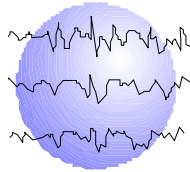


LONG-TERM VNS EXPERIENCE IN NORMAL AND MENTALLY RETARDED ADULTS AND CHILDREN

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REVISED ABSTRACT

RATIONALE: The vagus nerve stimulator (VNS) has been FDA approved for adjunctive use in refractory partial epilepsy in patients >12-years-old. Post-approval experience has included patients with broader epileptic syndromes, ages & general levels of function. Guardians & caregivers of mentally retarded (MR) patients have hesitated to utilize VNS fearing increased complications & less successful outcomes. We determined to evaluate our 8-year experience with the VNS in patients with refractory epilepsy, comparing patients with normal IQs & those with MR for efficacy & safety.

METHODS: A retrospective chart review was conducted of all patients with VNS implants with at least 1-year follow-up at Minnesota Epilepsy Group since 1997. Also, patient/guardian input was solicited via a mail survey that included questions of their subjective experience of safety & efficacy with the VNS.

RESULTS: 262 charts were reviewed: 178 adults (A), 84 children (P), ages 2 to 66-years-old. Nine were deceased. IQ was >75 in 75 patients & <75 in 138 (MR) & unknown (U) in 49. Twenty-five were lost to recent follow-up. Seizure (SZ) freedom occurred in 7% A and 13% P. >75% SZ reduction occurred in 22% A, 36% P. >50% SZ reduction occurred in an additional 21% A and 28% P. Szs were worse in 9% A and 4% P. Children did significantly better in efficacy than adults. Complications (CX) were mild to none in 75-87%; children had fewer CXs than adult patients. VNS was removed or turned off in 10% A and 16% P and replaced in 24% A and 31% P. Duty cycles utilized were more often intermediate or rapid settings in the MR-P group.

151 (59%) returned surveys. 64% of the whole group were more alert: 63% of normal groups, 47% MR with MR-P doing less well than the other groups. VNS judged to be helpful in 77% of normals, 44% of MR, less often in MR-P. The magnet helped 50% of normal IQ, 56% of MR (78% MR-A; 38% MR-P).

CONCLUSION: Both MR-A & MR-P do well with VNS. 70% P (66% MR-P) & 56% A (32% MR-A) achieve 50% or greater seizure reduction. MR populations also received marked benefit in subjective alertness & overall improvement. Additional benefits were reported from magnet use. CXs were mild in all groups. Neither age nor IQ status predicts response. Refractory epilepsy patients can be considered good candidates for successful treatment no matter what IQ status or age. Other associated indications of patient satisfaction and function will be reported.

Introduction:

The vagus nerve stimulator (VNS) is approved for use in refractory partial epilepsy in patients >12 years old. Post approval experience has reported use in patients with broader epileptic syndromes, younger ages, and a wide range of mental abilities. Guardians of patients with mental retardation (MR) and/or parents of younger children have hesitated to utilize VNS fearing increased risk of complication and less successful outcomes. Our preliminary data in adults suggested that MR patients did well with VNS and had no increase in complications and had good clinical outcomes.¹

We are presenting our 8 year experience with the VNS in children and adult patients with refractory epilepsy. In addition, we evaluated if there was an effect of IQ on efficacy and safety outcomes.

Methods:

A retrospective review of 262 charts was conducted of all patients with VNS implants with at least 1-year follow-up at the Minnesota Epilepsy Group. Implantation of VNS began in 1997 and cutoff for this review was 8/1/04. Also, patient/guardian input was solicited via a mail survey which included questions of the subjective experience of safety and efficacy with the VNS (Figure 1). Clinical efficacy was also assessed by evaluation of seizure frequency, reduction of medications, VNS settings, continued use of the device, and documentation of adverse effects at clinic visits (Figure 2).

