditation of Pain was realized through an instrument called EVA, and for the case of the Anxiety and depression were through HAD, achieving the baseline of each one of the variables. The EG group attended three psychological sessions of Hypnosis, with intervals of one month each. In these sessions, the perception of pain with an EVA was measured at the beginning and at the end. After a month, the subsequent evaluation was performed, measuring the same initial variables, in order to make the comparison of the pre and pos.

Results: The U of MANN Whitney was applied and it was identified that in the pre-test measurement, there were no statistically significant differences in the variables. However, in the pos measurement, differences were found in the patient's pain perception (z=-2.84, p<0.05), anxiety (z=-2.36, p<0.05) and The depression (z=-2.68, p<0.05). In addition, a Wilcoxon test was developed to determine differences between the pre-test score and the pos-test score in the EVA of each session. Statistically significant differences were found in the first session (Z=-3.65, p=0.001), second session (Z=-3.67, p=0.001) and third session (Z=-3.56, p=0.001).

Conclusions: Hypnosis, as a behavioral technique, has shown efficacy in patients with chronic pain. In this research, a significant decrease in patients' perception of pain has been demonstrated.

References:

- [1] Chopra, A. (2013). The COPCORD world of musculoskeletal pain and arthritis. *Rheumatology (United Kingdom)*, 52(11), 1925–1928.
- [2] Matcham, F., Rayner, L., Steer, S., & Hotopf, M. (2013). The prevalence of depression in rheumatoid arthritis: A systematic review and meta-analysis. *Rheumatology (United Kingdom)*, 52(12), 2136–2148.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6983

AB0428 A SYSTEMATIC REVIEW ON EFFICACY AND SAFETY OF SELECTIVE GLUCOCORTICOID RECEPTOR MODULATORS IN COMPARISON TO GLUCOCORTICOIDS IN ARTHRITIS

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Background: Glucocorticoids (GCs) can cause unwanted effects. Both rheumatologists and patients classify osteoporosis, hyperglycemia/diabetes mellitus, cardiovascular diseases, and infections as the most worrisome adverse effects of GCs. Alternatives with less adverse effects but with good efficacy are needed, thus with a better efficacy/safety ratio. Selective GC receptor modulators (SGMRs) are designed to engage the receptor with dissociative characteristics: less transactivation of genes, mainly responsible for unwanted effects, while trans-repression of genes, inducing anti-inflammation, is maintained. Hereby, SGMRs are expected to have a better efficacy/safety ratio. A systematic review providing an overview of the efficacy and safety data of SGMRs is lacking.

Objectives: To systematically review the current literature on efficacy and safety of SGMRs in arthritis, compared to those of GCs.

Methods: A search was performed in Medline, Embase and the Cochrane Library, from inception dates of databases to October 5th, 2016. Experimental studies involving animal arthritis models or human material of arthritis patients, as well as clinical studies in patients of arthritis were included, if they reported original data. All types of arthritis were included. Data was extracted on the SGRM studied and on the GC as reference standard, design or setting of the study and whether or not safety and efficacy parameters had been reported.

Results: A total of 437 articles was retrieved of which 15 articles were eligible for our analysis. The following SGMRs were investigated: Compound A¹⁻⁶, PF-04171327⁷, LGD-5552⁸⁻⁹, Compounds 4¹⁰, 5¹⁰, and 14¹¹, (R)-16¹², (R)-18¹³,

(R)-21¹³, (R)-35¹⁴, (R)-37¹², Ginsenoside Rg¹⁵ and Org 214007–0¹⁶. Results are shown in Table 1. (R)-16 showed better efficacy and safety compared to prednisone. Compound A, Ginsenoside Rg 1, Compounds 14, (R)-18, and (R)-21 had better safety profiles than a GC, but with similar efficacy. (R)-35 and (R)-37 showed better efficacy than a GC, but safety data was lacking. Org 214007–0, LGD-5552, Compounds 4 and 5 and PF-04171327 showed similar efficacy as a GC, but no safety data was provided.

