

SLEEP-WAKE DISORDERS AFTER TBE

Background

After the acute phase of TBE, up to 50% of patients develop neurologic and neuropsychological sequelae, among which are headache, cognitive and neuropsychiatric disturbances (e.g., apathy, irritability, memory, and concentration disorders), hearing loss, vision disturbances, balance and coordination disorders, flaccid paresis, and paralysis. Sleep-wake and circadian disorders (SWCD) have often anecdotally been reported, but the extent thereof and how long they persist is unknown. The current knowledge about SWCD caused by TBE has been reviewed and has been analyzed in infant rats experimentally infected with Langkat virus.

Results

A systematic literature search has been done using the terms „tick-borne encephalitis“ AND „sleep disorders“ OR „sleep disturbances“ and among 187 identified references, 15 studies which fulfilled a standardized quality assessment, were included in a review. The term SWCD is poorly defined, and phenomenon analyzed in the literature consist of sleep-wake disorders/sleep disorders or disturbances, fatigue, excessive daytime sleepiness, hypersomnia, circadian rhythm disorders, insomnia, sleepiness/somnolence and restlessness. The literature search suggested that SWCD after TBE is under-investigated and likely underreported, and the publications often do not have a high quality.

The clinical burden of SWCD after TBE impairs the quality of life. However, the true prevalence of SWCD is difficult to assess from data in the literature, since very few studies have used a long-term prospective design or a standardized measurement tool at different observation periods after TBE.

Most studies assessed symptoms in the acute phase of illness.

In children, SWCD persisted in up to one-third of subjects for 12 months or more. Fatigue was significantly more pronounced after TBE compared to children with neuroborreliosis or to other pediatric infections. The same trend was seen for SWCD after TBE in adults.

The mechanisms causing SWCD after TBE are largely unknown and the pathology of TBE virus-induced sleep dysfunctions have been analyzed in an infant rat model, in which animals were infected by the Langkat virus (this virus belongs to the TBE virus complex. it is naturally attenuated and causes no disease in humans, nor in rodents, but can induce encephalitis in laboratory rats after intracerebrally infection).

In infected infant rats, some chemokines, cytokines and Neurofilament light chain were assessed in the CSF, and the concentrations were significantly higher (e.g., IL-6 and IFN- γ) compared to control animals at day 4, 9, and 21 pi.

Examination of the general locomotor activity was assessed by total walking distance, and infected animals moved less than control animals, and infected animals had a reduced willingness to explore new environment.

Infected animals spent significantly more time awake than controls during the total light period and during the dark period, and during the dark period were less time in NREM and REM sleep. Infected animals also had a lower number of state changes, and the duration of a wake period in the dark phase was elongated.

Discussion

The experimental model revealed clear changes in the sleep macrostructure which were measured with objective parameters compared to a matched control group under identical conditions. Therefore, this study gave an indication that SWCD could be a result of the virus infection and

were not caused by changes of the TBE patient's circumstances. Infected animals also had a reduction in motor coordination and spontaneous locomotion as well as anxiety-like behavior.

The literature review and the experimental data warrant additional clinical and experimental research conducted by interdisciplinary teams to understand the frequency and the impact of sleep-wake disorders caused by TBE virus infections.

Literature

Chiffi et al.

Sleep-wake and circadian disorders after tick-borne encephalitis

Microorganisms 2022, 10, 304, doi.org/10.3390

Chiffi et al.

Tick-borne encephalitis affects sleep-wake behavior and location in infant rats

Cell Biosc. 2022. 12:121, doi.org/10.1186/s3578-022-00859-7

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Compiled: September 2022
