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Outcomes of vagal nerve stimulation in a pediatric population: A single center experience

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ABSTRACT

Objective: To evaluate the efficacy of vagus nerve stimulation (VNS) in pediatric patients with medically refractory epilepsy.
Method: We reviewed the medical records of 252 consecutive patients who underwent VNS implantation at a single center over a 5-year period. Patients with complete 6- and 12-month follow-up data were included. Analysis was also done across various subgroups including gender, age at implantation, seizure type, abnormal MRI findings pre-implantation, number of medications at baseline, history of SE, and duration of epilepsy.
Results: Complete follow-up data were available for 69 patients. Median seizure reduction for these patients was 50% (Q1: 0%; Q3: 73%) at 6 months and 40% (Q1: −25%; Q3: 75%) at 12 months. When stratified by baseline seizure frequency, there was a significant reduction from baseline of 61% at 6 months and 69% at 12 months for patients in the high-baseline frequency group. There were no significant reductions at month 6 or 12 months for the lower-baseline frequency group. Adverse events were reported in 40.6% (28 out of 69 patients). Six patients had the VNS removed for reasons including lack of efficacy and side effects and were excluded from the study group.
Conclusion: VNS provides significant seizure reduction, in particular in pediatric patients with a higher baseline seizure frequency.

1. Introduction

Vagus nerve stimulation (VNS) is an established adjunctive therapy for medically refractory epilepsy.[1,2] The therapy was approved in 1997 by the US Food and Drug Administration for use in adolescents and adults.[3] Combined analysis of these trials concluded that VNS therapy allowed 1/3 of treated patients to achieve a greater than 50% reduction in seizure frequency, a reduction which may continue even with long term use.[4] While the VNS is established for use in adults,[5–8] its potential value in the treatment of drug-resistant epilepsy in a pediatric population has not been conclusively established. Recently a small prospective study has been published suggesting that VNS may be effective in some children and adolescents, though not in others.[9,12,26] To date, few investigators have explored the efficacy and safety of VNS for refractory epilepsy in large pediatric populations over time.[10–13]

In this retrospective study, we aimed to expand the reported experience of VNS use in a pediatric population, with data from a single center. In addition, we also attempted to determine whether any specific clinical characteristics were associated with more favorable outcomes after VNS placement.

2. Methods

2.1. Patient selection

Prior to chart-review, institutional review board approval was obtained for this study. We reviewed the medical records of all

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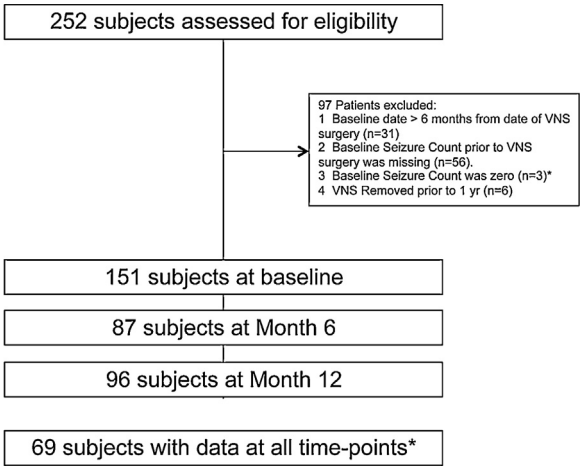

Fig. 1. Consort diagram. Only patients with complete data at baseline, month 6, and month 12 were included in statistical analysis. Sixty-nine patients were included. *Search using ICD-9 codes used returned some patients who did not undergo VNS implantations, but who underwent similar procedures for treatments in otolaryngology.

patients treated for epilepsy by VNS from December 1997 to March 2011 at Boston Children's Hospital. Patients were identified using the International Classification of Diseases, Ninth Revision codes 02.93, 89.15, 86.94, 86.95, 86.96, and 86.98. All medical records and reports of MRI findings were reviewed. Seizure outcome and VNS side effects were derived from the patient records and evaluated along with brain MRI findings, seizure type and localization, and previous seizure treatments.

