Continuous headache post Covid

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- Unrestricted research grants from Medtronic and Boehringer Ingelheim
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Headache and other neurological symptoms in acute Covid infection

Onset of the first general COVID-19 symptom to the onset of neurological symptoms in the most frequently represented categories of manifestations.

García-Azorín, David et al. "Neurological presentations of COVID-19: Findings from the Spanish Society of Neurology neuroCOVID-19 registry." *Journal of the neurological sciences*vol. 423 (2021):



Headache with vaccine- and dose-specific headache pattern associated with vaccine against SARS-CoV-2 in patients with migraine





Kuan et al Cephalalgia 2023, Vol. 43(10) 1–10



Post-COVID-19 persistent headache

- A multicenter 9-M study from 6 different 3rd level hospitals 2020 with follow-up of 905 patients with headache in the acute phase
- Aim: evaluate the long-term duration of headache in patients that presented headache during the acute phase of COVID-19.
- Results:
 - median age 51, 67% female, 53% had a prior history of primary headache.
 - median duration of headache 14 (6-39) days
 - 6 months: 19% chronic daily headache
 - 9 months: 16% chronic daily headache
- Headache intensity during the acute phase was associated with a more prolonged duration of headache (Hazard ratio 0.66; 95% CI 0.58-0.74)



Protracted headache after COVID-19: A case series of 31 patients from a tertiary headache center

- 31 adults Stanford Headache Clinic 2022 with new or worsening headaches after COVID-19
- Results:
 - Headache duration of 7.4±4.8 months after infection
 - 81% had a **previous** history of **headache**
 - specific features of the headache varied considerably
 - 74% met ICHD-3 criteria for **migraine**, 65% chronic migraine
 - Only 16% met these criteria before COVID infection
 - Full-time employment decreased from 81% to 55%
 - 72% of the patients started on **preventive medications** reported effect

Moskatel LS, Smirnoff L. Headache. 2022 Jul;62(7):903-907.











Protracted headache after COVID-19: A case series of 31 patients from a tertiary headache center

- Conclusions:
 - patients with a history of migraine are at risk of converting from episodic to chronic migraine
 - Recognition of this risk may fall to primary care providers
 - Validation of the use of migraine preventive treatments in this patient group will also help guide future treatments for protracted headache after COVID-19 infection

Moskatel LS, Smirnoff L. Headache. 2022 Jul;62(7):903-907.











Headache onset after vaccination against SARS-CoV-2 a systematic literature review and meta-analysis.

- 84 papers, 1.57 million participants
- 94% BNT162b2 or ChAdOx1.
- Headache 3rd most common AE
- 22% after 1st vaccine dose
- 29% after 2nd vaccine dose
- No differences were detected across different vaccines
- onset <24 h in 1/3
- migraine-like features
- No information on persistent headadche

	N. of studies	Pooled headache incidence (95%CI)	Q (p-value)	l ²
All vaccines recipients, 1 st dose	84	22% (18–27%)	270,544.2 (p<.01)	100%
All vaccines recipients, 2 nd dose	46	29% (23–35%)	16,478.5 (p<.01)	100%
Placebo recipients, 1 st dose	21	10% (6–13%)	2203.7 (p<.01)	99%
Placebo recipients, 2 nd dose	10	12% (7–17%)	955.7 (ρ<.01)	99%
mRNA vaccine recipients, 1 st dose	43	22% (17–27%)	84,389.3 (p<.01)	100%
Traditional vaccine recipients, 1 st dose	54	23% (18–29%)	44,406.8 (p<.01)	100%
BNT162b2, 1 st dose	41	21% (16–27%)	82,671.2 (p<.01)	100%
BNT162b2, 2 nd dose	26	30% (23–38%)	6784.6 (p<.01)	100%
ChAdOx1, 1 st dose	19	53% (39–66%)	29,819.7 (p<.01)	100%
ChAdOx1, 2 nd dose	3	29% (11–51%)	5.4 (p=.07)	63%
mRNA-1273, 1 st dose	5	28% (10–51%)	64.4 (p<.01)	94%
mRNA-1273, 2 nd dose	3	54% (32–74%)	12.6 (p<.01)	84%
NVX-CoV2373, 1 st dose	3	25% (24–26%)	1.5 (p=.46)	0%
NVX-CoV2373, 2 nd dose	3	31% (18–47%)	80.9 (p<.01)	100%
PiCoVacc, 1 st dose	9	11% (5–19%)	1283.8 (p<.01)	100%

