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**ONLINE RHEUMATOLOGY RESEARCH AND PUBLISHING
AMIDST THE COVID-19 PANDEMIC**
MREŽNO ISTRAŽIVANJE I OBJAVLJIVANJE U REUMATOLOGIJI
U TIJEKU PANDEMIJE COVID-19

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The ongoing COVID-19 pandemic has impacted all fields of scientific research. Rheumatology, as a rapidly developing clinical discipline, has embraced positive trends in online research and offered some valuable survey data. Depending on target populations, their size, and geographic coverage, the obtained survey data may form a basis for rheumatology practice guidelines.

The validity of online surveys is subjected to employing reliable channels for questionnaire dissemination and timeline of collecting responses. The strengths and limitations of online surveys share similarities with those of other observational studies. The reliability of the data change over time, necessitating revised surveys. Although full ethics review is not mandatory for most surveys, some precautions are warranted to preserve the anonymity of surveyees and avoid unjustified promotion of (repurposed) drugs amidst the COVID-19 pandemic.

The EQUATOR Network endorsed the CHERRIES standard for online surveys. We have proposed a set of recommendations that concentrate on designing questions, validating questionnaires, disseminating questionnaires via social media, choosing advanced platforms for data processing, and targeting journals. Given the relatively low citations of surveys, most high-impact journals decline related submissions outright. Nonetheless, some influential surveys, particularly those on COVID-19 vaccines for rheumatic patients, have been successfully published by top rheumatology journals.

During the ongoing pandemic, several other types of online research have gained their momentum. Bibliometric and altmetric analyses of COVID-19 publications, including those in rheumatology, have revealed trends successful use of Twitter and Mendeley platforms for disseminating reliable information and ranking the most influential topics. It is expected that more and more clinicians will embrace the benefits of online research for their daily practice.

Keywords: COVID-19, rheumatology, questionnaire and surveys, bibliometric and altmetric analyses

Ključne riječi: COVID-19, reumatologija, upitnik i ankete, bibliometrijske i altmetrijske analize

ADDITIONAL HETEROLOGOUS VERSUS HOMOLOGOUS BOOSTER VACCINATION IN IMMUNOSUPPRESSED PATIENTS WITHOUT SARS-COV-2 ANTIBODY SEROCONVERSION AFTER PRIMARY mRNA VACCINATION: A RANDOMIZED CONTROLLED TRIAL

DODATNO HETEROLOGNO CIJEPLJENJE U ODNOSU NA HOMOLOGNO POJAČANO CIJEPLJENJE U IMUNOSUPRIMIRANIH PACIJENATA BEZ SEROKONVERZIJE ANTITIJELA SARS-COV-2 NAKON PRIMARNOG CIJEPLJENJA mRNA: RANDOMIZIRANO KONTROLIRANO ISPITIVANJE

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Objectives. Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2)-induced coronavirus disease 2019 (COVID-19) has led to exponentially rising mortality, particularly in immunosuppressed patients, who inadequately respond to conventional COVID-19 vaccination.

Methods. In this blinded randomized clinical trial we compare the efficacy and safety of an additional booster vaccination with a vector versus mRNA vaccine in non-seroconverted patients. We assigned 60 patients under rituximab treatment, who did not seroconvert after their primary mRNA vaccination with either BNT162b2 (Pfizer-BioNTech) or mRNA-1273 (Moderna), to receive a third dose, either using the same mRNA or the vector vaccine ChAdOx1 nCoV-19 (Oxford-AstraZeneca). Patients were stratified according to the presence of peripheral B-cells. The primary efficacy endpoint was the difference in the SARS-CoV-2 antibody seroconversion rate between vector (heterologous) and mRNA (homologous) vaccinated patients by week four. Key secondary endpoints included the overall seroconversion and cellular immune response; safety was assessed at weeks one and four.

Results. Seroconversion rates at week four were comparable between vector (6/27 patients, 22%) and mRNA (9/28, 32%) vaccine ($p=0.6$). Overall, 27% of patients seroconverted; specific T-cell responses were observed in 20/20 (100%) vector versus 13/16 (81%) mRNA vaccinated patients. Newly induced humoral and/or cellular responses occurred in 9/11 (82%) patients. No serious adverse events, related to immunization, were observed.

Conclusions. This enhanced humoral and/or cellular immune response supports an additional booster vaccination in non-seroconverted patients irrespective of a heterologous or homologous vaccination regimen.

Trial registration: EudraCT 2021-002348-57

Keywords: SARS-CoV-2, Rituximab, vaccination, immune response

Ključne riječi: SARS-CoV-2, rituksimab, cijepljenje, imunološki odgovor

HOW WE ADAPTED OUR WORK DURING THE PANDEMIC. WERE WE SUCCESSFUL? KAKO SMO PRILAGODILI SVOJ RAD TIJEKOM PANDEMIJE. JESMO LI BILI USPJEŠNI?

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CONTROVERSIES IN THE TRETAMENT OF COVID-19 PATIENTS KONTROVERZE U ZBRINJAVANJU I LIJEČENJU COVID-19 BOLESNIKA

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Since we started to treat first COVID-19 patients and find out the gloomy perspectives of positive outcome, there was a desperate desire to improve survival by introducing new, “logical” treatment options beside oxygenation, following the rapid elucidation of the pathogenesis of the disease. An intriguing option appeared that beside targeting SARS-CoV-2, modulation of devastating inflammatory response and supression of extensive coagulation might increase survival rates. Severe COVID-19 is usually bilateral pneumonia with characteristics of ARDS, multiorgan dysfunction and disseminated intravascular coagulation. These are characteristics of sepsis. The same pattern of thinking developed as over thirty years ago. The idea was that survival might be increased with early pathogen oriented therapy (remdesivir), neutralization of viral S antigen with monoclonal antibodies (bamla-nivimab, etesevimab, casirivimab/imdevimab), supression of inflammation with steroids (dexamethasone), supression of the production and neutralisation of activity of proinflammatory cytokines IL-6 (tocilizumab, sarilumab), IL-1 (anakinra), janus kinase (baricitinib, tofacitinib). Heparin and 5NOK inhibitors were used to supress and threat thrombosis. Unfortunately, in nineties we needed more than ten years to admit that only targeted antibacterial therapy, fluids, sympatomymetics, and in a selected group of patients hydrocortisone are of clinical importnace, while other antiinflamamntory therapeutic approaches were only the futile attemps. In Covid-19 pandemic that became clear after only one year due to the huge number of patients.

Our capabilities to supress viral replication by antiviral drugs (remdesivir) are still poor performing. Dexamethasone (6 mg daily) improve outcome in patients who need oxygen. Prophylactic heparin doses are as effective as therapeutic, and 5NOK inhibitors might be useful in very selected group of patients with proven extensive thromboses. Other therapeutic approaches are of little clinical significance. Intensive oxygen supplementation is needed. High-flow oxygenation became a standard therapy, but the outcome of mechanically ventilated patients is extremely poor, particularly in elderly. Early ECMO therapy is very useful but limited with low number of experienced and well equipped centers. Since pandemics continue these facts should be considered to prevent doing harm instead of helping severely ill patients.

Key words: COVID-19, treatment, controversies

Ključne riječi: COVID-19, treatment, controversies