

Press Release

New data: German Society of Neurology analyzes sinus and cerebral vein thrombosis after COVID-19 vaccination in Germany

04.05.2021 - Today, a study conducted in Germany was published describing the occurrence of cerebrovascular events, especially cerebral sinus and cerebral venous thrombosis (CVT), after vaccination against SARS-CoV-2. A main finding was that not only younger women had a higher risk of CVT after vaccination with the vaccine ChAdOx1 (AstraZeneca) but also older women. Conclusion of the German Society of Neurology: Although the overall risk of CVT after vaccination with ChAdOx1 is very low, individuals of all ages, especially women, should be fully informed about CVT as a possible adverse reaction to this vaccine.

A study published today as preprint by the German Society of Neurology (DGN) showed that significantly more cerebral sinus and cerebral venous thrombosis (CVT) events occurred after vaccination with the COVID-19 AstraZeneca vaccine than after vaccination with the mRNA vaccines. The CVT event rate that occurred was more than nine times higher after initial vaccination with the ChAdOx1 vaccine than after initial vaccination with the mRNA vaccines within each demographic group. Furthermore, the incidence rate for females was more than three times higher compared to that of non-females.

The DGN has contacted all neurological hospitals in Germany under the project leadership of professor Jörg Schulz (University Hospital Aachen) on April 6, 2021. It was requested to report all cases of cerebral sinus and cerebral venous thrombosis (CVT) as well as ischemic and hemorrhagic strokes that had occurred within one month after SARS-CoV-2 vaccination in a web-based questionnaire until April 14, 2021.

A total of 87 reports were received, of which the expert team confirmed 62. In 95.2% of cases, the adverse events had occurred after the first dose of the vaccine. Forty-five cases were CVT, nine were ischemic strokes, four were cerebral hemorrhages, and four were other cerebrovascular events. The mean age of the cases was 46.7 years, and 77.4% were under 60 years of age.

Fifty-three of the total 62 confirmed cases (85.5%) had occurred after vaccination with the AstraZeneca vaccine ChAdOx1, and nine cases (14.5%) had occurred after vaccination with the BioNTech vaccine BNT62b2. No events were observed after administering the vaccine mRNA-12783 from Moderna (with, however, only 1.2 million doses of the latter administered, as opposed to 16.2 million doses of BNT62b2 and 4.6 million doses of ChAdOx1 in Germany until mid-April). Thirty-seven of 45 cases of CVT had been reported after vaccination with ChAdOx1, and eight cases had been reported after BNT62b2. Of the nine ischemic strokes reported after vaccination, eight had occurred after vaccination with AstraZeneca, and one after administration of the BioNTech vaccine. The four cases of intracerebral hemorrhage had been observed after vaccination with ChAdOx1.

Three-quarters of all cerebral thrombotic events (75.8%) had occurred in women. Of the 45 people who had cerebral venous thrombosis after vaccination, 35 (77.8%) were female, 36 (80%) were under 60 years of age.

The team of professor Tobias Kurth, Director of the Institute of Public Health at Charité - Universitätsmedizin, a leading expert in neuroepidemiology, performed the statistical analysis of the data. The cases that occurred in the different groups were referenced to the total number of first vaccine shots administered in the different age, sex, and vaccine groups. In this way, it was possible to calculate the event rate per 100,000 person-years for each group. This measure also allows comparing the event rates with the spontaneous incidence of CVT, independent of vaccination.

In women under 60 years of age who had received vaccination with ChAdOx1, the event rate for CVT within one month from the first dose was 24.2/100,000 person-years, compared with 8.9/100,000 person-years for non-females of the same age, a significantly lower rate. Among those under 60 years of age who had received the BioNTech vaccine, the event rate was 3.6/100,000 person-years in females and 3.5/100,000 in non-females. Women over 60 years of age had a very low event rate of 0.8/100,000 person-years after vaccination with BioNTech, and there were no events in non-females over 60 years of age, regardless of the vaccine applied.

"Until this point, the data did not surprise us. However, we did see a new safety signal," explains professor Kurth. "The incidence rate of sinus and cerebral venous thrombosis in women under 60 after administration of the AstraZeneca vaccine was 24.2/100,000 person-years, and that of women over 60 after administration of the same vaccine was quite close with 20.5/100,000 person-years. Thus, our data indicate that older women are also at increased risk of sinus and cerebral venous thrombosis after administering the AstraZeneca vaccine. Whether this leads to a change in the recommendation for administering the AstraZeneca vaccine should be rapidly evaluated with the available data in a risk-benefit analysis."

