The Efficacy Of VNS In Patients With Pharmacoresistant Epilepsy Of Temporal Versus Extra-Temporal Locations.

A Abubakr, I Wambacq

Citation

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Abstract

Objective: Evaluating the effectiveness of VNS therapy in patients with refractory epilepsy of temporal versus extra-temporal locations.

Methods: Retrospective record review of 31 patients with refractory epilepsy was carried out. Patients were divided into TLE group and extra TLE group based on the epileptogenic foci. Changes in seizures frequency was assessed at one year following VNS implant. Those with >50% reduction in seizures frequency from the base line were considered responders to VNS therapy.

Results: Out of 31 patients one died from unrelated cause and another asked their device to be removed due to AEs. There were 9 patients with TLE and 20 with extra TLE. There were no significant differences in demographic characteristics or seizures frequency (TLE 1-450/month and extra TLE 3-900/month). All the patients were taking an average of 2- 5 AEDs a day. No significant differences were observed in responder rate between groups at one year (p= 0.88; 66% in TLE and 55% in extra-TLE).

Conclusion: The study demonstrates that VNS is an effective therapy in epilepsy patients irrespective of thelocation of the epileptogenic foci.

INTRODUCTION

Epilepsy is well controlled in 60% to 70% of patients with seizures due to recent advances in AEDs therapy, which provides several options for physicians who treat patients with epilepsy. However, about one third of patients has drug resistant epilepsy or are unable to tolerate medications due to adverse effects (1, 2). In this group of patients with drug resistant epilepsy generally the accepted non-medical therapy is limited to ketogenic diet, resective epilepsy surgery and VNS. The ketogenic diet may not be helpful or practical in adults, and a considerable proportion of patients with pharmacoresistant partial onset seizures is not a candidate for or is opposed to intracranial surgery. For such patients, VNS may be an alternative therapeutic option (3, 4)

The FDA has approved VNS since 1997 for use as an adjunctive therapy to reduce the frequency of seizures in adults and adolescents over 12 years of age with partial onset seizures, and who are refractory to AEDs. Since 1997 the VNS has been an alternative treatment for refractory epilepsy, and the long-term outcome of VNS treatment has been reported with variable results in a number of studies (5, 6). However, it is unclear whether VNS is equally effective irrespective of the location of the epileptic focus. Recently, it has been suggested that VNS is more efficacious in frontal than temporal lobe epilepsy (7). In this study we aimed to evaluate the efficacy of VNS in patients with partial seizure of temporal lobe versus extra-temporal origin.

METHODS

The medical records of all patients implanted with VNS between 1998 and 2001 were reviewed.(Refer to prior study of long-term outcome of VNS; JCN 2008).

All the patients were admitted to EMU for phase 1 presurgical evaluation. The evaluation consisted of detailed history, physical examination, interictal EEG, video EEG for ictal recording and clinical semiology, MRI of the brain and neuropsychology test. All patients were being treated with 2 to 4 AEDs. Patients were offered VNS therapy if their surgical evaluation indicated that they would not benefit from resective surgery. The record review collected patients' data regarding seizures frequency before and one year following VNS implantation. The patients were divided into

TLE and extra-TLE groups based on the epileptogenic foci. Changes in seizures frequency was assessed at one year following VNS implant. Patients with >50% reduction in seizure frequency were considered responder to VNS therapy.

Statistical analyses (Student *t* test) were conducted on seizure outcome and the responder rate for any significant difference between groups ($P<0.05$).

RESULTS

Thirty-one patients were implanted with VNS. Out of 31 patients one died of unrelated cause, and another patient asked for the device to be removed due to adverse effects, such as pain in her chest and hoarseness of the voice. There were 9 patients with temporal lobe epilepsy (5 males and 4 females) with age range between 27 and 61 years. They were taking an average of 2-5 AEDs daily, had suffered from epilepsy between 4-40 years and had seizure frequencies of 1-450/month. There were 21 patients with extra-temporal lobeepilepsy (9 males and 11 females) with age range between 14 to 62 years. They were taking 2-4 AEDs daily, had epilepsy duration of 8-54 years, and seizure frequencies of 3-900/month. There were no significant differences between the two groups in these subject characteristics.

