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Q: What is vagus nerve stimulation?

A: Originally approved for the treatment of epilepsy, vagus nerve stimulation (VNS) is a U.S. Food and Drug Administration-approved intervention for treatment-resistant depression, indicated for “the adjunctive, long-term treatment of chronic or recurrent depression for patients 18 or older who are experiencing a major depressive episode and have not had an adequate response to four or more adequate antidepressant treatments” (U.S. Food & Drug Administration, 2005). VNS involves indirect stimulation of neural networks via the vagus nerve, one of the cranial nerves. VNS often involves an invasive procedure wherein a pulse generator (similar to a pacemaker) is implanted below the skin in the patient’s chest and connected to the left vagus nerve in the neck via an electrical lead (VA/DoD, 2022). Following implantation, the pulse generator is controlled by a computer, and is programmed to periodically send electrical impulses 24 hours a day (typically for 30 seconds every five minutes), usually for a 10-week period.

Q: What are the potential mechanisms of action underlying VNS?

A: VNS was first considered as a treatment for major depressive disorder (MDD) based on clinical observations of improved mood and cognition in studies of VNS for epilepsy (Rush et al., 2000). It has been hypothesized that stimulation of the vagus nerve alters neurotransmitter levels and modulates activity of brain regions (Rush et al., 2005). VNS has been shown to alter concentrations of neurotransmitters in the cerebrospinal fluid of epilepsy patients (Carpenter et al., 2004) and has been shown to modulate the functional activity of regions of the brain in neuroimaging studies (Chae et al., 2003). However, the mechanisms of action of VNS are still unclear.

Q: Is VNS recommended as a treatment for MDD in the Military Health System (MHS)?

A: No. The 2022 VA/DoD Clinical Practice Guideline for the Management of Major Depressive Disorder gives a “weak against” recommendation for VNS for patients with MDD, including patients with severe treatment-resistant depression, outside of a research setting. This guideline is based on the lack of evidence of efficacy, the presence of safety concerns, and concerns about the associated costs.

The MHS relies on the VA/DoD clinical practice guidelines (CPGs) to inform best clinical practices. The CPGs are developed under the purview of clinical experts and are derived through a transparent and systematic approach that includes, but is not limited to, systematic reviews of the literature on a given topic and development of recommendations using a graded system that takes into account the overall quality of the evidence and the magnitude of the net benefit of the recommendation. Recommendations for or against a treatment may be characterized as strong or weak based on a variety of factors (e.g., confidence in the quality of the evidence, weight of treatment benefits versus risks, feasibility). The CPGs also state if there is insufficient evidence to develop a recommendation. A further description of this process and CPGs on specific topics can be found on the VA clinical practice guidelines website.

Q: Do other authoritative reviews recommend VNS as a treatment for MDD?

A: No. Other authoritative reviews have not substantiated the use of VNS for MDD.

Other recognized organizations conduct systematic reviews and evidence syntheses on psychological health topics using grading systems similar to the VA/DoD CPGs. Notable among these is Cochrane, an international network that conducts high-quality reviews of healthcare interventions.

- Cochrane: No systematic reviews of VNS for depression were identified.

Q: What conclusions can be drawn about the use of VNS as a treatment for MDD in the MHS?

A: The 2022 VA/DoD Clinical Practice Guideline for the Management of Major Depressive Disorder suggests against the use of VNS for the treatment of MDD due to the potential benefits of VNS being outweighed by the harms and burdens. For additional guidance on selecting a treatment for MDD, please visit the PHCoE Clinician Resources section of the intranet and navigate to clinical support tools.

References

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