Table 3 Pooled rates and 95% CI for headache onset after injection against SARS-CoV-2

Castaldo M, et al. Headache onset after vaccination against SARS-CoV-2: a systematic literature review and meta-analysis. J Headache Pain. 2022 Mar 31;23(1):41.

Post-vaccination headache reporting: Trends according to the Vaccine Adverse Events Reporting System



Cocores AN, Goadsby PJ, Monteith TS. Headache. 2023

FIGURE 3 Patient ages, stratified by sex, for reports of an adverse event after vaccination in the Vaccine Adverse Events Reporting System from July 1990 until June 2020, for all symptoms (All) versus all headache (HA) reports. Of headache cases, there were 1280 (4.1%) reports with unknown age and 515 (1.7%) with unknown sex.











	Headache attributed to SARS-CoV-2-infection		Headache attributed to SARS-	
	Acute phase Covid-19	Post acute phase Covid-19	Cov-2-vaccination	
Prevalence	50%	31% after 1 M 16% after 9 M	40%	
Age	Most in young	Most in young	Most in young	
Sex	Both	Most female	Most female	
Previous headache	More common	No association with persistent headache at 9-M	More common	
Characteristics	Disabling in 50%	Episodic, chronic	Onset median at 10-14 days	









	Headache attributed to SARS-CoV-2-infection		Headache attributed to SARS-	
	Acute phase Covid-19	Post acute phase Covid-19	CoV-2-vaccination	
Phenotype	TTH most common Migraine	TTH most common Migraine	TTH most common Migraine	
Symptoms significantly associated w/headache	Anosmia-Ageusia	Fatigue, brain fog	Fatigue, fever, chills	
Presentation in patients with migraine	I 50% worse than usual migraine	Migraine chronification	I 50% worse than usual migraine	
Median duration	14 days inpatient Unknown outpatients	Unlikely to occur after 2 M	14-16 h Unknown in persistent ha	
Putative mechanisms	 Activation of trigeminovascular system by local or systemic inflammatory signals Direct viral damage? 	 Persistent activation of trigeminovascular system? Autoimmunue Activation of latent migraine 	 Fever, meningeal sensitisation by TNF-alfa Nocebo 	







12

UiO **: University of Oslo**



	Headache attributed to SARS-CoV-2-infection		Headache attributed to SARS-	
	Acute phase Covid-19	Post acute phase Covid-19	CoV-2-vaccination	
Acute treatment	 Up to 50% may not respond; Potential improvement with corticosteroids in 40% Response of GON in 85% of those unresponsive to paracetamol Response to indomethacin 	• Variable response to the use of triptans in patients with migraine-like phenotype	 NSAIDS (ibuprofen) and paracetamol most used acetylsalicylic acid among the best rated 	
Preventive treatment		 Unknown, potential benefit of AMT and variable response to BTX Avoid medication overuse 	• no data	
Etiologies	CVT, meningitis, encephalitis, intracranial hypertension	CVT (delayed), intracranial hypertension	CVT / VITT RCVS, aseptic meningitis	







Caronna E, et al Cephalalgia. 2023;43(1)



13

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Effect of COVID vaccination on monthly migraine days: a longitudinal cohort study



van der Arend BWH,. *Cephalalgia*. 2023;43(9). doi:<u>10.1177/033310242311987</u>











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New-onset headache following COVID-19: An Italian multicentre case series

