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Vagus nerve stimulation for refractory idiopathic generalised epilepsy

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We reviewed our experience with vagus nerve stimulation (VNS) in 165 patients with medically refractory epilepsy (138 partial epilepsy (PE), 13 symptomatic generalised epilepsy (SGE), 14 idiopathic generalised epilepsy (IGE)). Average duration of VNS therapy was 21.6 months. A 50% or greater reduction in seizure frequency was achieved in 47.1% of the PE group, 46.1% of the SGE group, and 57.1% of the IGE group. A 50% or greater reduction in seizure frequency and reduced antiepileptic drug (AED) regimen were achieved in: PE (9.4%), SGE (7.7%), and IGE (35.7%). These preliminary results suggest that VNS is an effective therapy for some patients with medically refractory IGE.

Key words: intractable seizures; vagus nerve stimulation; generalised epilepsy.

INTRODUCTION

Vagus nerve stimulation (VNS) is a palliative treatment for medically refractory epilepsy in patients over 12 years of age with partial onset seizures[1]. Off-label use of VNS has included children ages nine months and older[2], as well as idiopathic and symptomatic generalised epilepsies (SGEs)[3]. Controlled data are not available for these off-label uses.

Labar *et al*. found that VNS was effective in a study of 24 patients, aged 4 years and older, with medication-resistant generalised epilepsy[4]. Short-term efficacy during a three-month period was compared to a one-month baseline period with stable antiepileptic drug (AED) therapy. Median reduction in seizure frequency was 46%, suggesting that VNS was an effective treatment for medication resistant generalised epilepsy.

We studied VNS treatment for a longer period in 14 patients with idiopathic generalised epilepsy (IGE) and compared them to results in 151 patients with partial epilepsy (PE) and SGE, examining seizure control and changes in AED therapy after implantation.

METHODS

We evaluated the results of VNS in patients implanted between 1994 and 2000 at the NYU Comprehensive Epilepsy Center. Data was gathered via systematic review of medical records. All patients were diagnosed with medically refractory epilepsy, and were implanted with a VNS. A baseline of three months was established, and patients were followed for a minimum of three months. We evaluated the reduction in seizure frequency in this cohort, as well as change in AED regimen after VNS implantation. Seizure type and epilepsy syndrome were defined using the International League Against Epilepsy criteria[5].

To identify patients with an excellent response to VNS therapy, we used stricter criteria for 'responders'. Responders were defined as having a 50% or greater reduction in seizure frequency and a concurrent reduction in medication regimen. Non-responders were defined as meeting at least one of these criteria: (1) less than 50% reduction in seizure frequency; or (2) no change or increase in AED regimen. Reduction in medication regimen was defined as any of the following: (1) decrease in dosage of AED regimen;

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(2) decrease in number of AEDs; (3) both; or (4) termination of all AEDs.

RESULTS

VNS were implanted in 165 patients for whom adequate follow-up was available. Fourteen patients had IGE. Of the remaining 151 patients, 138 had PE and 13 had SGE. Eighty-eight patients (53%) were male; 77 (47%) were female. For the IGE group, 7 (50%) were male. Mean age at the time of study was 27.3 years (range, 6–73 years). For the IGE group, the mean age at time of study was also 27.3 years (range, 13–45 years). Mean age of seizure onset was 8.5 years (range, 0–56 years). For the IGE group, the mean age of seizure onset was 8.2 years (range, 0.5–23 years). Among the 151 patients with PE and SGE, the cause was unknown in 77. In these two groups, perinatal anoxia or other early life vascular insults ($n = 19$), head injury ($n = 14$), encephalitis ($n = 12$), benign brain tumor without evidence of growth during the study period ($n = 8$), hydrocephalus ($n = 7$), and tuberous sclerosis ($n = 4$) were the most commonly identified sources. No etiology for epilepsy was present in the patients with IGE. MRI results for the overall group were negative in 78 (47.2%), abnormal in 74 (44.8%), and not available in 13 (7.8%). Full scale IQ (FSIQ) for the overall group revealed severe developmental delay in 27 (16.4%) and mental retardation (MR) in 32 (19.4%). FSIQ results were not available for 16 patients. Of the remaining 90 patients, FSIQ mean was 84.5.

