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ACTA PÆDIATRICA NURTURING THE CHILD WILEY

BRIEF REPORT

Preliminary observations on the immunogenicity and safety of vaccines to prevent COVID-19 in patients with juvenile idiopathic arthritis

Patients with autoimmune diseases have a higher risk of COVID-19, hospitalisation and death than the general population and are a priority for vaccination.[1]

Two messenger ribonucleic acid vaccines from Pfizer and Moderna have been approved for patients with rheumatic disease.[1] It is not completely clear whether these vaccines could make underlying rheumatic disease flare up, as a result of immune activation, but adult studies have reported that they are safe and effective.[1]

Juvenile idiopathic arthritis (JIA) is the most common paediatric rheumatic disease.[2] The Pfizer vaccine has been shown to be safe and effective in adolescents with JIA.[3] In spring 2021, the Pfizer vaccine was approved for children aged 12 years and above with rheumatic disease,[4] but data about the Pfizer vaccine for children with JIA have been lacking.

This monocentric, retrospective, observational study aimed to compare the immunogenicity and safety of the Pfizer vaccine in patients with JIA aged 12–16 years and healthy controls. It was approved by the Research Ethical Committee of the University of the Study of Campania Luigi Vanvitelli in Naples, Italy, and informed parental consent was obtained.

We approached 85 patients aged 12–16 years and 36 (75% female) agreed to be vaccinated: 24 refused due to fear of being vaccinated and 25 had already had COVID-19, with 13 experiencing JIA reactivation. The 33 healthy controls (75% female) were relatives of patients.

The JIA subtype, the disease activity, according to the Juvenile Arthritis Disease Activity Score (JADAS-10)[5] and the pharmacological treatment were recorded. Virus antibodies and vaccination side effects were recorded for patients and controls.

Juvenile idiopathic arthritis was diagnosed according to the International League of Association for Rheumatology criteria and treated in line with the American College of Rheumatology recommendations.[2] The demographic and clinical characteristics of both groups are shown in Table 1.

The patients and controls received two intramuscular Pfizer vaccines 3 weeks apart, according to national guidelines.[6] Blood samples were collected on enrolment and 1 month after the second vaccination to identify viral antibodies.[1] Immunoglobulin antibodies against the virus' S1/S2 spike were quantified by chemiluminescent immunoassay, using the LIAISON SARS-CoV-2 Trimeric S-IgG (Diasorin SpA, Piemonte, Italy). A signal/cut-off ratio of ≥14 binding antibody units (BAU)/ml was deemed positive. All subjects were seronegative at baseline.

Follow-up visits were planned 1, 2 and 3 months after the second dose. Disease activity was evaluated with JADAS-10, and all patients were in clinical remission at the time of vaccination, with a score ≤1.[4]

Differences in continuous variables were analysed with the independent-sample *t*-test if the variables were normally distributed and with the Mann–Whitney *U* test if they were not. The differences in proportions were tested with the chi-square test or Fisher's exact test, as appropriate. p values of <0.05 were considered statistically significant.

There were no statistically significant differences in the average levels of antibodies in the patients and controls ($p = 0.65$) (Table 1), in line with studies of Pfizer immunogenicity in adolescents with JIA.[3]

Juvenile idiopathic arthritis was treated according to the published recommendations (Table 1).[2] Methotrexate was discontinued during the weeks of the first and second vaccines, but non-steroidal anti-inflammatory drugs (NSAIDs) and biological drugs were not discontinued.[4] No statistically significant differences were noted when we examined the influence of treatment on antibody production between the different treatment arms. Patients with systemic JIA produced fewer antibodies than patients with oligoarthritis ($p = 0.05$), polyarthritis ($p = 0.03$) and enthesitis-related arthritis ($p = 0.02$). This agreed with Kostik et al who reported that the lowest levels of protective antibodies were found in systemic arthritis, rather than oligoarthritis and polyarthritis.[7]

No disease flares were noted, based on the JADAS-10 score before the first vaccination and follow-up visits.

We recorded any local pain and/or swelling and/or rash, asthenia, fever (>38°C), lymphadenopathy, chills, arthralgia, myalgia, gastrointestinal symptoms and need for NSAIDs by telephone 7 days after the first and second injections. The controls had more local pain and needed NSAIDs more often than the patients ($p = 0.006$ and $p = 0.04$, respectively). Lymphadenopathy was absent in patients. The other side effects were comparable in both groups (Table 1).

Abbreviations: JADAS-10, Juvenile Arthritis Disease Activity Score; JIA, juvenile idiopathic arthritis; NSAIDs, non-steroidal anti-inflammatory drugs.

TABLE 1 Baseline characteristic, treatment and side effects in JIA patients and healthy controls after immunisation with the Pfizer vaccine

	Cases ($n = 36$)	Controls ($n = 33$)	p-value
Female (%)	27 (75)	25 (75)	ns
Age (yrs)	14.5 (±4.1)	14.8 (±3.7)	ns
JIA(%)			
Systemic	4 (11.1)	0	na
Oligoarticular	15 (41.6)	0	na
Poliarticular	13 (36.1)	0	na
Enthesitis-related arthritis	4 (11.1)	0	na
Treatment (%)			
NSAIDS	6 (16.6)	0	na
Methotrexate	16 (44.4)	0	na
Abatacept	1 (2.7)	0	na
Adalimumab	6 (16.6)	0	na
Etanercept	6 (16.6)	0	na
Canakinumab	4 (11.1)	0	na
Tocilizumab	6 (16.6)	0	na
Mean antibodies (range) in BAU/ml	1417 (679–2155)	1311 (112–2510)	ns
Side effects			
Local pain	19 (27.5%)	28 (40.6%)	0.006
Needed NSAIDs/paracetamol	7 (10.1%)	14 (20.3%)	0.04
Local swelling/redness	2 (2.9%)	5 (7.2%)	ns
Lymphadenopathy	0 (0%)	4 (5.8%)	na
Fever >38°	6 (8.7%)	7 (10.1%)	ns
Arthralgia	4 (5.8%)	8 (11.6%)	ns
Asthenia	7 (10.1%)	14 (20.3%)	ns
Gastrointestinal symptoms	5 (7.2%)	1 (1.4%)	ns

Abbreviations: BAU, binding antibody unit; ml, millilitre; na, not applicable; ns, not significant.

This preliminary study did not find any difference in the safety and immunogenicity of the Pfizer vaccine between children with JIA and healthy controls. Although this was a small cohort, the vaccine had an adequate safety and tolerability profile. Further research should investigate whether the differences we observed affected the long-term protection offered by vaccine.

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CONFLICT OF INTEREST

None.

Maria Francesca Gicchino
Fabio Giovanni Abbate
Alessia Amodio
Emanuele Miraglia del Giudice
Alma Nunzia Olivieri

Department of Woman, Child and General and Specialized Surgery, University of the Study of Campania "Luigi Vanvitelli", Naples, Italy

Correspondence
Maria Francesca Gicchino, Department of Woman, Child and General and Specialized Surgery, University of the Study of Campania "Luigi Vanvitelli", via De Crecchio, 4 – 80138 Naples, Italy.
Email: francesca.gicchino@gmail.com

ORCID

Maria Francesca Gicchino https://orcid.org/0000-0003-0329-6583

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