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Efficacy of Vagal Nerve Stimulation in Iraqi Patients with Refractory Epilepsy: Two-Year Experience

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Abstract

Background Refractory epilepsy patients who fail to respond to two antiepileptic drugs used appropriately are likely to have medically refractory seizure disorder and should be investigated for alternative forms of treatments like experimental drug trial, surgical treatment, electrical stimulation and combination of these. Vagal nerve stimulation is an adjunctive treatment for certain types of epilepsy.

Objectives To evaluate the efficacy of vagal nerve stimulation in refractory epilepsy, as an adjunctive therapy to antiepileptic drugs in Iraqi patients.

Methods A retrospective study recruiting 34 patients at Neurosciences Hospital in Iraq between Feb. 2008 and Jan. 2011. Diagnosed as refractory epilepsy according to International League Against Epilepsy criteria; the epilepsy state, number of the anti-epileptic drugs, frequency and severity of the attacks (using Chalfont scale) was assessed before and after the vagal nerve stimulation implantation. Programming was done every two weeks depending on clinical assessment.

Results Severity of the attacks was reduced totally 100% in 26.5% of the patients and 50-99% in 26.5% of patients. The number of attacks per month was decreased by 100% in 26.5% of patients and showed more than 50% improvement in 38% of patients. The number of the drugs used after the implantation decreased by 17.6% (P = 0.007). The most common side effects were hoarseness of voice 55.8% and dysphagia 41% only during the on time of the device.

Conclusion Vagal nerve stimulation is effective safe and well tolerated in Iraqi patients.

Key words Vagus nerve stimulation, Refractory epilepsy, Anti-epileptic drugs, Iraqis.

Introduction

According to International League against Epilepsy (ILAE) criteria "Patients who fail two antiepileptic drug (AED) medications used appropriately are likely to have a medically refractory seizure disorder and should be investigated for alternative forms of treatment [1,2]. Potential treatment options include experimental drug trials, surgical treatment, electrical stimulation and combination of the above [1].

Vagus nerve stimulation (VNS) is approved by Food and Drug Administration (FDA) for management of intractable epilepsy in 1997 [3]. It is possible that VNS may interrupt the spread of epileptiform activity if delivered at a theoretically critical time; it is possible that VNS causes small changes in brain dynamics resulting in larger effects that inhibit the brain from becoming dynamically entrained, thus interrupting any progression towards a clinical seizure [4].

Two published retrospective case series discussed the long-term outcome of patients receiving VNS therapy [5,6]. A series reporting five-year or greater outcomes of 26 patients from the University of Wisconsin noted that the median frequency of seizures reported after one year of VNS therapy was decreased from baseline (-28%), but had decreased even more by the long-term follow-up (-72%) [7].

The aim of the present study is to evaluate our first experience in Iraq and to assess the results of vagal nerve stimulation in refractory epilepsy in Iraqi patients as an adjunctive therapy to antiepileptic drugs.

Methods

A retrospective study evaluating thirty-four patients diagnosed as refractory epilepsy according to ILAE criteria who had been operated for VNS implantation by a team of neurologists and neurosurgeons in Neurosciences Hospital in Baghdad for the period between Feb. 2008 and Jan. 2011, they were interviewed at epilepsy clinic, by taking thorough history and revaluation of the epilepsy state, frequency and severity of the attacks, number of the anti-epileptic drugs (AEDs), duration of the epilepsy before and after the implantation of the device was assessed. Seizure severity was assessed by using Chalfont seizure severity scale [8].

All the patients with implanted devices from the first case which is carried out in 24th Feb. 2008 till the last one at 5th Jan. 2009 were included in the study. All subjects were consented to participate in the research prior to their inclusion in the study, and the local ethics committee approved the study protocol.

Ten patients (29.4%) out of the tested were on full doses of two AEDs (tried before with three drugs with failure due to side effects); seventeen patients (50%) were on three drugs, and seven patients (20%) on four drugs. The age of the patients ranges between 12 years and 35 years. Six (17.6%) patients were having generalized tonic clonic epilepsy, fifteen (44%) with focal and secondary generalized epilepsy, thirteen (38%) with multiple types (generalized tonic clonic, myoclonic and atonic).

The devices (Cyberonic, Houston, Texas, model 102, and 102R) were implanted by neurosurgeons with the assistance of a biomedical engineer. First programming was done two weeks after implantation and then periodic programming every two weeks depending on the clinical assessment.

Statistical Analysis

Statistical Package of Social Sciences (SPSS) version 18 was used for the purpose of data entry and data analysis. Paired t test was used to compare between numerical variables before and after the implantation of the VNS device. A *P* value of ≤ 0.05 was considered as statistically significant.

