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Review

Neurological adverse effects after SARS-CoV-2 vaccinations: Etiology should be warranted

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ABSTRACT

The coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has claimed a global health crisis of unpredictable amount. Due to its high mortality, many COVID-19 vaccines are being developed, approved, and manufactured rapidly. However, some serious neurological adverse events (AEs) were reported after the application of them.

This review was conducted to collect and discuss published data about neurological side effects of SARS-CoV-2 vaccines in order to discover type, frequency, treatment, and outcome of these side effects. The most frequent neurological side effects of SARS-CoV-2 vaccines are headache, Guillain-Barre syndrome (GBS), venous sinus thrombosis (VST), and transverse myelitis. Healthcare practitioners, particularly neurologists involved in the management of patients having undergone SARS-CoV-2 vaccinations, should be aware of these side effects and should recognize them early and treat them significantly. However, some neurological conditions like headache and GBS are found in patients with COVID-19 infection and patients after the SARS-CoV-2 vaccinations. Further studies should be warranted to differentiate the etiology.

Keywords: adverse effects, neuropathy, vaccination, COVID-19, SARS-CoV-2

INTRODUCTION

According to the World Health Organization (WHO), more than 143 vaccine candidates are currently in clinical trials, and 9 of them (AstraZeneca/Oxford Vaccine, Johnson and Johnson, Moderna, Pfizer/BioNTech, Sinopharm, Sinovac, Bharat Biotech BBV152 COVAXIN, Covovax, and Nuvaxovid) have been granted emergency use authorization. However, during the past few months, serious adverse effects such as cerebral venous sinus thrombosis (CVST), splanchnic vein thrombosis, and thrombocytopenia were reported after vaccinations, and some cases have even proved fatal.^{1,2} The earliest reports from Wuhan found that 36.4% of patients showed a certain extent of neurological involvement, which included central nervous system (CNS) manifestations (dizziness, headache, impaired consciousness, acute cerebrovascular disease, and epilepsy), peripheral nervous system (PNS) manifestations (anosmia, hypogeusia, visual impairment, and neuralgia), and skeletal muscular damage.³

In a cohort study of 3,744 patients with clinically diagnosed or laboratory-confirmed COVID-19 at 28 centers, neurological manifestations were found in approximately 80% of patients; the most common self-reported symptoms included headache (37%) and anosmia or ageusia (26%), whereas the most common neurological signs and/or syndromes were acute encephalopathy (49%), coma (17%), and stroke (6%).⁴

More seriously, some of the above symptoms still bothered many survivors 1 year after discharge from hospitals, 10.4% suffered from anxiety, 2.3% from headache, 1.4% from taste change, and 1.3% from impaired sense of smell. Recently, by searching literature on thyroid dysfunction in patients with COVID-19, the entire hypothalamic-pituitary-thyroid axis could be the target of damage by COVID-19. Specifically, it could manifest as thyrotoxicosis or hypothyroidism.⁵⁻⁶

METHODS

A literature search in the databases PubMed using the search terms “SARS-CoV-2 Vaccination,” “side effects,” “adverse reactions,” and “neurological,” was conducted for the period December 2022 to February 2023. Initially detected were 80 titles in PubMed. Included were only original articles which reported a neurological adverse reaction. Excluded were articles that were repetitive and articles in which a causal relation between the vaccination and the complication could not be convincingly established. All approved vaccines were considered.

RESULTS

Fourteen case studies reported the neurological adverse effects and identified them in mass vaccination campaigns (Table 1). The vaccine AZD 1222 reported Guillain-Barré syndrome,⁷⁻¹¹ cerebral venous sinus thrombosis,¹²⁻¹⁷ and transverse myelitis.¹⁸⁻²² The vaccine Ad26.COVS.2 reported cerebral venous sinus thrombosis,^{23,24} and transverse myelitis.²⁵ The vaccine mRNA-1273 reported Bell’s palsy,²⁶⁻²⁹ cerebral venous thrombosis,³⁰ Parsonage-Turner syndrome.^{31,32} The vaccine BNT162b2 reported Bell’s palsy,³³ Guillain-Barré syndrome,³⁴ cerebral venous thrombosis,³⁰ small fiber neuropathy,³⁵ Parsonage-Turner syndrome,^{31,32} and Delirium.³⁶ The vaccine AstraZeneca and Pfizer reported headaches in the 3051 patients.^{37,38}

Table 1: Case reports of neurological adverse effects after SARS-CoV-2 Vaccination.

Vaccine	Neurological adverse effects
AZD1222 (Astrazeneca)	Guillain-Barré syndrome
	Cerebral venous sinus thrombosis
	Transverse myelitis
	Headache
Ad26.COVS.2 (Johnson)	Cerebral venous sinus thrombosis
	Transverse myelitis
mRNA-1273 (Moderna)	Bell’s palsy
	Cerebral venous thrombosis
	Parsonage-Turner syndrome
BNT162b2 (Pfizer)	Bell’s palsy
	Guillain-Barré syndrome
	Cerebral venous thrombosis
	Small fiber neuropathy
	Parsonage-Turner syndrome
	Delirium
	Headache

DISCUSSION

The most frequent neurological side effects of SARS-CoV-2 vaccines are headache, Guillain-Barré syndrome, venous sinus thrombosis, and transverse myelitis as per this review. Other neurological side effects occur at a very low frequency. The most common neurological adverse effect of SARS-CoV-2 vaccination is headache, which can occur with any of the licensed vaccines. The majority of the time, the headache begins within a few hours following the vaccine and subsides spontaneously within 48 hours.³⁷ The pathophysiological mechanism of Guillain-Barré syndrome after SARSCoV2 vaccination is unknown, however, molecular mimicry is thought to be the most feasible theory. Given that SARS-CoV-2 vaccines induce immunization against the spike protein and that the SARS-CoV-2 spike protein can bind to sialic acid-containing glycoproteins and gangliosides on cell surfaces, an antibody cross-reaction appears to be the most likely causal link between Guillain-Barré syndrome and SARSCoV2 immunization.³⁹ The third most common consequence of SARS-CoV-2 vaccines is venous sinus thrombosis, which is explained by hypercoagulability. The activation of platelets by the virus, which shifts endothelium from an antithrombotic to a prothrombotic state, and direct activation of complement pathways, which promotes thrombin production, have been linked to hypercoagulability following a SARSCoV2 vaccine.⁴⁰ The headache and GBS were also reported as neurological complications in the patients with COVID-19 infection.⁴¹

CONCLUSION

This study shows that safety concerns against SARS-CoV-2 vaccines are backed by an increasing number of studies reporting neurological side effects. The most frequent of them are headache, Guillain-Barré syndrome, venous sinus thrombosis, and transverse myelitis. Healthcare practitioners, particularly neurologists, involved in caring for patients who have received SARS-CoV-2 vaccinations should be aware of these side effects, recognize them early, and treat them significantly. However, some neurological conditions like headache and Guillain-Barré syndrome are found in patients with COVID-19 infections and patients after the SARS-CoV-2 vaccinations, further studies should be warranted to differentiate the etiology.

Conflict of Interest

The authors declare no conflicts of interest relevant to this article.

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