Author, year	SGRM tested	Reference compound	Clinical trial	Pre-clinical human	Pre-clinical animal	Efficacy	Safety	Conclusion on efficacy and safety in comparison to reference compound
Dewint et al., 2008	Compound A	Dex		X	X	X	X	Similar efficacy. Better safety of Compound A.
Gossye et al., 2009	Compound A	Dex		X				Similar efficacy. No safety data.
Gossye et al., 2010	Compound A	Dex		X	X			Less efficacy of Compound A. No safety data.
Rauch et al., 2011	Compound A	Dex		X		X	X	Similar efficacy. Better safety of Compound A.
Rauner et al., 2013	Compound A	Dex			X	X	X	Less efficacy of Compound A. Better safety of Compound A.
Malaise et al., 2015	Compound A	Pred		X		X	X	Similar efficacy. Better safety of Compound A.
Yang et al., 2015	Compound 4 and 5	Pred			X	X		Similar efficacy of compound 4, better efficacy of compound 5. No safety data.
Razavi et al., 2014	Compound 14	Pred			X	X	X	Similar efficacy. Better safety of Compound 14.
Riether et al., 2010	Compound (R)-16 and (R)-37	Pred			X	X	X	Better efficacy of (R)-16. Better safety of (R)-16 and (R)-37.
Harcken et al., 2014	Compound (R)-18 and (R)-21	Pred			X	X	X	Similar efficacy. Better safety of (R)-18 and (R)-21.
Weinstein et al., 2011	Compound 35 and 37	Pred, dex			X	X		Better efficacy of compounds 35 and 37. No safety data.
Miner et al., 2007	LGD-5552	Pred			X	X		Similar efficacy. No safety data.
Lopez et al., 2008	LGD-5552	Pred			X	X		Similar efficacy. No safety data.
Du et al., 2011	Ginsenoside Rg1	Dex			X	X		Similar efficacy. Better safety of Ginsenoside Rg1.
Van Lierop et al., 2012	Org 214007-0	Pred			X	X	X	Similar efficacy of Org-214007-0. No safety data.
Conrado et al., 2015	PF-04171327	Pred	X			X		Similar efficacy. No safety data.

Table 1. Efficacy and safety results of selective glucocorticoid receptor modulators (SGRMs).

Conclusions: Studies both assessing efficacy and safety parameters of SGRMs are scarce. Currently, there is insufficient evidence for the presumed superior efficacy/toxicity balance of SGRMs compared to that of GCs.

References:

[1] Dewint P et al. J Immunol. 2008;180:2608–15.
[2] Rauch A et al. FASEB J. 2011;25:1323–32.
[3] Rauner M et al. Endocrinology. 2013;154:3719–28.
[4] Malaise O et al. Rheumatology. 2015;54:1087–92.
[5] Gossye V et al. Arthritis Rheum. 2009;60:3241–50.
[6] Gossye V et al. Ann Rheum Dis. 2010;69:291–6.
[7] Conrado DJ et al. J Pharmacokinet Pharmacodyn. 2016;43:325–41.
[8] Miner JN et al. Proc Natl Acad Sci U S A. 2007;104:19244–9.
[9] López et al. Endocrinology. 2008;149:2080–9.
[10] Yang MG et al. J Med Chem. 2015;58:4278–90.
[11] Razavi H et al. Bioorg Med Chem Lett. 2014;24:1934–40.
[12] Riether D et al. J Med Chem. 2010;53:6681–98.
[13] Harcken C et al. J ed Chem. 2014;57:1583–98.
[14] Weinstein DS et al. J Med Chem. 2011;54:7318–33.
[15] Du J et al. J Immunol. 2011;187:942–50.
[16] Van Lierop MJ et al. PLoS One.2012;7:e48385.

Disclosure of Interest: M. Safy Grant/research support from: MS was supported by a research grant from Astra Zeneca. Astra Zeneca was not involved in this study., M. De Hair: None declared, J. Jacobs: None declared, F. Buttgerit: None declared, M. Kraan: None declared, J. van Laar: None declared
DOI: 10.1136/annrheumdis-2017-eular.3254

AB0429 SHORT-TERM EFFECTS OF LOW DOSE GLUCOCORTICOIDS ON BONE METABOLISM IN EARLY RHEUMATOID ARTHRITIS

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Background: Glucocorticoids (GCs) are frequently used in the treatment of Rheumatoid Arthritis (RA). Studies in humans about the effects on bone turnover markers and modulators are poor, and results are discordant and controverse, probably because conducted with different doses and underlying diseases.
Objectives: To evaluate changes in serum bone turnover markers and Wnt inhibitors at 7- and 30-days after initiation of low dose GCs treatment of early RA.
Methods: 27 adult patients suffering from early RA were prospectively enrolled. Blood tests including C-Reactive Protein (CRP), amino-terminal propeptide of type 1 procollagen (P1NP, marker of bone formation), carboxy-terminal telopeptide of

type 1 collagen (CTX, marker of bone resorption), Sclerostin, and Dickkopf-related protein 1 (DKK1) were detected at baseline and 7 and 30 days after starting low dose of GC (methylprednisolone 4 mg/day).

