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ORIGINAL ARTICLES

Vagus nerve stimulation therapy improves quality of life in patients with intractable postencephalitic epilepsy, a study of five patients

Ayataka Fujimoto *MD PhD*, Toru Okanishi *MD PhD*, Mitsuyo Nishimura, Sotaro Kanai *MD*, Keishiro Sato *MD*, Hideo Enoki *MD PhD*

Comprehensive Epilepsy Center, Seirei Hamamatsu General Hospital, Shizuoka, Japan

Abstract

Introduction: To evaluate the utility of vagus nerve stimulation (VNS) therapy for patients with intractable postencephalitic epilepsy in the reduction of seizure frequency and quality of life (QOL). *Methods:* We studied five patients with intractable postencephalitic epilepsy, the age ranged from 21 to 46 years. QOL of the patients was evaluated with the questionnaire, QOLIE-31-P. *Results:* VNS therapy improved seizure frequency in four patients (80%). One patient (20%) had no reduction of seizure frequency. Three patients had improvements in QOLIE-31-P ($p < 0.024$) and became socially independent. Two other patients continued to be dependent, and have lesser degree of improvements in their QOLIE-31-P scores.
Conclusion: VNS is effective for patients with intractable postencephalitic epilepsy and is able to improve the QOL.

Keywords: Postencephalitic epilepsy, vagus nerve stimulation therapy, quality of life, QOLIE-31-P

INTROUDCTION

Acute encephalitis is a debilitating neurological disorder with a rapidly progressive encephalopathy caused by inflammation secondary to an infection or non-infectious autoimmune reaction.[1,2] Patients with postencephalitic epilepsy may develop intractable epilepsy.[3-7] Open cranial surgery is not able to achieve satisfactory seizure outcomes in these patients.[8-10] We have earlier reported that vagus nerve stimulation (VNS) was effective in treatment of intractable epilepsy and early response was a predictor for long term outcome[11] or patients with intractable postencephalitic epilepsy, VNS may also be beneficial.[12-14] There were two previous case reports of beneficial effect of VNS for intractable postencephalitic epilepsy.[15,16] However, none has reported effects of VNS, on the quality of life (QOL).[17] In this study, we aimed to evaluate the utility of VNS therapy for patients with intractable postencephalitic epilepsy in seizure frequency and to compare QOL before and after implantation.

METHODS

We selected patients who (1) had a history of encephalitis with a known etiology, (2) were healthy before the encephalitis, (3) experienced refractory seizures in the chronic period after the encephalitis, (4) had complete clinical records, and (5) did not undergo open cranial epilepsy surgery between 2010 and 2016. Five patients (one woman and four men) met the criteria. One patient who underwent VNS implantation during the acute period was excluded.[18] All the patients were treated with VNS (Aspire HC; VNS Therapy® System, Cyberonics, Inc., Houston, TX, USA).

Quality of life in epilepsy evaluation

We used the QOLIE-31-P scale,[19,20] which is a scale of health-related QOL for adults with epilepsy. There are 38 questions about patients' health and daily activities.

Medications

We compared the numbers of anti-epileptic drugs (AEDs) before implantation and at 2 years after

Address correspondence to: Ayataka Fujimoto, 2-12-12 Sumiyoshi, Nakaku, Hamamatsu, Shizuoka 430-8558, Japan. Tel: +81-53-474-2222, E-mail: ataka_fuji@sis.seirei.or.jp

implantation. All the patients underwent Wechsler Adult Intelligence Scale III (WAIS-III) testing 2 years after VNS implantation.

Statistical analysis

In the statistical analyses of the QOLIE-31-P scores, we used the paired t-test. We examined the relationships between pre- and post-VNS implantation scores. Statistical significance was set at $p < 0.05$. All analyses were done using KaleidoGraph® software (Hulinks Inc.,Tokyo, Japan).

Ethical approval

This study was approved by the Ethical Committee for Epidemiology of Seirei Hamamatsu General Hospital. All procedures performed in this study were in accordance with the 1964 Helsinki Declaration.

RESULTS

Clinical details of the study patients are shown in Table 1. The ages ranged from 21 to 46 years (mean, 33 years). Patients 1, 2, and 4 had autoimmune encephalitis.[1] Patient 3 had herpes simplex encephalitis. Patient 5 had acute encephalitis with refractory, repetitive partial seizures (AERRPS).[21-23]

Patient 1 had a weekly aura of pounding palpitation followed by secondary generalized tonic-clonic seizure (sGTC). Patient 2 showed monthly independent right or left-hand twitching followed by complex partial seizure (CPS), which sometimes proceeded to sGTC. Patient 3 had weekly sudden, brief staring episodes followed by sGTC. Patient 4 had weekly independent right or left fencing posturing followed by sGTC. Patient 5 had daily brief CPS followed by sGTC.

The follow-up period ranged from 2.1 to 5.3 years. Patients 1 and 2 continued to have short-term memory loss and working memory deficits. However, their intelligence quotients were maintained within normal range. Magnetic resonance imaging (MRI) of their brains showed bilateral medial temporal lobe abnormalities on fluid-attenuated inversion recovery (FLAIR) imaging. Electroencephalogram showed bitemporal independent epileptiform discharges interictally in both patients. Patient 3 continued to have working memory deficits with normal intelligence. FLAIR imaging showed multiple demyelinated areas in both hemispheres. FLAIR imaging of Patient 4 showed high-intensity areas in the bilateral frontoparietal regions. Even though he maintained normal intelligence, he continued to experience psychiatric symptoms including depression and auditory hallucinations of mechanical sounds. Patient 5 had moderate intellectual disability.

