POS0641

INCIDENCE OF GASTRO-INTESTINAL COMPLICATIONS IN RHEUMATOID ARTHRITIS PATIENTS RECEIVING BIOLOGICAL DMARDS IN OBSERVATIONAL COHORT STUDIES: A SYSTEMATIC LITERATURE REVIEW AND META-ANALYSIS

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Background: Rheumatoid arthritis (RA) patients are at increased risk of gastro-intestinal (GI) perforations compared with non-RA patients, resulting in increased mortality. Clinical trials, post-marketing studies and registries have reported an increased risk of GI perforations in RA patients treated with tocilizumab.

Objectives: The aim of our study was to assess the incidence of GI complications among RA patients receiving bDMARDs in observational cohort studies

Methods: A systematic literature review was carried out through September 2020 on the Pubmed, Embase and international congress databases, selecting observational cohort studies assessing the incidence of GI complications, including perforations and diverticulitis, in RA patients receiving bDMARDs. Keywords were “gastrointestinal perforation”, “gastrointestinal disease”, “diverticulitis”, “biological DMARDs” and “rheumatoid arthritis” with no publication date limit. Studies were selected independently by two readers. Data were extracted by one investigator and independently checked by another. A meta-analysis was performed with Review Manager Software, with random-effects models, whenever methodologically possible and relevant.

Results: The literature search revealed 232 articles and abstracts of potential interest, and further examination resulted in 7 studies fulfilling required criteria. Among bDMARDs, Tocilizumab was associated with an increased incidence of GI perforations, with an overall incidence of 2.40 per 1000 person-years (95% confidence interval [95% CI] 1.45-3.35). The overall incidences of GI perforations were 1.01 per 1000 PY [0.75-1.27] for TNF inhibitors, 1.07 per 1000 PY [0.53-1.62] for abatacept and 1.12 per 1000 PY [0.16-2.08] for rituximab (Figure 1). In RA patients treated with tocilizumab, most of the perforations were located in the lower GI tract, with an incidence of 2.24 per 1000 PY [1.24-3.52]. The incidences of upper GI perforations were similar across the different bDMARDs. The incidences of diverticulitis were 4.99 per 1000 PY [4.08-5.99] in RA patients receiving tocilizumab and 1.81 per 1000 PY [1.47-2.19] in those receiving TNF inhibitors.

Conclusion: In our meta-analysis, focused in RA patients receiving bDMARDs in observational cohort studies, tocilizumab was associated with an increased incidence of GI perforations, mainly located in the lower GI tract. An history of diverticulitis and long-term corticosteroid therapy were associated with an increased risk of GI perforations.

Figure 1. Meta-analysis of the incidences of gastro-intestinal perforations in RA patients receiving bDMARDs in observational cohort studies

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THE IMPACT OF AGE ON DISCONTINUATION OF BIOLOGIC DMARDs IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is the most common autoimmune disease. Older patients treated with biologic DMARDs (bDMARDs) are at a significantly greater risk of adverse effects (AEs) [1]. However, the rate of drug discontinuation because of adverse effects caused by bDMARDs has not differed in elderly compared to younger patients in different registries.

Objectives: Determine if drug discontinuation of bDMARDs differs by age in patients with rheumatoid arthritis in the Mexican Adverse Events Registry (BIOBADAMEX).

Methods: BIOBADAMEX is a Mexican ongoing cohort of patients using bDMARDs since 2016. In this analysis we included all patients with diagnosis of RA with at least two assessments. Survival on bDMARDs was estimated using Kaplan-Meier analysis. Predictors of discontinuation, including age older than median age in the sample were investigated by Cox regression analyses.

