

Reduced frequency of migraine attacks following COVID-19 disease

Roland Houben (✉ houben_r@ukw.de)

University Hospital Wurzburg: Universitätsklinikum Wurzburg <https://orcid.org/0000-0003-4538-2324>

Research Article

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Abstract

Introduction:

SARS-CoV-2 is a virus affecting different organs and causing a wide variety and severity of symptoms.

Case Presentation:

Here we report on a 57-year old male patient with chronic migraine and medication overuse headache who fell ill with COVID-19. For many years prior to his Sars-Cov2 infection he suffered from very frequent migraine attacks and for control of headache he had been taking triptans almost daily. In the 16-month period before outbreak of COVID-19 on 98% of the days triptans were taken with only a 21-day prednisolone-supported triptan holiday, which, however, had no longer-lasting consequences on migraine frequency. Upon Sars-Cov2 infection, the patient developed only mild symptoms including fever, fatigue and headache. Directly following recovery from COVID-19 the patient surprisingly experienced a period with largely reduced frequency and severity of migraine attacks. Indeed, during 80 days following COVID-19, migraine as well as triptan usage were restricted to only 25% of the days no more fulfilling criteria of chronic migraine and medication overuse headache.

Conclusion:

SARS-CoV-2 infection might be capable of triggering mitigation of migraine.

Introduction:

Coronavirus disease 2019 (COVID-19) is a life-threatening condition caused by the severe-acute-respiratory-syndrome-corona-virus-2 (SARS-CoV-2) and affected patients present with a wide variety of symptoms [1]. In this respect, also a multitude of neurological manifestations of COVID-19 have been reported [2–4]. While these were generally pathological complications associated with the disease, we here report on a 57-year old male patient who experienced a beneficial neurological effect, evident directly following his SARS-CoV-2 infection.

Case Presentation:

His medical history revealed that he suffered from migraine with aura for almost 40 years. The individual attacks typically persisted between 8 and 16 hours and, when left untreated, the pain severely affected the patient's ability to participate in daily life. While in the early phase of his disease no effective treatment could be established, headache became better controllable after the advent of the triptans [5]. The patient applied sumatriptan in early years and later zolmitriptan (requiring prescription) for very heavy attacks and naratriptan (available as OTC drug in Germany) for less severe migraine. However, while migraine attacks occurred before triptan therapy approximately every 5 days, the frequency increased since triptans were applied finally resulting in almost daily migraine and as a consequence

almost daily triptan usage. Approximately since 2003 the patient fulfilled the criteria of medication overuse headache, i.e. (i) headache present on more than 15 days/month, (ii) regular overuse of a symptomatic treatment (> 10 days per month for triptans) for more than three months and (iii) markedly worsened headache during medication overuse [6, 7]. Throughout his adult life, the patient was treated with several prophylactic therapies including beta-blockers, tricyclic antidepressants, topiramate, acupuncture, neural- and psychotherapy as well as dietary changes and relaxation techniques. Out of these measures topiramate was most effective, significantly reducing migraine frequency. However, this outcome was transient and several started therapies always ended with discontinuation of topiramate treatment due to return of daily migraine and triptan usage after a few month or weeks. In combination with topiramate but also with other prophylactic therapies, the patient had - over a period of 13 years - in total seven prednisolone-supported drug holidays from triptans. However, long-lasting effects on migraine frequency and reduction of triptan overuse could never be achieved, particularly not in recent years.

In December 2020, the patient had extended contact to a SARS-CoV-2 positive person, developed COVID-19 symptoms and two positive SARS-CoV-2 PCR tests confirmed the infection. The course of his COVID was mild, with fever, fatigue and headache, as well as weak respiratory symptoms. Headache was bilateral but developed every day into a unilateral migraine attack. However, after approximately 20 days, the patient not only felt as if he had completely recovered from COVID-19 but surprisingly also experienced thereafter 24 days with only three migraine attacks. This was unprecedented and with the exception of periods of high-dose corticosteroid treatment had - according to the patient's memory and his written migraine diary - not occurred in the previous 15 years. Reduced frequency of migraine attacks and triptan usage compared to the pre-COVID-19 phase persisted for 80 days (Fig. 1). Only 20 migraine attacks and 20 days with triptan usage, respectively, during this period (25% of the days) imply that the patient neither fulfilled the criteria for chronic migraine nor for medication overuse headache during this time. Almost as sudden, as the period with reduced migraine had started it ended with a return to almost daily migraine (Fig. 1).