Results

262 charts were reviewed: 178 Adults (A), 84 children < 18 years (P). Patients were implanted between the ages of 2-66 years. The collected data reflected from the last available clinic note. Survey return was 59%. The survey was answered by the patient in 32%; by family member 49%, or by other observer 19%. Epilepsy surgery occurred after the VNS had been implanted in 29 patients: 22 corpus callosotomies and 7 resections. VNS generator was replaced due to battery life in 68 patients.

Table 1 reports the group epidemiology. Table 2 reports the efficacy results as defined by % seizure reduction after at least one year of implantation. There was no significant change in the number of medications before or after the VNS implant by any group analysis or within the group as a whole. Emergency room visits decreased by 40% for the group (Figure 1).

There were no significant differences among groups for tolerability (Table 3 and Figure 2). The duty cycle setting was different between groups (Table 4). Normal IQ adults were more likely to have regular duty cycles while children were more likely to have intermediate cycles. Normal IQ adults tended to be treated with regular cycles while normal IQ pediatric patients had intermediate cycles. These analyses approached significance. The group as a whole was evenly distributed among the VNS settings (Figure 3).

Survey results are illustrated in Figures 4 and 5. There were no significant differences between IQ or age subgroups for any of the survey results although the seizure frequency improvement approached significance for the combined (A + P) normal groups compared to the combined (A + P) MR groups.

Discussion:

The VNS has proved to be an important addition to therapeutic options for patients with medically refractory epilepsy and meets criteria by the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology.² The VNS registry data has supported efficacy in both children and adults who have had epilepsy for less than and greater than 6 years. There is a better likelihood of seizure freedom in patients who are implanted with early treatment intervention, 7.8% at 3 months and 11.8% at 12 months.² Report of the VNS registry data regarding use in children in all age groups documents efficacy which is equivalent to reported adult efficacy. This population was comprised of 70% mentally retarded/developmentally delayed, a group which is at greater risk for refractory epilepsy. Frost's review of the VNS registry data describes marked efficacy in patients with Lennox-Gastaut syndrome for all seizure types.³ Long term evaluation of responses for tolerability and efficacy in adults and children and whether the patient's IQ changes the outcome, have not been reported. This report is one center's longitudinal experience in real life practice. There was no control on settings, medication changes or other therapy decisions. Despite this lack of organized prospective control of variables and settings, reduction in seizures and tolerability were not different significantly between any patient groups. This study also solicited the patient and caregiver's evaluation of the therapy by means of a survey so that no medical provider influenced the responses, such as could happen in the office setting. Assuming that this would likely encourage any negative responses, we were surprised and encouraged that such a positive response had been experienced by our patients; 70% reported better quality of life, 64% were more alert, and 75% would have the VNS placed again.

Conclusions:

Both adult and pediatric patients do well with VNS. Whether or not a patient has mental retardation does not affect the safety or efficacy profile. MR populations received marked benefit in subjective alertness and overall seizure and reported quality of life improvement. Additional benefit by both normal IQ and MR patients was reported with magnet use, which afforded a sense of having some personal control over the seizures. Complications were mild in all groups. Refractory epilepsy patients can be considered good candidates for successful treatment regardless what the IQ status or age.

References:

1. Penovich P, Korby B, Moriarty G, Gates, J. Vagal Nerve Stimulation (VNS) Use In Patients With Epilepsy And Mental Retardation. *Epilepsia* 43(S7): 344, 2002
2. Fisher RS, Handforth A. Reassessment: vagus nerve stimulation for epilepsy: A report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. *Neurology* 1999;53:666-9.
3. Helmers SL, Griesemer DA, Dean JC, et al. "Observation on the Use of Vagus Nerve Stimulation Earlier in the Course of Pharmacoresistant Epilepsy: Patients with Seizures for Six Years or Less" *The Neurologist* 2003; 9:160-164.
4. Frost M, Gates J, Helmers SL, et al. "Vagus nerve stimulation in children with refractory seizures associated with Lennox-Gastaut syndrome." *Epilepsia* 2001;42:1148-1152.

