Frequency and severity of COVID-19 in patients treated with biological disease-modifying anti-rheumatic drugs for inflammatory rheumatic disease: a cross-sectional study

Sirs,

The outbreak of the coronavirus disease 2019 (COVID-19) (1) has left behind more than 1 million deaths among the 35 million diagnosed cases. In children and young adults, COVID-19 is usually mild, and not even symptomatic, while in older and frail people, especially in subjects with immunity disorders, it can result in multiple organ failure, with death in about 4% of cases (2). Biological disease-modifying anti-rheumatic drugs (bDMARDs), have been classified as potentially immunosuppressive drugs due to the increased risk of severe infection (3). The French Society of Rheumatology (SFR) recommended that persons with immunosuppression acquired by immunosuppressive therapy, biotherapy and/or corticosteroid therapy, may request to be put on sick leave. In the lack of a COVID-19 infection sign, they must continue the treatment (cDMARDs, DMARDs, corticotherapy). If signs of COVID-19 infection, patients must stop treatment except for corticosteroids and hydroxychloroquine. Patients should restrict their social interactions and postpone non-emergency care. However, the preliminary reports showing beneficial effects of IL-6 (4) and IL-1 blockade (5) in Sars-CoV-2 ARDS can paradoxically suggest a possible 'protective' effect of certain bDMARDs on COVID-19 severity. The Nord Franche-Comté hospital is located in north-eastern France, an area severely impacted by the COVID-19 outbreak (more than 700 patients hospitalised and 180 deaths). The aim of the present work was to estimate the impact of COVID-19 in patients treated with bDMARDs for inflammatory rheumatic disease (IRD) and to compare it to a control group of patients not treated with bDMARDs

This single-centre, observational, case-control trial included 100 consecutive patients, treated with bDMARDs for IRD and 100 patients who did not take bDMARDs. All completed a standardised questionnaire after they have given their informed consent. The following information was recorded: gender, age, body mass index, professional activity, family status, number of children and number of children under 18, rheumatic disease diagnosis, current treatments for rheumatism, close contact with COVID-19 patients, Covid-19 symptoms, COVID-19 test result and hospitalisation for COVID-19. bDMARD patients mostly suffered from rheumatoid arthritis (RA) (47%) and ankylosing spondylitis (42%). TNFα inhibitors were the most prescribed of the bDMARDs (57%). IL-6 blockers and JAK inhibitors were prescribed in 12% and 11%, respectively. The mean duration of the current biologic treatment was 38.6 months. Patients from the control group were suffering chiefly from osteoarthritis (45%) and RA (21%). The between-group comparison is summarised in Table I. The 36 patients from the control group who suffered from IRD did not differ from those with other musculoskeletal disorders in age, BMI, sex, number of children under 18. They differed from patients with bDMARDs with regard to age (p=0.008), number of children under 18 (p=0.05) and professional status (p=0.05). They were more likely to take corticosteroids (16.6% *vs*. 7%, p=0.007) and methotrexate (50% *vs*. 29%, p=0.005) and have been more frequently in contact with COVID-19 patients (16.6% *vs*. 5%, p=0.04). Eighteen patients from the bDMARD group stopped their biological treatment. Among them, only 1 stopped because of COVID-19 evidenced by PCR, 11 because of symptoms that suggested COVID-19. Six asymptomatic subjects stopped treatment due to fear of contracting the disease. Twelve patients, including the one Sars-CoV-2 +, resumed their treatment after a few weeks of interruption. There was no severe COVID-19 infection in the bDMARD group. Thereby, our results suggest that taking a biologic is not a significant risk factor for contracting the disease. However the number of infected subjects was very low in the two groups. Larger-scale studies, carried out outside a containment period, are necessary before affirming that biologics do not expose patients to an increased risk of COVID-19 and complications.

Table I. Characteristics of patients treated with biological disease-modifying anti-rheumatic drugs (bDMARDs) or not (Controls).

Variables	All	bDMARDs	Controls	p-values
Age (years), mean (range)	59 (23-89)	54 (25-81)	64 (23-89)	<0.001
Weight (kg), mean (range)	75.3 (41-145)	75.7 (45-121)	74.5 (41-145)	0.64
Height (cm), mean (range)	166.4 (140-195)	166.4 (148-187)	165.8 (140-195)	0.62
Body Mass Index, mean (range)	27.2 (16.8-48.1)	27.3 (17.9-48.1)	27.0 (16.8-44.9)	0.74
Sex ratio (F/M)	127/93	62/48	65/45	0.66
n. children, mean (range)	1.71 (0-5)	1.7 (0-5)	1.78 (0-4)	0.87
n. of children <18, mean (range)	0.54 (0-5)	0.7 (0-5)	0.36 (0-3)	0.02
Life in couple/alone (n)	156/44	80/20	76/24	0.69
Retired (%)	87	31	56	0.001
Sick or incapacity leave (%)	48	31	17	0.02
Working from home/short-term working (%)	36	27	9	<0.0001
Work with public or patients (%)	17	4	13	0.01
Methotrexate or leflunomide (%)	47	29	18	0.04
Corticosteroid (%)	13	7	6	0.90
Covid-19 symptoms (yes/no)	27/173	12/88	15/85	0.45
PCR assessment (%)	11	4	7	0.55
PCR+ (%)	4	1	3	0.84
Contact with Covid-19 subject (yes/no/uncertain)	27/156/18	10/84/6	17/72/11	0.16
Stop biologic (yes/no)	18/182	18/82	NA	NA

Availability of data and materials

All data generated or analysed during this study are available at the Unité de Recherche Clinique, Hôpital Nord Franche-Comté, Belfort, France.

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