Conclusions:

Prevalence of chronic migraine depends on age. The American migraine prevalence and prevention study revealed that for males a prevalence maximum of 0.79% is reached between 40 and 50 years and that prevalence drops to 0.26% for men above 60 [8]. This may imply that spontaneous regression of the disease is not a very unlikely event for a 57-year old man and it cannot be excluded that the observed reduced migraine attacks in the reported case are not related to the SARS-CoV-2 infection. Nonetheless, the very strict chronological association of the two events, the rapid and significant reduction of headache episodes as well as the transient nature of phenomenon, suggest that the mitigation of chronic migraine was triggered by COVID-19. It will be interesting to study whether other migraine patients experienced similar effects following SARS-CoV-2 infection.

Attempts to explain how SARS-CoV-2 triggered migraine mitigation might be mediated mechanistically can only be highly speculative because we have only little knowledge on the interaction of SARS-CoV-2

with the nervous system [9] and even the molecular pathology of migraine is not completely understood [10]. However, a possible convergence point could be the blood-brain barrier, which has been suggested to be affected during the headache attack of migraine patients [11]. On the other hand using brain organoid models it has been shown that SARS-CoV-2 can damage the choroid plexus epithelium [12]. Therefore, it may be speculated that during repair of virus-induced blood brain barrier damage a migraine-suppressing environment might be produced.

Declarations:

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- ii. **Conflict of interest:** The author declares no conflict of interest.
- iii. **Ethics approval:** Not applicable
- iv. **Consent to participate:** Not applicable
- v. **Consent to publication:** The patient gave written consent for publishing this case report.
- vi. **Availability of data and material:** All data are included in the publication.
- vii. **Code availability:** Not applicable
- viii. **Author's contribution:** RH wrote the manuscript about himself.

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Figures

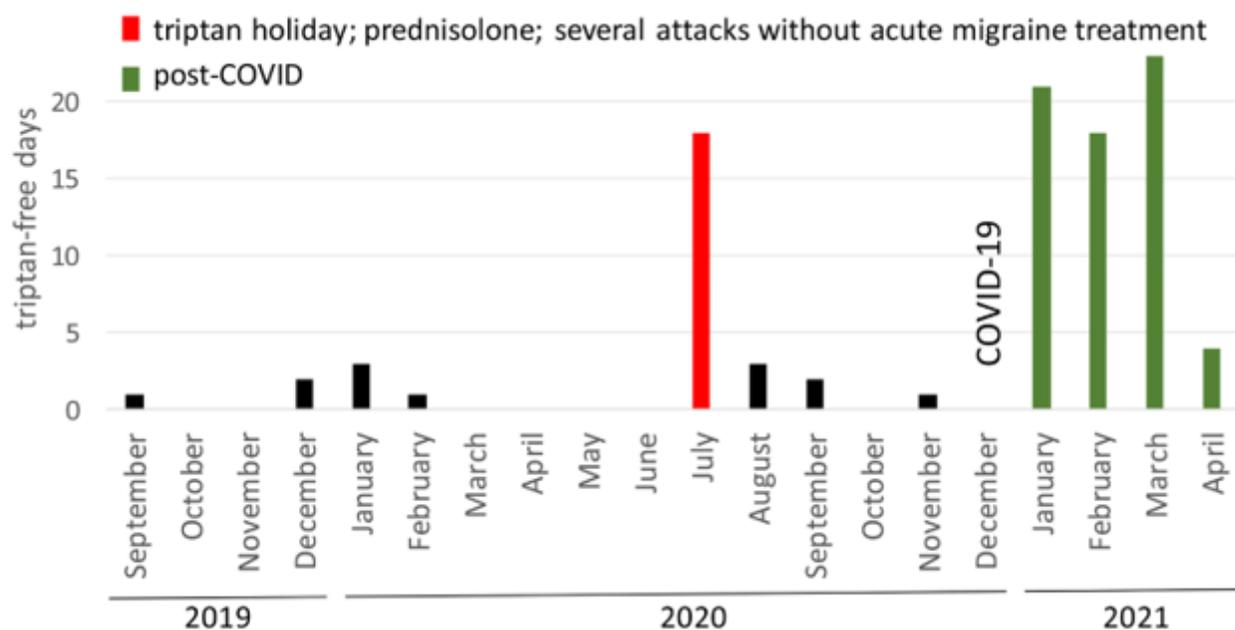


Figure 1

Dramatic increase in triptan-free days directly following COVID-19 disease. Displayed is the number of days per month without triptan consumption from September 2019 to April 2021 based on the recordings of the patient. The number of migraine-free days was identical to the depicted triptan-free days with the

exception of July 2020, when the 57-year old patient experienced 4 migraine attacks without triptan intervention during a drug holiday associated with 12 days of prednisolone treatment (100 mg on the first two days and stepwise reduction to 10 mg on the last two days). The first SARS-CoV-2-positive PCR test was on December 21, 2020. The patient had COVID-19 symptoms until January 4, 2021 and a period of 80 days with only 20 migraine attacks started on January 7, 2021. Starting on 28th of March the patient returned to having almost daily migraine attacks.