Table 1

Epidemiology of VNS Patients Implanted between 7/1997 to 8/2004*

| Adults | N |
|-----------------------------|----------|
| IQ >75 | 64 |
| IQ <75 | 91 |
| Pediatric <18 yrs | |
| IQ >75 | 11 |
| IQ <75 | 47 |
| Deceased | |
| Adult | 8 |
| Pediatric | 1 |

*Numbers of patients with noted IQ's reflect only documented data.

Table 2 **% Seizure Frequency Outcome Documented by Chart Notes***

| | Adult (n=144) | Pediatric (n=76) |
|---------------------|----------------------|-------------------------|
| Seizure Free | 7 | 13 |
| > 75% reduction | 22 | 36 |
| >50% reduction | 21 | 28 |
| <50% reduction | 28 | 14 |
| No change | 12 | 5 |
| Worse | 9 | 4 |

*Data was incomplete in 13 adults and 24 children

Figure 1

Emergency Room Visits

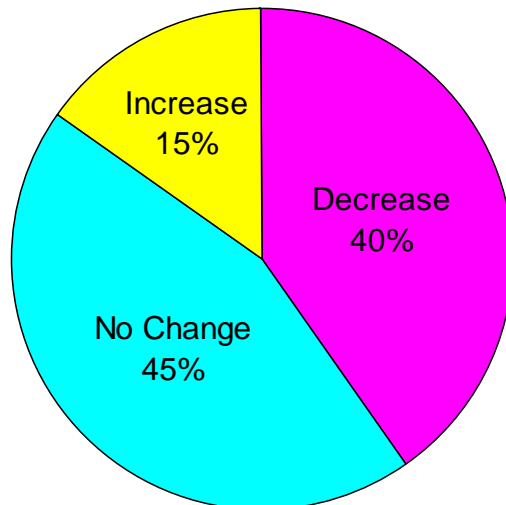


Table 3

Adverse Effects

| | Adults (%) | Pediatric (%) |
|-----------------|------------|---------------|
| Mild | 80 | 77 |
| Moderate | 17 | 10 |
| Severe | 2 | 10 |

Mild = temporary hoarseness or cough with stimulation
 Moderate = catching breath
 Severe = pain, prolonged cough

