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Vagus Nerve Stimulation in the treatment of Epilepsy: Our initial experience

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Abstract

Introduction: Vagus nerve stimulation (VNS) is a neuromodulation therapy used to treat intractable seizures that do not respond adequately to antiepileptic drugs. The therapy involves implanting a device that delivers electrical impulses to the vagus nerve, potentially reducing seizure frequency and severity. While initially approved for partial epilepsy, VNS is now being explored for various seizure disorders, including generalized epilepsy and Lennox-Gastaut syndrome.

Material and Methods: Two patients with intractable epilepsy were treated with VNS therapy. The VNS device was surgically implanted and programmed with a current charge of 0.5 mA, a pulse width of 250 microseconds, a pulse frequency of 20 Hz, and an on/off duty cycle of 10 seconds/10 minutes. Both patients were followed up after surgery to monitor seizure frequency and any complications.

Results: In the first case, a 15-year-old boy experienced complete seizure cessation within 8 weeks post-VNS implantation. In the second case, a 20-year-old boy initially experienced an increase in seizure frequency, but after adjusting the current charge, his seizures were controlled. Both cases highlight the positive outcomes of VNS, although individual response and device adjustments may vary.

Conclusion: Our initial experience with VNS therapy in treating intractable epilepsy shows promising results. While the number of cases is limited, VNS appears to be an effective option for seizure reduction. However, the high cost of the device limits its accessibility. Governmental assistance is needed to make this therapy available to more patients.

Introduction:

Vagus nerve stimulation (VNS) is a neuromodulation therapy which is used to treat intractable seizures not responding well with antiepileptic drugs.This procedure involves the implantation of a device that delivers electrical impulses to the vagus nerve, which in turn modulates neural activity in the brain, potentially reducing the frequency and severity of seizures. Vagal nerve stimulation (VNS) was first approved for treating partial epilepsy but is now showing promise for various seizure disorders, including generalized epilepsy and Lennox-Gastaut syndrome. The exact mechanism of this device is unclear, but it is believed to work at multiple levels, initially by desynchronizing brain activity. Implanting the VNS device is generally safe, with infection being the most common complication. Vocal cord paralysis is the primary neurological issue post-implantation,alongside transient effects like hoarseness, cough, and nausea, which typically don't require stopping treatment.

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Methods of stimulating Vagus Nerve:

Vagus nerve stimulation (VNS) is a well-established therapy for epilepsy since long time, particularly for individuals who haven't responded well to anti epileptic drugs alone. There are many ways known to stimulate the vagus nerve in epilepsy treatment:

1. Vagus Nerve Stimulation (VNS) Implant: This involves surgically implanting a device under the skin in the neck and chest area,usually on the left side, since the right vagus nerve supplies the sinoatrial node. The device is connected to the vagus nerve in the neck via a lead wire. It delivers regular electrical impulses to the nerve, helping to reduce seizure frequency and severity. The settings of the device can be adjusted by a healthcare professional based on the individual's needs.[1]
2. Transcutaneous Vagus Nerve Stimulation (tVNS): This is non invasive method of stimulating vagus nerve. It involves applying electrical stimulation to the vagus nerve through the skin, typically via electrodes placed on the earlobe or another part of the body. Research has shown promising results in reducing seizure frequency and improving seizure control in some individuals with epilepsy.[2]

3. Vagus Nerve Stimulation During Seizures: Some research suggests that delivering vagus nerve stimulation specifically during a seizure may help abort the seizure or reduce its duration and intensity. This approach requires real-time detection of seizure activity, often achieved through responsive neurostimulation devices or similar technologies.[3]

4. Focused Ultrasound: Focused ultrasound is an emerging technique that allows non-invasive stimulation of deep brain structures, including the vagus nerve. This method has shown potential in preclinical studies for the treatment of epilepsy. By targeting specific areas of the vagus nerve, researchers aim to modulate its activity to reduce seizure occurrence.

5. Physical Exercise and Rehabilitation: Certain physical activities, such as aerobic exercise, have been shown to increase vagal tone, which may have a beneficial effect on seizure control. While exercise itself doesn't directly stimulate the vagus nerve, it can indirectly modulate its activity through autonomic nervous system regulation.[4]

Mechanism of action:

The mechanism of action of vagus nerve stimulation (VNS) in epilepsy involves several complex pathways that ultimately modulate brain activity to reduce seizure occurrence.

1. Modulation of Neurotransmitters: VNS influences neurotransmitter systems within the brain, such as increasing the release of gamma-aminobutyric acid (GABA), which is an inhibitory neurotransmitter. GABA helps to reduce the excitability of neurons, which can help prevent the spread of abnormal electrical activity associated with seizures.

2. Neuromodulation of Limbic System: The vagus nerve has extensive connections to key areas of the limbic system, including the hippocampus and amygdala, which are involved in seizure generation and propagation. VNS may modulate activity within these structures, thereby reducing seizure frequency and severity.[5]

3. Brainstem Modulation: The vagus nerve sends signals to the brainstem, which plays a crucial role in regulating autonomic functions and modulating cortical excitability. By stimulating the vagus nerve, VNS may exert effects on brainstem nuclei, leading to changes in overall brain activity and reducing the likelihood of seizure initiation.[6]

4. Anti-Inflammatory Effects: VNS has been shown to have anti-inflammatory effects by suppressing the release of pro-inflammatory cytokines and modulating immune responses. Inflammation is believed to contribute to the development and progression of epilepsy, and reducing inflammation may help to stabilize neuronal excitability and prevent seizures.