2.2. VNS implantation

Implantation was performed by the same neurosurgeon following standard procedures (J.R.M.). Stimulation parameters were initially set at 0.25–0.5 mA current, 20–30 Hz frequency, 250–500 μs pulse width, 30 s on time and 5–10 min off time; the magnet current was generally set 0.25 mA higher with a stimulation duration of 60 s. Parameter adjustments were made at subsequent follow-ups by the patient's neurologist according to accepted adult guidelines.[14]

2.3. Follow-ups

Seizure frequency data was acquired at baseline (within 180 days prior to VNS implantation), at 6 month (±2 month window) and at 12 month (±3 month window) follow-up visits. Patients were required to have complete seizure data at all three of these time points to be included in the analysis.

Given the wide range of seizure frequencies at baseline, subjects were categorized by seizure frequency into a high-frequency group (those with a baseline frequency above the group median) and a low-frequency group (those with a baseline frequency below this median).

2.4. Statistical analysis

The primary outcome measure was the percentage change from baseline seizure frequency at the 6- and 12-month follow-ups. Differences in seizure percentage change were assessed using a Wilcoxon signed-rank test.

Subgroup comparisons were undertaken to assess if the median percentage change from baseline to 12 month follow-up was significantly different between the various groups stratified by demographic characteristics as specified in Table 3. P values <0.05 were considered statistically significant. All statistical analyses were performed using SAS, 9.3 (SAS, Cary, NC).

3. Results

3.1. Patient inclusion (Fig. 1)

Sixty-nine patients had complete data both at baseline and the two follow-up periods and formed the study group. Patients who had the VNS removed before 12 months were excluded from the analysis, though outcomes for this group are reported separately (Figs. 2 and 3.).

3.2. Population demographics

The median seizure frequency at baseline was 45 seizures/month (Q1: 10 seizures/month; Q3: 150 seizures/month). Patients were grouped according to the baseline median with Group 1 (low

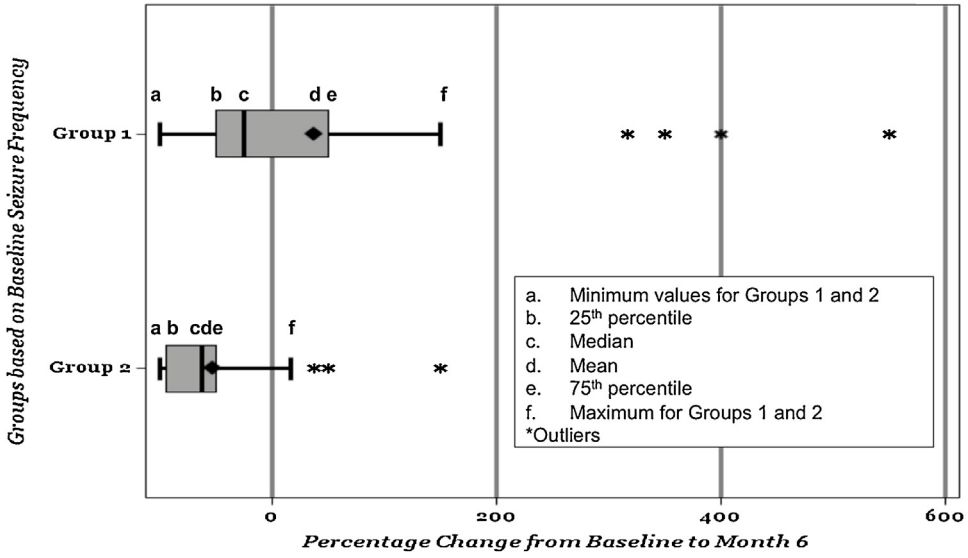

Fig. 2. Percentage change of seizures from baseline to 6 months. Patients in the low baseline group (Group 1) experienced a median seizure reduction of 25% (25% quartile, −50%; 75% quartiles, 50%) at 6 months ($p = 0.94$). Patients in the high baseline group (Group 2) experienced a median seizure reduction of 61% (25% quartile, −93%; 75% quartile, −50%) at 6 months ($p < 0.001$).