Results: At baseline we observed a significant positive correlation between CRP and DKK1 serum levels (r=0,63; p<0,05) and between DKK1 and CTX serum levels (r =0,38; p<0,05). A significant decrease in serum levels of CRP, P1NP, and Sclerostin was observed after 7 and 30 days of GC treatment (p<0,05). About DKK1, it has been detected a not significant tendency to decrease after starting GC. CTX serum levels showed no significant changes.

Conclusions: This study has shown that a low dose GC treatment might have complex and conflicting short-term effects on bone metabolism in early RA (a reduction of bone formation, without increase of bone resorption), different from those observed with higher dose, in other diseases or in healthy subjects. The observed decrease in P1NP and Sclerostin serum levels might mean that also low dose of GC could acutely suppress bone formation and induce loss of function and/or number of osteocytes.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4667

AB0430 LEFLUNOMIDE AS A SECOND LINE DMARD AFTER METHOTREXATE HAS LIMITED IMPACT ON RHEUMATOID ARTHRITIS IN REAL LIFE

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Background: If rheumatoid arthritis (RA) is not in remission or at least low disease under methotrexate (MTX), leflunomide is an approved conventional synthetic DMARD, which is commonly used in some countries.

Objectives: To investigate in a real life situation whether patients with RA benefit from instituting leflunomide after methotrexate.

Methods: The clinical data of all RA patients who had at least once received leflunomide, and who agreed to the pseudonymized analysis of their data (approved by the local ethics committee), were analyzed from the time of leflunomide initiation on to the time of stopping leflunomide or the last visit in 2015, which ever came first.

Results: In total, 145 RA patients treated with leflunomide were identified. Of these, 87 received leflunomide after MTX had failed as a first line DMARD, and 8 received leflunomide as a first line DMARD. 50 patients had another first line therapy. Of the first line leflunomide patients 3 (38%) were still on leflunomide at the last visit, as compared to 7 of the 44 patients (16%) who were switched from MTX to leflunomide, and 0 of the 27 patients in whom leflunomide was added to MTX (p<0.01 vs 1st line leflunomide). For leflunomide monotherapy, 29% and 19% were still on the drug after 24 and 48 months, respectively, as compared to 14 and 0% under the combination with MTX. Of all patients who started leflunomide, remission (at least low disease activity) as per CDAI (≤2.8 (≤10)) was reached by 23% (57%) 3 months, 20% (40%) 6 months, and 16% (34%) one year after initiating leflunomide monotherapy, with corresponding percentages of patients of 39% switched to other approaches at six months and of 60% switched at one year. Under the combination of leflunomide and MTX, remission (at least low disease activity) was seen in 18% (53%) at 3 months, 20% (37%) at 6 months, and 8% (20%) at one year, and 55% and 71% had switched to other modes of action at six months and one year, respectively. Gastrointestinal and mucocutaneous adverse events and hypertension were common, and 4 our patients experienced serious bacterial infections.

Conclusions: Leflunomide constitutes a longer term option for a subgroup of RA patients with contraindications to MTX or after MTX failure. After one year, leflunomide had led to sustained acceptable disease control in approximately one third of the patients, but only in one in five under leflunomide combined with MTX. These results are supportive of the EULAR recommendations that patients should be switched to a second conventional DMARD in the absence of predictors of bad outcome only. If leflunomide is initiated, the patients need to be followed closely for potential secondary loss of efficacy.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3531

AB0431 POST-MARKETING SURVEILLANCE OF TOFACITINIB IN JAPANESE PATIENTS WITH RHEUMATOID ARTHRITIS: AN INTERIM REPORT OF SAFETY DATA

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Background: Tofacitinib is an oral JAK inhibitor for the treatment of rheumatoid arthritis (RA). Efficacy and safety of tofacitinib have been shown in RA patients in global Phase 2, Phase 3 (one study included Japanese patients) and long-term extension (LTE) studies and in two Phase 2 and one LTE study in Japanese patients.