Results: Among 743 patients in the registry, 497 had RA diagnosis, from which, 214 had at least two assessments. At baseline, patients had a median (IQR) age of 53.4 (45-61) years old, median disease duration of 10.7 (6-17) months and median DAS28 of 4.7 (3-6). Conventional DMARDs were used by 185 (87%) patients and 94 (44%) patients used corticosteroids. Comorbidities were present in 194 (91%). The most common bDMARDs received at baseline were abatacept 59 (27%), tocilizumab 45 (21%), adalimumab 31 (15%) and certolizumab 30 (14%). At the time of analysis, the median bDMARDs treatment duration was 21.0 (13-34) months, 128 (59%) had discontinued treatment, 66 for inefficacy, 32 for adverse events and 30 for others. Fig 1 shows discontinuation rate curves in patients younger and older than median age. Cox proportional-hazards demonstrated no significant differences regarding age older than median age (HR 1.1, 95% CI 0.8-1.4, p=0.7), female sex (HR 1.2, 95% CI 0.7-1.9, p=0.44), use of corticosteroids (HR 1.2, 95% CI 0.9-1.6, p=0.20), comorbidities (HR 0.9, 95% CI 0.6-1.5, p=0.78), DAS28 (HR 0.9, 95% CI 0.9-1.1, p=0.93) or other factors.

Conclusion: This analysis did not show a role of age on discontinuation of bDMARDs in Mexican RA patients. Further longitudinal analyses will be performed including more patients to assess retention rate of bDMARDs and identify predictive variables of discontinuation in Mexican population.

Figure 1. Discontinuation rate curves in patients younger and older than median age (< 53.4 and ≥53.4 years old)

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ARE BIOLOGIC AND TARGETED SYNTHETIC DMARDS SAFE TO USE IN PATIENTS WITH RENAL IMPAIRMENT?

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Background: Chronic kidney disease (CKD) is defined as a permanent (minimum three month) reduction in glomerular filtration rate.^[1] 10-30% of rheumatoid arthritis (RA) patients have CKD, compared to 5% of the general population.^[1] There are several causes of CKD associated with RA including persistent inflammation, cardiovascular risk factors, frequent use of non-steroidal anti-inflammatory drugs and amyloidosis.^[1] CKD in RA patients is associated with increased mortality.^[2]

The use of biologic and targeted synthetic DMARDs for treating RA has increased significantly in recent years. Studies have shown these therapies might reduce the risk of developing CKD in RA.^[3] However, conversely, biologics have been linked to the development of glomerulonephritis.^[4]

Surprisingly few studies have explored the use of biologics in patients with pre-existing renal disease and whether they contribute to renal impairment themselves.

Objectives: Our objectives were to explore the renal safety profile of biologic and targeted synthetic DMARDs in a real-world cohort of RA patients with and without pre-existing CKD.

Methods: A retrospective observational study was completed using the Biologic Therapy Database at Cannock Chase Hospital. Inclusion criteria were a diagnosis of RA and current treatment with a biologic or targeted synthetic DMARD.

Demographic data, renal function at biologic initiation and any deterioration of renal function were among the recorded information for each patient. Patients with insufficient information available via electronic patient records were excluded.

Results: 998 RA patients on biologics were identified, of whom 213 were excluded. Of the 785 remaining patients, a 3:1 female to male ratio was noted with a mean age of 62. 40% of patients were on an anti-TNF, 22% rituximab, 15% abatacept, 15% JAK inhibitors and 9% anti-IL6 respectively. At biologic initiation 92% of the patients had a GFR of >60 ml/min per 1.73m², 4.8% had a GFR of 30-60 (CKD stage 3a-3b), <1% stage 4 CKD. No patients in the cohort had CKD stage 5 at biologic initiation.

Overall, 13 patients had significant pre-existing CKD (eGFR <45) of these, 6 were treated with abatacept. 7/13 patients had no co-morbid risk factors for CKD – of those remaining, 2 were hypertensive, 2 diabetic and 2 both. None of these 13 patients experienced a drop in renal function by more than 1 stage since initiation of current biologic.