Average duration of VNS therapy in the overall group was 21.6 months: PE group (20.7 months), SGE group (27.5 months), and IGE group (16.5 months).

Table 1 summarises the changes in seizure frequency after VNS for different patient groups. In the PE group, 65 (47.1%) had a 50% or greater reduction in seizure frequency, 57 (41.3%) had less than 50% reduction in seizure frequency, and 16 (11.6%) had an increase in seizure frequency. In the SGE group, six (46.1%) had a 50% or greater reduction in seizure frequency, six (46.1%) had less than 50% reduction in seizure frequency, and one (7.7%) had an increase in seizure frequency. In the IGE group, eight (57.1%) had a 50% or greater reduction in seizure frequency, five (35.7%) had less than 50% reduction in seizure frequency, and one (7.1%) had an increase in seizure frequency (Table 1).

Fourteen patients with IGE were compared to 151 patients with PE and SGE. Of the 14 patients with IGE, 5 (35.7%) were responders as we define them. One (7.7%) of 13 patients with SGE was a responder. Thirteen (9.4%) of 138 patients with PE were responders.

Of the IGE responders, MRI was negative in two, abnormal in one, and not available in two. The SGE responder had an abnormal MRI. Of the PE responders, MRI was negative in seven, abnormal in five, and not available in one. Of the IGE responders, one had severe developmental delay, one was MR, and three had FSIQ >70. The SGE responder did not have a FSIQ available. Of the PE responders, one had severe developmental delay, three were MR, and eight had FSIQ greater than 70. One PE responder did not have FSIQ available.

All five responders in the IGE group had reductions in the dosage of their AED regimens. The responder in the SGE group also had a reduction in AED regimen dosage. Of the PE group responders, eight had a reduction in AED regimen dosage, four had both a reduction in dosage and number of medications, and one responder had all AEDs stopped.

Table 1: Results of VNS treatment.

	Partial ($n = 138$)	Symptomatic generalised ($n = 13$)	Primary generalised ($n = 14$)
Average age	28.1	18.7	27.3
Sex	72 (52%) male 66 (48%) female	4 (30.8%) male 9 (69.2%) female	7 (50%) male 7 (50%) female
Number of years w/epilepsy	19.3	16.4	17.8
VNS treatment duration (months)	20.7	27.5	16.5
Mean VNS (A)	1.3	1.15	1.11
Mean % reduction in seizure frequency (all)	58.9	57.3	72.9
Percent of patients with decrease in AEDs	20.3 (28)	23.1 (3)	35.7 (5)
Percent responders with >50% reduction seizure frequency and decrease in AEDs	9.4 (13)	7.7 (1)	35.7 (5)
Percent responders with <50% reduction in seizures or no change	41.3 (57)	46.2 (6)	35.7 (5)
Percent responders with increased seizure frequency	11.6 (16)	7.7 (1)	7.1 (1)
Percent responders with >50% reduction in seizure frequency but non-responders (no decrease in AEDs)	37.7 (52)	38.5 (5)	21.4 (3)

DISCUSSION

Our findings suggest that VNS is an effective therapy for some patients with medication resistant IGE. These uncontrolled, retrospective observations suggest that patients with refractory IGE may enjoy both a greater reduction in seizure and medication burden with the VNS than those with refractory PE. We did not specifically look at quality of life issues with regard to decreased AED regimen. Advantages to patients and their families likely include decreased financial burden and psychological burden. Furthermore, the medication burden could possibly be further decreased with increased duration of VNS treatment.

Our findings support and expand the prior findings of Labar's group[4]. We also found that within the group of patients with generalised epilepsies, those with idiopathic disorders may have a better response to VNS than those with symptomatic forms. We studied patients for a longer interval after VNS implantation than in Labar *et al.*'s study (mean 21.6 months vs. 3 months)[4]. Our observations suggest that the duration of VNS efficacy in generalised epilepsies is sustained.

Our criteria for responders were stricter than most prior studies, requiring a reduction in medication number or dosage, as well as a reduction in seizure frequency. Specifically, we were interested in the subset with IGE. Individuals with IGE had a larger proportion of responders than groups with individuals with PE or SGE. Additional prospective studies are needed to better define the role of VNS in medically refractory IGE and determine if specific IGE may respond better to this therapeutic modality.

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