15. Streszczenie w języku angielskim

In November 2019, patients with an atypical course of pneumonia and multi-organ complications were observed in Wuhan Province, China. Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) was found to be responsible for these infections, leading to a global pandemic declared by the World Health Organisation in March 2020. SARS-CoV-2 is composed of single-stranded RNA and structural proteins: the spike protein (S), the nucleocapsid protein (N), the membrane protein (M) and the envelope protein (E). The most clinically significant is the S protein which binds to the receptor for angiotensin-converting enzyme II and infects host cells via this pathway. The N protein is also important as it serves a protective function for the genetic material of the virus and is responsible for its replication. Antibodies against the S-protein are produced after both passive and active immunisation, and show neutralising abilities, i.e. protecting against infection. Antibodies against the N protein typically develop after natural infection and have no protective abilities.

The course of COVID-19 in multiple sclerosis (MS) patients has been of particular interest since the start of the pandemic. Currently available data indicate that in patients with MS, the course of COVID-19 is not significantly different from that in the general population. MS is an autoimmune disease of the central nervous system with more than 50,000 patients in Poland. The mainstay of MS treatment are disease-modifying therapies (DMTs) which is available to patients in Poland on the National Health Fund.

The aim of the PhD thesis was to analyse antibodies against SARS-CoV-2 S and N proteins in patients with the relapsing-remitting form of MS treated with selected DMTs in North East Poland.

Prior to commencement of the research, analysis of the available literature on the serological status of patients with nervous system diseases who had had COVID-19 was performed. Following the analysis, and at the time of starting the study, a review paper that aimed to systematise the existing knowledge on the subject was published in a peer-reviewed journal.

The study group consisted of patients with the relapsing-remitting form of MS treated with selected DMTs. The majority of patients were treated with beta interferon, glatiramer acetate and dimethyle fumarate.

During the first stage of the study, the presence of antibodies against the S protein in IgG and IgA class (hereafter: IgG-S, IgA-S), and against the N protein in IgG class (hereafter: IgG-N) of SARS-CoV-2 was determined. The presence of IgG-S and IgA-S antibodies was assessed by immunoenzymatic ELISA using anti-SARS-CoV-2 IgA and IgG kits (Euroimmun, Medizinische Labordiagnostika AG, Germany). During the first stage of the study, laboratory determinations were performed twice (visit one: May–June 2020, n=186; visit two: May–June 2021 n=88). During the second stage of the study, antibodies against the receptor binding domain (RBD) of the S1 subunit of SARS-CoV-2 in IgG class (hereafter designated as IgG-S1RBD) and antibodies against the N protein in IgG class were determined qualitatively and quantitatively by chemiluminescence (CMIA; Abbott, IL, USA). During the second stage of the study, laboratory determinations were performed twice (visit three; December 2021–February 2022, n=38; visit four: December 2022–February 2023, n=38).

During the first stage of the study, it was demonstrated that vaccination statistically significantly induced the presence of antibodies against the S protein (IgG-S and IgG-A), but did not induce antibodies against the N protein (IgA-S, $p<0.0001$; IgG-S, $p<0.0001$; IgG-N $p = 0.91$). Statistical analysis of the results of the second stage of the study demonstrated that vaccination increased the level of IgG-S1RBD (visit three $p<0.001$ and visit four $p=0.038$), while there was no statistically significant difference in the presence of IgG-S1RBD neutralising antibodies in vaccinated and unvaccinated patients (third visit: $p = 0.089$; fourth visit $p = 0.501$). Furthermore, during the second stage of the study (2022–2023), no significant differences were found in the presence of neutralising antibodies between the group of patients who had had SARS-CoV-2 infection confirmed by an antigen or PCR test and the group of patients who had not had a confirmed SARS-CoV-2 infection (third visit $p=0.309$; fourth visit $p=1.0$). Study participants who had had SARS-CoV-2 infection (positive antigen/PCR result) had a statistically significantly higher level of IgGS1RBD antibodies during the third visit ($p=0.001$), but no differences were found in antibody levels during

the fourth visit (p=0.410). An increase in the level of neutralising antibodies in patients without a confirmed previous SARS-CoV-2 infection indicates a widespread presence of the virus in the studied population and numerous mildly symptomatic/asymptomatic infections. Patients with a confirmed past SARS-CoV-2 infection had a statistically significantly higher level of IgG-N antibodies on the third visit (p=0.040) in comparison to COVID (-) patients, but no differences were found on the fourth visit (p=0.363). Drugs modifying the course of MS used in the study group did not affect the production of neutralising antibodies. Analysis of the obtained data allowed us to arrive at the following conclusions:

- Patients suffering from relapsing-remitting MS treated with interferon beta, glatiramer acetate and dimethyle fumarate are immunocompetent. Vaccination against SARS-CoV-2 in the study group significantly induced the production of neutralising antibodies and increased their level.
- The observed increase in the percentage of seropositive patients who had not had a confirmed infection and had not been vaccinated against SARS-CoV-2 during the subsequent years of the pandemic indicates numerous mildly symptomatic/asymptomatic infections. Vaccination did not affect the production of antibodies against the N protein in the study group.
- The overall incidence of COVID-19 infection in the study group at various points during the pandemic was similar to that observed in the general Polish population. All study participants with a confirmed previous SARS-CoV-2 infection and vaccinated against COVID-19 showed the presence of neutralising antibodies, which suggests that hybrid immunity is of great importance for protection against infection in the studied group of patients and indicates the usefulness of vaccinating individuals who have already had SARS-CoV-2 infection.

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