

Treatment adherence of patients with systemic rheumatic diseases in COVID-19 pandemic

We read with great interest the preliminary German Society of Rheumatology recommendations for the management of patients with autoimmune inflammatory rheumatic diseases (AIRD) during the COVID-19 pandemic.¹ As other regulatory bodies suggest^{2,3} patients should not discontinue their anti-rheumatic treatment because of fear.¹

Herein, we investigated to which extent patients with AIRD altered their treatment during COVID-19 pandemic and whether there are any factors that affected their decision. We telephone-interviewed (14 April 2020–22 April 2020), 500 consecutive AIRD-patients followed-up in our centre and recorded the following parameters: age, sex, cohabitation, region of residence (urban, semiurban, rural), level of education (first, second, third), employment status, disease duration, current treatment and presence of co-morbidities (hypertension, hyperlipidemia, coronary heart disease, diabetes mellitus, chronic obstructive pulmonary disease (COPD), depression, anxiety).

Specific questions referred to the COVID-19 pandemic period in Greece, starting on 26 February 2020, with predefined answer-options, were asked: discontinuation of any medication received for AIRDs, possible reasons that led to drug discontinuation (including fear of immunosuppression and lack of resources/drug shortage), whether advice was received from a clinician or other sources, symptomatology compatible with COVID-19 infection, subjective assessment (on a five-point Likert scale) of disease activity and a questionnaire to detect nocebo behaviour (cut-off score: 15).⁴ Univariate and binary logistic regression analyses were performed using 'discontinuation of medication due to fear of infections', 'discontinuation of medication due to lack of resources/drug shortage' and 'consultation by a clinician' as dependent variables, in three different models.

We interviewed 500 patients (73.2% female, mean (±SD) age: 53.7±15.3 years, disease duration: 10.0±9.4 years) with various AIRDs: inflammatory arthritis: 52.4%, connective tissue diseases: 33% (systemic lupus erythematosus: 16%, systemic sclerosis: 11%, anti-phospholipid syndrome: 3.6%, Sjogren's syndrome: 1.2%, polymyalgia rheumatica: 1.2%), vasculitis: 9.4%, auto-inflammatory diseases: 5.2%. Of them, 65.8% were cohabiting with another person, 83.6% were living in urban area, 47.6% and 38.2% had a second and third level of education, respectively and 6% were unemployed. Half (46.6%) of our patients were on steroids, 73.4% were on conventional disease modifying anti-rheumatic drugs (cDMARDs), 6.8% on targeted DMARDs and 43.8% on biologics (bDMARDs).

Collectively, 11/500 (2.2%) discontinued AIRD treatment due to fear of immunosuppression; all but two were on bDMARDs. Nineteen (3.8%) patients stopped their treatment because of lack of resources/shortage of drug; 7/19 (36.7%) were on treatment with hydroxychloroquine. Noteworthy, 53.8% (7/13) of patients who discontinued treatment with hydroxychloroquine did so because of drug shortage. Additionally, 13/500 (2.6%) and 30/500 (6.0%) discontinued their medication due to a respiratory infection or for other reasons (eg, side-effects), respectively. In total, 124 (24.8%) patients received advice about possible modification of their treatment. All but three, were guided by a clinician.

Therapy withdrawal due to fear of immunosuppression was associated with underlying COPD in univariate analysis ($p=0.022$), and with unemployment (OR, 95% CI: 9.19, 1.30 to 64.7, $p=0.03$) and COPD (OR, 95% CI: 27.53, 3.17 to 239.1, $p=0.003$) in regression analysis. Treatment discontinuation due to lack of resources/drug shortage was not associated with any parameter tested. Decision about consulting a clinician was associated with unemployment status, COPD and male gender ($p=0.001$, $p=0.03$ and $p=0.03$, respectively) in univariate analysis. Regression analysis confirmed these findings: unemployment (OR, 95% CI: 3.55, 1.58 to 7.93, $p=0.002$); COPD (OR, 95% CI: 3.93, 1.11 to 13.95, $p=0.03$); male gender (OR, 95% CI: 1.82, 1.13 to 2.93, $p=0.01$).

COVID-19 infection symptomatology was reported in 39 patients, two of whom were tested and found negative. For most patients (66%) the disease remained stable during the pandemic. Ninety-three (18.6%) patients reported improvement and 77 (15.4%) deterioration from their last visit. Treatment discontinuation due to fear of infections or lack of resources/shortage of drugs was not associated with a disease exacerbation ($p=0.472$). Nocebo behaviour was detected in 10.2% of the patients.

In conclusion, discontinuation rate due to fear of immunosuppression in our cohort was low, mostly observed in patients on bDMARDs. Hydroxychloroquine shortage was a considerable problem for our patients. Special consideration should be given to patients with certain social or clinical characteristics, such as unemployment status and COPD.

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