Letter to the Editor

Induced Hypoglossal Dysfunction as a Cause of Obstructive Sleep Apnea in Mefloquine-Exposed Veterans

Dear Editor:

I read with interest the recent study by Sarber and colleagues,1 in which they demonstrated the effectiveness of hypoglossal nerve stimulation in veterans with obstructive sleep apnea. Although strongly limited by sample size, the authors found suggestive evidence of increased effectiveness among veterans with comorbid mental health conditions.

It is not clear how many of the veterans in the authors’ study may have been exposed to mefloquine, a neurotoxic antimalarial drug of the quinoline class that has been widely used among military personnel during deployments over the past quarter century.

Unmeasured exposure to mefloquine may be the cause of several of the comorbid mental health conditions observed in the authors’ analysis, including anxiety, depression, and symptoms that may be attributed to posttraumatic stress disorder (PTSD). For example, military authors have noted that “the significant overlap in symptoms associated with mefloquine toxicity and [PTSD] obscures the distinction between these diagnoses.”

Antimalarial quinolines related to mefloquine have been found to induce focal neurotoxic injury to various brainstem nuclei,3 including to the hypoglossal nucleus and the vestibular nuclei.4 Exposure to mefloquine specifically has been associated with development of central vestibulopathy, consistent with lasting dysfunction of the vestibular nuclei.2,5 It is thus tempting to speculate that exposure to mefloquine may induce a similar lasting dysfunction of the hypoglossal nucleus, with resultant loss of tone in the genioglossus. Such a mechanism would be consistent with a postulated cause of obstructive sleep apnea,6 for which hypoglossal nerve stimulation might be expected to be particularly effective.

Unmeasured mefloquine exposure has been identified as a concern in the interpretation of recent studies of sleep disorders among veterans.7 Researchers conducting such studies should measure prior symptomatic mefloquine exposure among their subjects8 and consider the effects of such exposure in their analysis. Our group has developed the two-question White River Mefloquine Instrument (WRMI-2) to assist clinicians and researchers in assessing such exposure in a standardized manner.9

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BIBLIOGRAPHY


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