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RELATIONSHIP BETWEEN COVID-19 VACCINES AND GUILLAIN-BARRÉ SYNDROME: A REVIEW OF THE LITERATURE

Ana Beatriz Vitorino e Silva
Cariri Federal University, Barbalha-CE
http://lattes.cnpq.br/7795300796627598

Marina Batista Gondim
Cariri Federal University, Barbalha-CE
http://lattes.cnpq.br/9858439304975585

Alvaro Maciel Oliveira
Cariri Federal University, Barbalha-CE
http://lattes.cnpq.br/3446069065327278

Luíza Alencar Moura
Cariri Federal University, Barbalha-CE
http://lattes.cnpq.br/7930110400194252

Pedro Henrique Matos Granjeiro Cruz
Cariri Federal University, Barbalha CE
http://lattes.cnpq.br/4191974662260296

Harianne Leite de Alencar
Cariri Federal University, Barbalha-CE
http://lattes.cnpq.br/8673298063089216

Hugo Mendes Alencar Furtado
Cariri Federal University, Barbalha-CE
http://lattes.cnpq.br/697259943534875527

Dara Almeida Mauricio de Alencar
Cariri Federal University, Barbalha-CE
http://lattes.cnpq.br/8282335046440847

Morgana de Alencar Oliveira
Estácio de Juazeiro do Norte Medical School
http://lattes.cnpq.br/9617479486146705

Brunno Alexander Oliveira
Federal University of Ceará, Sobral campus
http://lattes.cnpq.br/5723350936631861

John Victor Luna Gregorio
Cariri Federal University, Barbalha campus
http://lattes.cnpq.br/7506006801451087

Abstract: Guillain-Barré syndrome is an immune mediated inflammatory polyradiculoneuropathy associated with numerous viral infections and the adverse reaction to some vaccines, including the vaccine for COVID-19. This is a systematic review of the literature where data collection was performed in the Databases PubMed (NCBI), Virtual Health Library (VHL) and Google Scholar, in october/2021, which aims to verify the prevalence of this adverse reaction in the world, considering the advance of vaccination for COVID-19 in the last months of 2021. Most of the patients who developed the syndrome did not present previous comorbidities, but all were adults, and the youngest person was a 25-year-old woman. The GBS presentations were the most varied, ranging from rapidly reversible unilateral paralysis to severe conditions requiring advanced respiratory support and evolving with sepsis due to white aspiration pneumonia. All patients underwent a large number of tests, which were mostly within the normal range, and the test was the analysis of cerebrospinal fluid. Almost all patients were treated with intravenous immunoglobulin, except for one patient who had no major systemic symptoms, most of which had almost complete remission of the condition with a return to activities of daily living. GBS is a potentially serious disease with low general incidence, several are the factors that can trigger its onset, among them vaccines stand out, however, the benefit of protecting against COVID-19 outweighs the risk of developing GBS.

Keywords: Guillain-Barré syndrome, Covid-19, vaccination.

INTRODUCTION

Covid-19 is an infectious disease caused by a single-tape RNA virus from the Coronaviridae family, was first detected in Wuhan, China, in

December 2019 and quickly spread around the world. The person-to-person transmission occurs mainly through respiratory droplets (KOIKE, KATSUNO, 2021; ZIVKOVIC *et al*., 2021).

The worldwide devastation caused by the COVID-19 pandemic has stimulated a large number of clinical trials investigating different vaccines. Vaccines made with biological products can cause side effects, which can raise suspicions about their safety and cause hesitation or refusal of immunization in certain populations (LUO *et al*. 2021; LUNN *et al*.2021; ZIVKOVIC *et al*.2021).

As with multiple vaccines, including hepatitis B, polio, tetanus, meningococcus, rabies, some studies suggest the association of the occurrence of Gillian Barre Syndrome (GBS) and Covid-19 vaccine. GBS is a rare acute polyradiculoneuropathy commonly associated with a previous infection that can lead to cross-reactions between peripheral nerve components, leading to inflammatory demyelinization. It is believed that the production of autoantibodies directed against the peripheral nerve components induced by the infection of these pathogens plays an important role in the pathogenesis of GBS (KOIKE; KATSUNO, 2021; LUNN *et al*.2021; DUFOUR, *et al* 2021).

In view of the above, we propose, in this article, to review the evidence on the relationship between GBS after vaccination against Covid-19 through the analysis of the evidence available in the literature.