Six patients, 2 in the TLE group and 4 in the extra TLE group developed transient adverse effect that were tolerable; 2 patients had hoarseness of the voice, 2 patients developed cough, one had pain at the generator site and another had transient dysphagia.

The patients in the TLE and extra-TLE groups responded equally well to VNS therapy at one year following VNS implantation ($p=0.88$). In the TLE group, 6 out of 9 patients (66%) were considered responders to VNS therapy (≥50% reduction in seizures frequency) compared to 11 out of 20 extra TLE patients (55%). It is of note, however, that none of the patients obtained complete seizure freedom during the follow-up period of one year post implantation.

Table 1

Patient characteristics and the responder rate

	TLE	Extra TLE
Number of patients	9 (5 females)	20 (11 females)
Age range	27-61 years	14-62 years
Epilepsy duration	4-40 years	8-54 years
Seizures frequency	1-450/month	3-900/month
Number of AEDs/day	2-5	2-4
Number of Responders	66% (6/9)	55% (11/20)

DISCUSSION

This retrospective study demonstrates that VNS is an equally effective therapy in patients with either TLE or extra TLE focus as the responder rate was similar between these groups of patients. Improving seizure control irrespective of epileptogenic focus supports the possibility of broad spectrum effect of VNS implantation on seizure control. However, none of our patients attained complete seizure freedom. This could well be due to selection of mostly refractory epilepsy patients.Our finding is in contrast to a report by Burakgazi et al. (7); they retrospectively evaluated the seizure outcome of VNS therapy in 46 patients with refractory epilepsy of temporal and frontal lobe. They classified the outcome into group A (Engel class1, 2 and 3) as satisfactory and group B (Engel class4) as unsatisfactory. They reported that 41.3% of their patients had satisfactory outcome. On further analysis of the satisfactory group 65% of the patients had epilepsy of frontal lobe origin and 15% of temporal lobe origin.This was found to be statistically significant ($P=0.004$) and they concluded that VNS is more efficacious in frontal lobe. In our study we did not find any significant difference in outcome between temporal lobe epilepsy and extra temporal lobe epilepsy, which, again, could be due to the selection of more refractory epilepsy patients in our study. However, in concordance with Burakgazi et al we observed that none of the patients obtained complete seizure freedom.

Overall there is a scarcity of studies concerning the relationship between seizure type and VNS outcome. Holmes et al. (8) assessed the success of VNS in children on generalized seizures of idiopathic and symptomatic etiology, and found that VNS significantly reduces seizures associated with falls. This is somewhat similar to the study by Blount et al. (9) where VNS showed a significant effect on atonic seizures in children. Hence both studies differed from our study as we evaluated the effect of VNS on focal seizures in an adult population. Similarly Casazza et al (10) carried out a study evaluating the efficacy of VNS on patients with focal refractory epilepsy and frequent falls due to secondary generalization. They found the best outcome in certain type of falls; especially retropulsive tonic compared to tonic postural seizures. Although they did not obtain an EEG during these events, they established that VNS significantly impacted the patients with focal temporal lobe onset compared to extra-temporal origin. This is in contrast to our study that we did not find any difference in the response rate between various foci. Frost et al (11) studied the outcome of

VNS therapy in children with Lennox-Gastaut syndrome.At 6 months, the greatest reduction in seizure frequency was in generalized seizures of tonic and atypical absence which was around 80% compared to complex partial seizure of 23% at 3 months. They did not provide the 6 months results or the seizures foci.

Similarly Kabir et al. (12) studied the efficacy of VNS in children with refractory epilepsy of various locations. They did not find any significant difference between temporal and extra-temporal lobe locations; however the number of the patients was too small (4 frontal and 3 temporal) to reach any statistical conclusion. Overall their limited findings of no difference between the two groups were similar to our conclusion that VNS is effective on seizures of temporal and extra-temporal lobe origin.

The shortcomings of our study are that it is retrospective and that there is no control group. However, our study is similar to many observational and interventional studies in such that we were able to demonstrate that VNS is an effective therapy in patients with either temporal or extra-temporal lobe focus and that there was no difference in the response rate between various epileptogenic foci. We suggest that further studies are warranted to verify our finding and reconcile contradicting reported results.

References

Author Information

Abuhuziefa Abubakr, MB. FRCP
University of Mississippi Medical Center
Jackson, MS

Ilse Wambacq, PhD.
Montclair State University
Montclair, NJ