Figure 2

Problems Tolerating

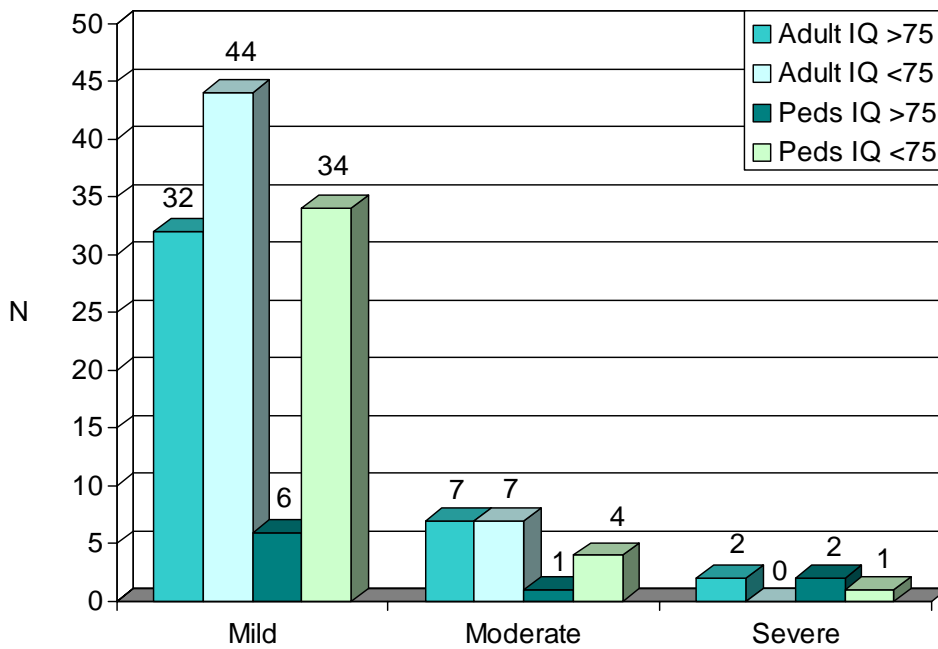


Table 4

VNS Cycle Settings

| | Adult % | | | Pediatric % | | |
|---------------------|---------|----|-------|-------------|----|-------|
| | NL | MR | Total | NL | MR | Total |
| Regular | 67 | 30 | 50 | 21 | 30 | 23 |
| Intermediate | 12 | 22 | 23 | 55 | 42 | 49 |
| Rapid | 20 | 23 | 26 | 21 | 25 | 23 |

Regular cycle = 30 seconds on, 5 minutes off
 Intermediate cycle = variable settings between regular and rapid
 Rapid cycle = 7 seconds on, 12 seconds off

Figure 3 **VNS Settings: Whole Population**

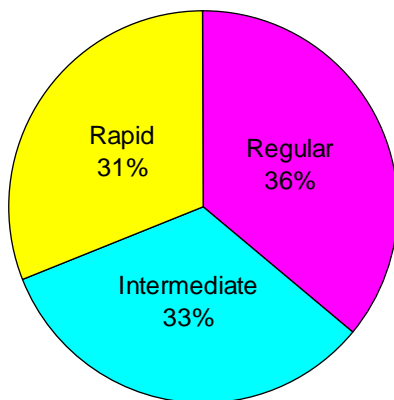


Figure 4 **Survey Results: Whole Population**

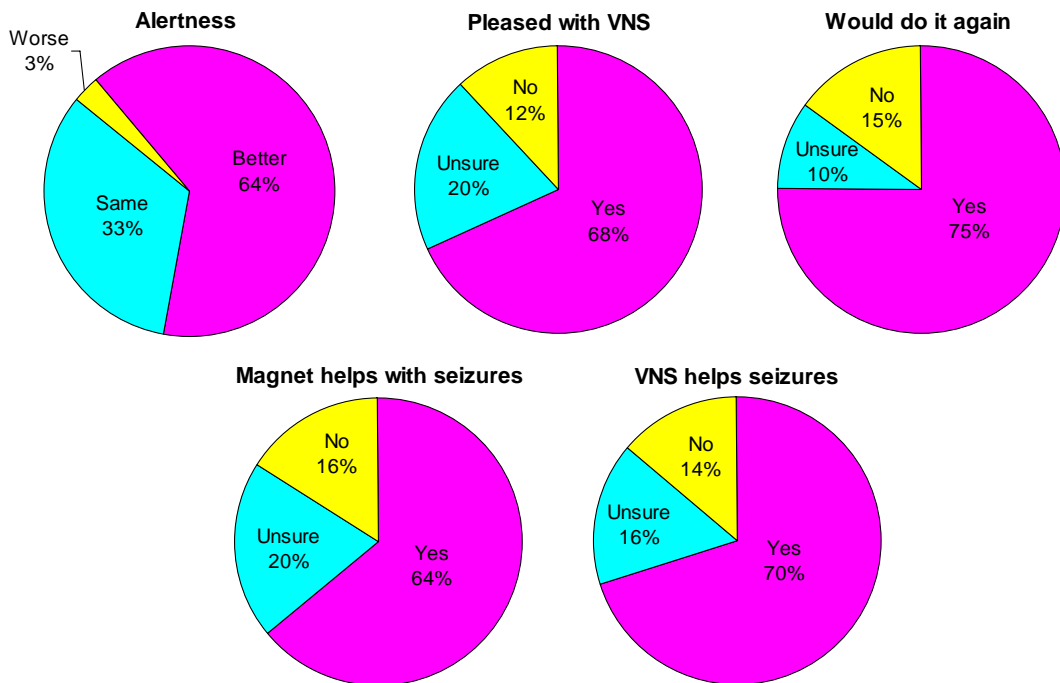


Figure 5 **VNS Effect on Seizures**