METHODOLOGY

Data were collected in the PubMed (NCBI), Virtual Health Library (VHL) and Google Scholar databases during October/2021, through the combination of Boolean descriptors in English, Portuguese and Spanish:

1 COVID-19 ; OR Vaccines; (Medical subject headers - (MeSH)) AND

2 "Guillain-Barre syndrome" (MeSH)

We selected: (1) articles that had at least one combination of two of the terms described in the search strategy and (2) articles with the full text available online. Additionally, textbooks, protocols from internationally recognized institutions such as the World Health Organization (WHO) were also consulted.

RESULTS AND DISCUSSION

During the research carried out in the databases, 24 articles were selected that met the eligibility prerequisites of which 18 of them had full text available online. Thus, 18 articles were included in this study and evaluated in an integral way. Thus, 17 are case reports (WAHEED, *et al*., 2021; FINSTERER, 2021; INTRONA, *et al*., 2021; FINSTERER, 2021; MATARNEH, *et al*., 2021; PRASAD; 2021; JAIN, *et al*.2021; OGBEBOR; SETH; MIN; BHANOT, 2021; OO; Giri; SOUZA, 2021; AOMAR-MILLÁN, *et al*., 2021; HASAN, KHAN, KHAN, HAMZA, 2021; GARCÍA-GRIMSHAW, *et al*., 2021; RAO *et al*., 2021; MCKEAN; CHIRCOP, 2021; RAZOK; SHAMS; ALMEER; ZAHID, 2021; ROSSETTI; GALINA GHEIHMAN; O'HARE; KOSOWSKY, 2021; MIN *et al*. 2021) and 1 article is an observational retrospective study (TRIMBOLI; ZOLEO; ARABIA; GAMBARDELLA, 2021).

Vaccines against the Covid-19 virus have recently been introduced with a variable degree of immunogenicity and safety (MATARNEH *et al*. , 2021). Although vaccines have been well tolerated, mild or severe adverse reactions, including neurological impairment, may occur in some cases (FINSTERER, 2021).

GBS is an acute immune mediated inflammatory polyradiculoneuropathy of peripheral nerves associated with numerous viral infections, the most common

causative agent being Campylobacter jejuni (INTRONA, *et al*. 2021). Although, most often precipitated after a viral infection, GBS has also been recorded as an adverse reaction to certain vaccines (PRASAD, 2021). The mechanism by which SARS-CoV-2 induces GBS is still unclear (AOMAR-MILLÁN, *et al*., 2021). The most useful diagnostic investigations include lumbar puncture with cerebrospinal fluid analysis (CFA) demonstrating albumin cytological dissociation and electrophysiological studies showing peripheral neuropathy that is of demyeloinizing or axonal origin (RAZOK; SHAMS; ALMEER; ZAHID, 2021).

In the selected articles, GBS were reported after receiving the first dose of AstraZeneca vaccine (AZ) against Covid-19 in 10 people aged between 37 and 76 years (37; 48; 51; 58; 62; 62; 65; 66; 69; 72 years). The time between vaccination and the onset of symptoms ranged from 3 days to 40 days, with an average of 14.5 days. Two people had received H1N1 influenza vaccine 8 weeks before receiving the Oxford immunizer (OO; Giri; SOUZA, 2021; HASAN, KHAN, KHAN, HAMZA, 2021; MCKEAN; CHIRCOP, 2021; FINSTERER, 2021; INTRONA *et al*. 2021; AOMAR-MILLÁN, *et al.,* 2021).

GBS is one of the main causes of flaccid paralysis and can manifest with varying degrees of weakness until almost complete paralysis of all extremity, facial, respiratory and bulbar muscles (AOMAR-MILLÁN, *et al*., 2021). Approximately one third of GBS patients may develop respiratory failure, requiring advanced respiratory support and intensive care unit admission (OO; Giri; SOUZA, 2021; HASAN, KHAN, KHAN, HAMZA, 2021). Although the exact pathophysiology is still unknown, it is believed that an autoimmune response plays a role in the pathogenesis of this disease (WAHEED, *et al*., 2021; OGBEBOR; SETH; MIN; BHANOT, 2021).

A cohort of Pfizer vaccine recipients in Mexico found 7 cases of GBS, all after the first dose, among the 3,890,250 people vaccinated. Of these, only one progresses to death, related to pneumonia associated with mechanical ventilation complicated with septic shock (GARCÍA-GRIMSHAW, *et al.,* 2021). Matarneh *et al.* (2021) described the case of a 61-year-old patient with GBS-compatible symptoms that started 4 days after receiving the second dose of the mRNA-based vaccine (Moderna), the patient presented bilateral weakness in the upper limbs, with inability to perform fine movements with her hands.