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ARTICLE INFO

ABSTRACT

Objective: To describe the characteristics of patients with new-onset headache following SARS-CoV-2 infection. <i>Background:</i> SARS-CoV-2 infection leads to several neurological manifestations, and headache is a frequent and disabling symptom, both exacerbating pre-existing headache syndromes and causing new-onset ones. <i>Methods:</i> Patients with new-onset headache after SARS-CoV-2 infection with consent to participate were included, while those ones with previous headaches were excluded. The temporal latency of headache after infection, pain characteristics, and concomitant symptoms were analysed. Moreover, the efficacy of acute and preventive medications was explored. <i>Results:</i> Eleven females (median age 37.0 [10.0–60.0] years old) were included. In most cases, headache onset occurred with the infection, the location of pain varied, and the quality was either pulsating or tightening. Headache was persistent and daily in 8 patients (72.7%), while it occurred in episodes in the remaining subjects. Baseline diagnoses were new daily persistent headache (36.4%), probable migraine (9.1%), and migraine-like headache secondary to COVID-19 (18.2%). Ten patients received one or more preventive treatments and six of them showed an improvement. <i>Conclusion:</i> New-onset headache following COVID-19 is a heterogenous condition with uncertain pathogenesis. This type of headache can become persistent and severe, with a wide spectrum of manifestations (new daily
This type of headache can become persistent and severe, with a wide spectrum of manifestations (new daily persistent headache being the most represented one) and variable response to treatment.



Design:

Multi-center prospective observational study of neurological symptoms in COVID-19 positive patients.

Aims

to study the natural course and to characterize the longterm functional impairment of patients with neurological symptoms 6 and 12-M after COVID-19 infection. Substudy with neuropsychological and psychiatric assessments.

Substudy of headache 6 and 12-M after COVID-19 infection





New-onset severe headache after Covid-19 vaccine CovaxHEAD

<u>The main aim</u> of the project is to describe the characteristics of severe new-onset headache after Covid vaccine and the treatment effects.

Secondary aim:

- Investigate potential mechanisms and analyse biomarkers to predict treatment effects.
- To assess at baseline and 6-month follow-up the rate of brain MRI pathology.
- To assess the change xof brain ¹⁸F-FDG PET metabolism from baseline and 6-month follow-up.
- To assess the levels of brain specific biomarkers.
- To assess the level of blood specific biomarkers

REK 351097, NCT05235776 EudraCT number 2021-005210-34



Background

- March 2021: cases with vaccine-induced immune thrombotic thrombocytopenia (VITT)
- From April 2021 patients at the ward and headache clinic with newonset severe headache after different Covid-19 vaccines
- Both patients with and without a previous headache history



Den erfarne intensivsykepleieren fikk Astra Zeneca-vaksinen. Siden da har hun vært sykmeldt i et halvt år med kronisk hodepine.

Norge Koronaviruset

162 personer har meldt om vedvarende hodepine etter at de fikk Astra Zenecavaksine mot covid-19. En av dem er intensivsykepleier Marit Erika Tøien. Hun har anfall med sterk hodepine flere dager i uken. Nå søker hun om erstatning.





- Prospective observational multi-center study
- Flowchart clinical interview



<u>All participating centres</u> complete the clinical interview at baseline and 6-month follow-up (complete CRF) and analyse routine clinical blood samples and baseline MRI according to the study protocol.

Follow-up at 3-month intervals during the study is recommended in severly affected patients in need of regular follow-up. Data from each follow-up is registered in follow-up CRF.

In selected centres PET scan at baseline and 6-M follow-up, 6-month follow-up MRI scan and sampling for biomarkers will be done.



CovaxHEAD



Examination of the patients

- Clinical assessmentBlood samples
- CSF



¹⁸F-FDG PET/CT cerebrum





Conclusions

- Long-lasting headache occur in a subset of persons after Covid infection and Covid vaccine
- Migraine phenotype common
- Good experience with migraine prophylactic treatment
- More data from the Norwegian NeuroCOVID and CovaxHEAD study



Thank you for your attention!





Headache Clinic Oslo University Hospital