What is the risk of thrombotic events after vaccination with the AstraZeneca vaccine ChAdOx1? After vaccination, vaccine-induced immunogenic thrombotic thrombocytopenia (VITT) may occur in very rare cases. The pathomechanism of this rare vaccine side effect is similar to heparin-induced thrombocytopenia (HIT) type II, in which antibody formation occurs against the complex of platelet factor 4 (PF4) and heparin. VITT was first described in a paper from the Institute of Immunology and Transfusion Medicine at the University of Greifswald [2], which was published in early April. When asked why VITT does not occur after vaccination with mRNA vaccines, professor Peter Berlit, Secretary General of the DGN, replied, "We suspect that the antibodies against PF4 do not cross-react with the spike protein of SARS-CoV-2, but that the vaccine complication is related to the adenoviral vector. This needs further investigation." In the present study, 57.8% of the reported cases of cerebral venous thrombosis could be attributed to such VITT with a very high probability by the clinicians. According to the findings, the same mechanism was probably present in five of nine patients with ischemic stroke and in two of the four cases of cerebral hemorrhage.

So, what can be drawn from the available data, and what do they mean for vaccination strategy?

"We think the AstraZeneca vaccine is associated with a very low risk of cerebral venous thrombosis in men. The rate was higher in women of all ages, but the event rate was still very low overall. When interpreting this, it must also be considered that the risk of venous thrombosis is increased in patients with a COVID-19 infection by a factor of 10. The disease relatively often leads to thrombotic

events resulting in death, while vaccination only very rarely does," said professor Diener, press spokesman for the DGN.

Professor Christian Gerloff, president of the DGN, continues: "The highest priority, especially in a situation with repeatedly emerging mutations of SARS-CoV-2, is to vaccinate the population as quickly as possible. From a global perspective, the benefits of the vaccines approved in Germany clearly outweigh the very low risks. But the safety signal that not only younger but also older women have an increased risk of thrombotic events after vaccination with the AstraZeneca vaccine is new and must be communicated transparently. Importantly, we are not questioning the global benefit of the AstraZeneca vaccine. Still, we propose that all individuals, especially women, be informed about this risk before vaccination and potential symptoms of CVT that they should be aware of after vaccination. Besides, the risk-benefit analysis should be updated by the regulatory authorities in due time."

Literature

[1] Schulz J, Berlit P, Diener H, Gerloff C, Greinacher A, Klein C, Petzold G, Poli S, Piccininni M, Kurth T Röhrig R, Steinmetz H, Thiele T. COVID-19 vaccine associated cerebrovascular events in Germany: a descriptive study. Preprint, <https://www.medrxiv.org/content/10.1101/2021.04.30.21256383v1>

[2] Greinacher A, Thiele T, Warkentin TE et al. Thrombotic Thrombocytopenia after ChAdOx1 nCov-19 Vaccination. N Engl J Med. 2021 April 9. <https://pubmed.ncbi.nlm.nih.gov/33835769/>

Pressekontakt

Pressestelle der Deutschen Gesellschaft für Neurologie

c/o Dr. Bettina Albers, albersconcept, Jakobstraße 38, 99423 Weimar

Tel.: +49 (0)36 43 77 64 23

Pressesprecher: Prof. Dr. med. Hans-Christoph Diener, Essen

E-Mail: presse@dgn.org

Die Deutsche Gesellschaft für Neurologie e.V. (DGN)

sieht sich als wissenschaftliche Fachgesellschaft in der gesellschaftlichen Verantwortung, mit ihren über 10.000 Mitgliedern die neurologische Krankenversorgung in Deutschland zu sichern und zu verbessern. Dafür fördert die DGN Wissenschaft und Forschung sowie Lehre, Fort- und Weiterbildung in der Neurologie. Sie beteiligt sich an der gesundheitspolitischen Diskussion. Die DGN wurde im Jahr 1907 in Dresden gegründet. Sitz der Geschäftsstelle ist Berlin. www.dgn.org

Präsident: Prof. Dr. med. Christian Gerloff

Stellvertretender Präsident: Prof. Dr. Gereon R. Fink

Past-Präsidentin: Prof. Dr. med. Christine Klein

Generalsekretär: Prof. Dr. Peter Berlit

Geschäftsführer: Dr. rer. nat. Thomas Thiekötter

Geschäftsstelle: Reinhardtstr. 27 C, 10117 Berlin, Tel.: +49 (0)30 531437930, E-Mail: info@dgn.org