In another study (JAIN, *et al.* 2021) a 65-year-old Caucasian woman, hypertensive, diabetic type II, allergic to some medications and egg white, presented dysarthria, dysphagia and bilateral facial weakness, 19 days after receiving the Vaccine Ad26.OV2.S.

A 38-year-old man with a previous diagnosis of anxiety and depression, using marijuana, in addition to ingesting 6 to 8 beers per day (ROSSETTI; GALINA GHEIHMAN; O'HARE; KOSOWSKY, 2021) and another 41-year-old morbidly obese man (PRASAD, 2021), also developed GBS-compatible symptoms after receiving the same vaccine.

Some patients presented themselves, on admission, in good clinical condition, without acute suffering and walking independently (ROSSETTI; GALINA GHEIHMAN; O'HARE; KOSOWSKY, 2021). Clinical neurological examination on admission of some patients revealed peripheral facial paralysis (FINSTERER, 2021; PRASAD, 2021 OO; Giri; SOUZA, 2021). Some patients presented absence of reflexes only in the lower limbs (TRIMBOLI; ZOLEO; ARABIA; GAMBARDELLA, 2021), while in others the deep tendon reflexes were absent (RAO, *et al.* 2021; INTRONA *et al*.2021).

Some patients presented more severe conditions, with disappearance of epicritic

and protopathic sensitivity, as well as decreased flex-extension strength of both feet and leg flexion (AOMAR-MILLÁN, *et al*., 2021). Another patient presented hypotonic quadriparesis and more severe symmetrical bilateral areflexia in the proximal lower limbs evolving two days after admission with respiratory distress and the need for orotracheal intubation (OO; Giri; SOUZA, 2021).

Cerebrospinal fluid investigations were not defining in some cases, polymerase chain reaction (PCR) tests for viruses and CSF bacteria were all negative (FINSTERER, 2021). In most cases, CFS analysis showed albumin cytological dissociation and one viral panel was negative (OO; Giri; SOUZA, 2021; ROSSETTI; GALINA GHEIHMAN; O'HARE; KOSOWSKY, 2021).

Several imaging studies were performed in the most diverse combinations in the cases presented from chest X-ray to computed tomography of the skull with multiphase and venous angiography and magnetic resonance imaging with venous angiography of the brain, showing no evidence to justify the symptoms presented, with the majority being within the normal range (JAIN, *et al.* 2021; OGBEBOR; SETH; MIN; BHANOT, 2021; MCKEAN, CHIRCOP, 2021; INTRONA, *et al*.2021). Nerve conduction studies have shown electrophysiological evidence of pure motor neuropathy with primary demyexinizing characteristics suggestive of demyexinizing polyneuropathy (MATARNEH, *et al.* 2021; PRASAD, 2021).

The vast majority of patients were treated with intravenous immunoglobulin (IVIG) at the most used dose of 2 g/kg for 3 to 10 days, most of which were used for 5 days, most of them responding well from the 3rd day of use (MATARNEH, *et al.* 2021; OGBEBOR; SETH; MIN; BHANOT, 2021; RAZOK; SHAMS; ALMEER; ZAHID, 2021; FINSTERER, 2021; OO; Giri; SOUZA, 2021). Some patients needed to receive, in addition to IVIG, plasmapheresis sessions due to immunoglobulin refractoriness (AOMAR-MILLÁN, *et al.*,2021; JAIN, *et al.* 2021; FINSTERER, 2021).

Some patients complaining of pain were treated with gabapentin, paracetamol, duloxetine and tramadol with moderate improvement of symptoms (MIN, *et al*,2021). Most patients received intense physiotherapy during hospitalization and discharge with referral to the Neurology outpatient clinic for follow-up (WAHEED, *et al.,* 2021; TRIMBOLI; ZOLEO; ARABIA; GAMBARDELLA, 2021; RAO, *et al*., 2021).

To date, there has been no evidence of increased risk of GBS resulting from Covid-19 infection or Covid-19 vaccines; however, individual cases and population cohorts should be examined in order to ensure the constant assessment of such risks (MCKEAN; CHIRCOP, 2021; TRIMBOLI; ZOLEO; ARABIA; GAMBARDELLA, 2021).

FINAL CONSIDERATIONS

Vaccines are a fast and safe public health strategy to combat the pandemic by Covid-19. Vaccines are expected to present adverse reactions with varying meanings in different populations. The exact prevalence of GBS associated with vaccines for Covid-19 remains uncertain. Health professionals should be aware of the appearance of neurological signs and symptoms suggestive of BGS in order to perform an increasingly early approach minimizing its effects and its morbidity and mortality as well as the notification of such events in order to promote and promote knowledge about the subject.

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