Case Report

Vagus Nerve Stimulation for Medically Refractory Epilepsy in Children with Brain Malformations

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Abstract

Vagal nerve stimulation is approved for medically refractory partial epilepsy in children older than 12 years of age. However, it has been shown in the literature that vagal nerve stimulation is also quite efficacious in children younger than 12 with generalized epilepsy and brain malformations. We report a case series of children younger than 12 who responded well to vagal nerve stimulation. A retrospective review was conducted at our institution for pediatric patients from 1997 to 2013 who were younger than 12 years of age and had pharmacoresistant epilepsy and brain anomalies resulting in static encephalopathy. Our institution's institutional review board approved the study. Three patients were identified who received vagal nerve stimulator were between 6-9 years of age. Two of these patients were diagnosed with generalized epilepsy and one with Lennox-Gastaut syndrome. The etiologies included lissencephaly, cortical dysplasias and asymmetry of the cerebral hemispheres, respectively. They were taking an average of 2-3 anticonvulsants and had failed treatment with at least 2 anticonvulsants. The patients showed marked decrease in the seizure frequency during the 6-month and 1-year follow-up. Vagal nerve stimulation was found to be efficacious in this subgroup of difficult pediatric patients with pharmacoresistant generalized epilepsy and epileptic encephalopathy.

ABBREVIATIONS

AED: Antiepileptic Drugs; VNS: Vagal Nerve Stimulation; MRI: Magnetic Resonance Imaging; EEG: Electroencephalogram

INTRODUCTION

Epilepsy is worldwide problem effecting millions of children and contributing to significantly increased risk of morbidity and mortality [1]. In children diagnosed with epilepsy, 60-70% become seizure free with antiepileptic drugs (AEDs) as monotherapy, leaving 30-40% of children with long-term refractory and difficult to manage epilepsy that may not be responsive to multiple AEDs [1]. Additionally, increasing numbers and dosages of AED’s can cause significant side effects, especially in children. Vagal nerve stimulation (VNS) has been approved for medically refractory partial epilepsy in patients 12 years and older since 1997. Since its introduction, VNS has become a popular method in reducing seizure frequency. However, it has been shown in the literature that vagal nerve stimulation is quite efficacious in children younger than 12 with generalized epilepsy and brain malformations [2]. Not only does VNS implantation seem to help immediately after implant, it also seems to have a cumulative effect over time with some patients becoming seizure free [2]. Colicchio et al showed that an earlier age of implantation (< 6 years) and shorter duration of epilepsy prior to implant had improved positive clinical outcome [3]. Given that maintaining good seizure control can improve long-term potential lessening the developmental, cognitive, and behavioral complications, our age group of interest (< 12 years) could gain significantly from this method of treatment. We report a case series of children younger than 12 years of age who responded well to vagal nerve stimulation.
METHODS

A retrospective review was conducted at our institution for pediatric patients from 1997 to 2013 who were younger than 12 years of age and had been diagnosed with pharmacoresistant epilepsy and brain anomalies resulting in static encephalopathy. The study was approved by our hospital's institutional review board. The variables included epilepsy type, current anticonvulsants, failed anticonvulsant, epilepsy type, imaging data, other comorbidities and effect of vagal nerve stimulation on seizure frequency.

RESULTS

Three patients were identified who received vagal nerve stimulator between the ages of 6-9 years. Two of these patients were diagnosed with generalized epilepsy and one was diagnosed with Lennox-Gastaut syndrome. The etiologies included lissencephaly, cortical dysplasias and asymmetry of the cerebral hemispheres, respectively. They were taking an average of 2-3 anticonvulsants and had failed treatment with at least 2 anticonvulsants. The patients showed a marked decrease in seizure frequency during the 6-month and 1-year follow-up.

CASE SERIES

Case 1

Our first case is of a boy with refractory generalized epilepsy hypotonia, microcephaly, and severe static encephalopathy. He experienced seizure onset at the age of 2 years. An Electroencephalogram (EEG) showed diffuse polyspike and wave discharges. A magnetic resonance imaging (MRI) of the brain revealed Type 1 lissencephaly with pachygyria in the frontal and occipital lobes and agyria in parietal regions (Figure 1). The seizures frequency ranged from 5-6 seizures on divalproex sodium, zonisamide and levetricateam polytherapy. The vagal nerve stimulator was implanted when he was 9 years old. The seizures frequency improved after 2-3 months to occasional clusters. Adjunctive therapy included divalproex sodium and zonegran.

Case 2

Our second case was also of a boy with refractory generalized epilepsy optic nerve dysplasia, hearing loss, septo-optic dysplasia and static encephalopathy. His seizure onset was at the age 6 years. An EEG showed diffuse polyspike and wave discharges. A MRI revealed hypoplastic optic nerves, with a small focus of heterotopic gray matter adjacent to right frontal horn, and a right choroidal fissure arachnoid cyst cortical dysplasia and neuronal migration disorder (Figure 2). He was intractable on divalproex sodium, zonisamide and levetricateam polytherapy and had failed phenytoin. The vagal nerve stimulator was implanted when he was 9 years old. The seizures frequency improved after 3 months, with occasional breakthrough seizures every 2-3 years. Adjunctive therapy included divalproex sodium and lamotrigine.

Case 3

Our third case is of a girl with Lennox-Gastaut syndrome, static encephalopathy, left hemiatrophy, spastic left hemiplegia, and deafness. She was 4 years old when she experienced seizure onset. The EEG showed slow spike and wave discharges consistent with Lennox-Gastaut syndrome. An MRI revealed asymmetry in the size of the hemispheres and decrease size of the right cerebral hemisphere (Figure 3).

She had absence seizures -- 10 to 20 times per day and generalized tonic/clonic episodes - 3 times per month on divalproex sodium and zarontin polytherapy. The vagal nerve stimulator was implanted when she was 6 years old. This patient became seizure free, except for occasional breakthrough after VNS implantation. Her adjunctive therapy included levetiracetam, lamotrigine or ethosuximide.

DISCUSSION

VNS was found to be efficacious in this subgroup of difficult
pediatric patients with pharmaco-resistant generalized epilepsy and epileptic encephalopathy.

This 3 case series showed improvement in children with multi-drug-resistant generalized epilepsy and brain malformations with implantation of vagal nerve stimulation. Not only did these children have clear improvement in their seizure activity, 2 of them became nearly seizure free. Additionally, in 2 of the cases, the total numbers of AED therapy were reduced from 3 drugs to 2 after implantation. There has been little research so far of VNS implantation in children younger than 12 since the device was first approved in 1997, as this age group was not included in the original study and indication for the device. Nevertheless, studies conducted to date have shown great promise (4-11). Considering the improved developmental outcomes that could possibly be addressed by stopping, or at least considerably reducing, seizure frequency in this younger age group, further research is warranted.

REFERENCES