Effect on seizure

At last follow up, Patient 1 has sGTC once every 2 to 3 months when he failed to use the VNS magnet. The seizure frequency has reduced by more than 80%, and he returned to participate in social activities. Patient 2 was free from sGTC, she has yearly CPS only. She was currently a mother of one son. Patient 3 had a 50%-79% reduction in seizure frequency. Currently, he was employed as a computer engineer. Patients 4 and 5 were not employed and spend most of their time at home. Patient 4's seizure frequency did not change after VNS. Even though Patient 5 obtained more than 80% seizure reduction after VNS, he only helped with his father's farms on a part-time basis (Table 1).

Quality of life in epilepsy

On comparing QOLIE-31-P before and after VNS therapy, all of the patients achieved better QOLIE-31-P outcomes ($p < 0.024$), especially in the "emotional well-being "($p < 0.045$), and "cognitive" ($p < 0.016$) parameters, which were statistically significant. Patients 1, 2, and 3 had larger score improvements and became socially independent. However, Patients 4 and 5 were still dependent without full-time employment and had only limited improvements in QOLIE-31-P scores. In both of these patients, almost no improvements were seen in the areas of energy/fatigue, medication effects, or social function (Table 2).

Medications

The total number of AEDs was reduced in Patients 2 and 3. Patient 1 was currently being treated with non-enzyme inducers. Patient 4 was previously on four AEDs but was currently on five AEDs (Table 1).

DISCUSSION

As AEDs often do not control seizures in patients with intractable postencephalitic epilepsy,[24-26] VNS therapy could be a last resort. In this study, VNS therapy was effective in reduction of seizure frequency, except for Patient 4. VNS therapy also improved QOLIE-P outcomes in all the patients.

Table 1: Clinical details of the study patients

Table 1; Clinical information									
	Sex	Age of VNS	Onset	Seizure	Before VNS	After VNS	Cognitive	AEDS at pre VNS implantation	AEDs at post VNS implantation
Pt.1	M	29	25	aura/sGTC	weekly	≥ 80% reduction	FIQ83	CBZ/VPA/PHT	ZNS/LEV/LCM
Pt.2	F	38	23	hand twitching/CPS/sGTC	monthly	≥ 80% reduction	FIQ117	ZNS/LTG/PHT/VPA	LEV/LCM
Pt.3	M	31	25	sGTC	weekly	< 80%, ≥ 50%	FIQ94	VPA/CBZ/LTG/LEV/CLB/GBP	LTG/LEV/PER/LCM
Pt.4	M	46	43	Fencing posturing/sGTC	weekly	No change	FIQ81	LTG/CBZ/CLB/LEV	LTG/CBZ/LEV/PER
Pt.5	M	21	14	CPS/sGTC	daily	≥ 80% reduction	FIQ67	PB/LEV/CBZ/CLB	PB/LEV/CBZ/TPM

Pt: patient; M: male; F: female; CPS: complex partial seizure; sGTC: secondary generalized tonic-clonic seizure; AED: anti-epileptic drug; VNS: vagus nerve stimulation; FIQ: full intellectual quotient (Wechsler Adult Intelligence Scale III); CBZ: carbamazepine; VPA: valproate; PHT: phenytoin; ZNS: zonisamide; LTG: lamotrigine; CBZ: clobazam; GBP: gabapentin; LEV: levetiracetam; PB: phenobarbital; LCM: lacosamide; PER: perampanel

Table 2: QOLIE-31-P before and after implantation of VNS

Table 2; QOLIE-31-P								
	Patient	Emotional-well being	Energy/fatigue	Cognitive	Medication effects	Social function	Overall score	
Pre VNS QOLIE-31-P	1	24	45	30	47.2	0	21.9	
	2	56	15	48.9	8.3	14	35	
	3	56	30	10	0	0	19	
	4	36	25	35.8	88.9	0	20.9	
	5	56	56	35	47.2	33.3	34.2	
	Patient	Emotional-well being	Energy/fatigue	Cognitive	Medication effects	Social function	Overall score	Score Increase
Post VNS QOLIE-31-P	1	72	65	61.1	75	32	51.5	135% ↑
	2	76	55	71.9	27.7	30	79.9	128% ↑
	3	88	60	16.7	77.8	14	41.9	120% ↑
	4	52	25	45	88.9	5	30.4	45% ↑
	5	56	55	57.2	25	32	44.35	30% ↑
p value*		$p < 0.045$	$p < 0.093$	$p < 0.016$	$p < 0.29$	$p < 0.08$	$p < 0.024$	

VNS: vagus nerve stimulation; QOLIE: quality of life in epilepsy; * The paired t-test was used to compare pre- and post-VNS therapy.

As VNS therapy has been shown to be efficacious in mood disorder and treatment-resistant major depression [27], this may partially explain the improvement of the QOL in patients undergoing VNS treatment.

As shown in Table 2, the difference in QOLIE-31-P scores before and after VNS implantation were statistically significant in "emotional well-being," "cognitive," and "overall" scores. One of the reasons that Patient 4 was unable to obtain a high score might have been continuing frequent seizures despite VNS therapy, and persistent depression. Even though VNS was efficacious for Patient 5, the severity of his seizure frequency and intellectual impairment were the worst among the five patients, which may have contributed to his lack of improvement in QOL.

This study was limited by the small number patients. However, it appeared to demonstrate a trend of improvement in QOL for intractable postencephalitic epilepsy patients treated with VDS.

DISCLOSURE

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Conflicts of interest: None

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