5. Neuroplasticity and Synaptic Remodeling: Chronic VNS has been associated with changes in synaptic plasticity and remodeling of neural circuits involved in seizure generation. By promoting neuroplasticity, VNS may help to reorganize aberrant neural networks and reduce hyperexcitability, leading to improved seizure control over time.[5]

6. Autonomic Nervous System Modulation: The vagus nerve is a major component of the autonomic nervous system, which regulates bodily functions such as heart rate, blood pressure, and respiratory rate. VNS may exert its antiepileptic effects by modulating autonomic function, leading to changes in cortical excitability and seizure threshold.[7]

Surgical Procedure:

Surgery is done under general anesthesia .

Surgery is performed under general anesthesia. The patient is positioned supine with the head turned slightly to the right to provide better access to the left side of the neck and chestFigure1.

Figure 1.Incision:Left side of the neck

After proper positioning, cleaning, and draping, the left side of the neck and chest are exposed.

First, an incision is made in the neck, about 2-3 cm above and anterior to the sternocleidomastoid muscle. The skin, subcutaneous tissue, and platysma are dissected. Blunt dissection is carried out to expose the carotid sheath, and then the left vagus nerve is identified and isolated Figure2.

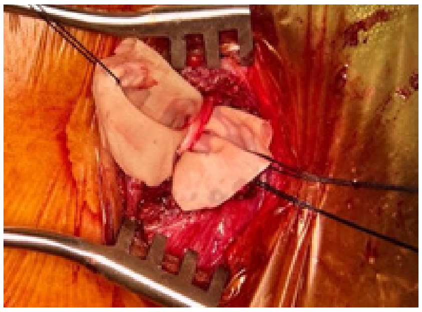

Figure 2. Vagus Nerve Identification

Care is taken to avoid damaging surrounding structures such as the carotid artery and jugular vein.

Another horizontal incision is made at the infraclavicular area using blunt dissection, a subcutaneous pocket is created where the pulse generator (the VNS device Figure3)

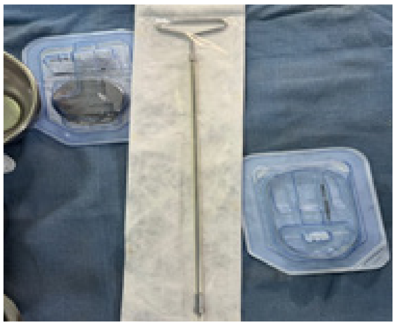

Figure 3.VNS Implant with Subcutaneous Tunnelling Trocar

will be housed. This pocket is typically situated between the pectoral muscles and the subcutaneous tissue.

The lead Figure 3,4, which consists of a pair of electrodes, is wrapped around the exposed vagus nerve Figure 6 . This is done using a helical design where the electrodes spiral around the nerve to ensure stable contact. Finally, the lead is secured in one of the muscle using non-absorbable sutures or ties to prevent movement. This ensures the electrodes remain in the correct position around the vagus nerve.Once electrode is secured , a subcutaneous tunnel is created from the neck incision to the chest pocket Figure 5. This is done using a tunneling instrument to create a pathway under the skin for the lead.

The lead is carefully threaded through the subcutaneous tunnel, connecting the electrodes around the vagus nerve to the pulse generator in the chest which later is connected to the pulse generator and is placed into the subcutaneous pocket created earlier in the chest Figure7.

Before closing the incisions, the device is tested to confirm proper electrical contact and
functionality. This is done using an external programming device Figure 8 .After the confirmation of its function, both wounds are closed in layers.

Complications:
Complications can be broadly classify in two groups: Surgical and Hardware complications.Complicatiions related to surgery consists of postoperative hematoma,infection,vocal cord palsy,lower facial weakness, pain and sensory related complications etc.Hardware related complications are fracture malfunction of the electrode,spontaneous VNS turn on and lead disconnection.

Case 1.
A 15-year-old schoolboy had been experiencing intractable seizures and had been on multiple anti-epileptic drugs for 8 years. His seizure frequency was 3-7 episodes per month. Imaging was essentially normal. Vagal nerve stimulation was performed with a programmed current charge of 0.5 mA, a pulse width of 250 microseconds, a pulse frequency of 20 Hz, and an on/off duty cycle of 10 seconds/10 minutes. At an 8-week follow-up, the boy had not had any episodes of seizures (Engels ClassI).
Case 2.
A 20-year-old schoolboy had been experiencing intractable seizures, sometimes monthly and sometimes 2-3 episodes daily, and had been on multiple anti-epileptic drugs since he was 2 years old. Imaging was essentially normal. Vagal nerve stimulation was performed, initially programmed with a current charge of 0.5 mA, a pulse width of 250 microseconds, a pulse frequency of 20 Hz, and an on/off duty cycle of 10 seconds/10 minutes. After the initial programming, the patient experienced an increased frequency of seizures but of shorter duration compared to his previous episodes. Consequently, his current charge was increased to 0.5 mA. Following this adjustment, his seizures were controlled(Engels Class II).
Conclusion:While cases of vagus nerve stimulation(VNS) for intractable epilepsy are currently limited, the initial results are encouraging.However,a significant disadvantage is the high cost of the device,which restricts its use for many patients in need. It is imperative to advocate for governmental assistance to make VNS devices more affordable and accessible.

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