Of those patients without prior CKD at the point of biologic initiation (GFR >45), only 15 patients (2%) developed new renal impairment whilst on biologic treatment. 10 patients' renal function dropped by one stage and five patients by two stages. Crucially, 12 of the 15 patients were aged ≥75yrs and 10 patients had at least one other associated risk factor (e.g. diabetes). Only one patient in the cohort developed renal impairment as a direct result of a biologic – minimal-change disease secondary to etanercept.

Conclusion: Our findings indicate that biologic treatments have a good renal safety profile – even with pre-existing CKD. RA patients most at risk of developing CKD whilst on biologics are likely to have other risk factors such as diabetes or hypertension. As previously stated, there is a very rare association of anti-TNF biologics causing glomerulonephritis.

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AIR POLLUTION IS A PREDICTOR OF POOR RESPONSE TO BIOLOGICAL THERAPIES IN CHRONIC INFLAMMATORY ARTHRITIDES

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Background: There is increasingly evidence that environmental air pollution is associated with both development of chronic inflammatory arthritides (CIA). The role of air pollutants on the treatment response of CIA (including psoriatic arthritis [PsA] and ankylosing spondylitis [AS]) is still unclear.

Objectives: The objective of the present study is to determine the association between the concentration of air pollutants and biological drug retention rates in CIA.

Methods: We retrieved longitudinal data of patients affected by CIA on biological therapies and of the daily concentration of air pollutants in the Verona area. We designed a case-crossover study to compare the exposure to pollutants in the 30-day and 60-day periods preceding a drug switch or swap due to disease progression referent to the 30-day and 60-day periods preceding a visit with stable treatment for at least 6 months.

Results: 1,286 patients with CIA (888 with RA, 260 with PsA and 138 with AS) with 5,454 follow-up visits were included in the study. 13,636 daily air pollution records were retrieved. We found an exposure-dependent relationship between exposure to air pollutants and CRP serum levels in CIA. At PM10 exposures of >50 µg/m³ and >40 µg/m³ we found a 150% and 65% higher risk of having CRP above 5 mg/L respectively (OR 2.564, 95% CI 2.114-3.110 and OR 1.659, 95% CI 1.440-1.910, respectively). If the threshold was set at >30 µg/m³ of PM10 (below the European Union health protection limit) we still found a 38% higher risk of having altered CRP (OR 1.383, 95% CI 1.206-1.588). Among CIA patients, 280 patients (21.7%) had at least 2 follow-up visits with at least one drug switch or swap due to drug inefficacy and one visit with stable treatment for at least 6 months, serving as our sample for the case-crossover study. We found that air pollutants concentrations were higher before a switch or swap due to drug inefficacy (Figure 1A). Figure 1B shows the receiver operating characteristic (ROC) curve for the prediction of switch or swap due to drug inefficacy. Discriminatory capacity of disease activity alone was the highest (AUC 0.841) but when the prediction model included the concentrations of air pollutants in the 60 days before the visit the discriminatory capacity increased (AUC 0.879).

Conclusion: We found that environmental air pollution was a determinant of poor response to biological treatment in a cohort of patients with CIA followed over a 5-year period. Intervention aimed to decrease the fossil combustion emissions might have beneficial effects on biologics persistence rate of patients with CIA.

Figure 1. A) Mean concentrations of air pollutants in the 60-day period before switch or swap visit compared to the stable treatment visit. p <0.001 between all groups. B) Receiving operating characteristics (ROC) curves for the prediction of switch or swap due to drug inefficacy

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RITUXIMAB THERAPY IN THE INTERSTITIAL LUNG DISEASE OF RHEUMATOID ARTHRITIS: A SYSTEMATIC REVIEW

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Background: Interstitial lung disease (ILD) is a severe manifestation of rheumatoid arthritis (RA), linked to increased mortality. There is still no consensus on the best therapeutic strategy as there aren't yet randomized controlled trials.

Objectives: To analyze the available scientific evidence on the efficacy and safety of rituximab (RTX) treatment of interstitial lung disease (ILD) associated with rheumatoid arthritis (RA).

Methods: A systematic search was carried out in PubMed until April 2020 following the PRISMA recommendations. Studies were selected according to the