Results

Age, sex, family history of epilepsy, age of seizure onset, and seizure types before and after the implantation of the device is shown in the table 1.

Severity of the attacks:

The severity of the attacks was decreased to 54 mean score as compared to 118.9 mean score prior to device implantation ($P < 0.005$) as seen in table 2.

The severity of the seizure attacks improved totally (100%) in 26.5% of the patients and about 50%-99% in 26.5% of the patients. In the rest 47% of the patients, the improvement was less than 50% as demonstrated in table 3.

Frequency of the attacks:

The number of the attacks after the implantation of the device is decreased from 225 attacks per month to 50.6 per month after the implantation of the device ($P = 0.022$) as noticed in table 2.

The frequency of the seizure attacks per month showed total improvement (100%) in 26.5% of the patients, 50% in 38% of the patients and less than 50% in 14.7% of the patients while 20.5% of the patients showed no improvement in the frequency of the attack (Table 3).

Table 1. Demographic feature of epileptic patients

	Age (year)	Gender	Age of seizure onset/year	Family history	Seizure type/before	Seizure type/after
1	8.5	F	0.33	No	PSG	PSG
2	12	M	0.5	No	PC, AS, MS	PC, AS, MS
3	15	M	6	No	PSG	PSG
4	16	M	4	YES	PSG	PSG
5	19	M	4	No	PSG	PSG
6	20	M	7	No	GTC, MS, AS	GTC, MS, AS
7	20	M	0.5	No	PSG	PSG
8	20	M	10	No	PSG	PSG
9	21	F	10	No	PSG	PSG
10	21	M	19	No	GTC	GTC
11	21	M	0.08	No	AS, MS, GTC, PCS, MR	AS, MS, GTC, PCS, MR
12	21	M	0.75	No	GTC	GTC
13	22	F	7	No	GTC, SE	GTC, SE
14	22	M	13	No	PSG, EPC	PSG, EPC
15	22	F	21	No	GTC, AS	GTC, AS
16	25	M	13	No	GTC, AS, PSG	GTC, AS, PSG
17	26	M	11	No	GTC	GTC
18	27	M	3	No	PSG	PSG
19	30	F	20	No	GTC, MS	GTC, MS
20	32	M	21	No	GTC	GTC
21	35	M	20	No	GTC, MS	GTC, MS
22	8.5	F	1	No	PSG	PSG
23	14	M	5	No	GTC	GTC
24	16	F	6	No	GTC, MS, AS	AS
25	25	M	16	YES	GTC, MS	Free
26	16	F	12	YES	GTC, MS	Free
27	17	F	7	No	GTC	GTC
28	30	M	17	No	PSG	PSG
29	25	F	10	No	GTC	Free
30	17	F	7	No	PSG	PSG
31	19	M	8	No	PSG	PSG
32	11	F	4	No	PSG	PSG
33	21	F	11	No	PSG	PSG
34	21	M	9	No	EPC	PSG

PSG = partial seizure with secondary generalization, PC = partial seizure, AS = absence seizure, MS = myoclonic seizure, GTC = generalized tonic clonic, EPC = epilepsia partialis continua, SE = status epilepticus.

Number of the drugs:

The number of the AED used by the patients after the implantation of the device is decreased by17.6% as compared to number of drugs at the end of the study ($P = 0.007$) (Table 2).

Adverse effects of the device implantation:

Hoarseness of the voice was the most common side effect in 55.8% of patients followed by dysphagia in 41%, cough, dyspnea, palpitation in 14.7%, and headache in 5.8%.

The implanted device was removed from 4 patients due to local infection in one, aspiration pneumonia in one, suicidal attempt in one and loss of contact in another patient.

Table 2. Severity of the attacks before and after the device implantation

Parameter	No.	Before implantation of device	End of the study	t	P value
Severity of the attacks	34	118.95 ± 40.36	54 ± 38.53	9.37	≤0.005
Frequency of the attacks/month	34	225.04 ± 244.2	50.65 ± 74.35	3.49	0.0022
No. of the drugs	34	2.95 ± 0.67	2.34 ± 0.81	2.95	0.007

Table 3. Improvement in the severity of the attacks

Parameter	100% improvement		50-99% improvement		<50% Improvement		No improvement	
	No.	%	No.	%	No.	%	No.	%
Severity of the attacks	9 (34)	26.5	9 (34)	26.5	16 (34)	47	0 (34)	0
Frequency of seizure attacks	9 (34)	26.5	13 (34)	38	5 (34)	14.7	7 (34)	20.5

Discussion

This study describes 34 patients, with refractory epilepsy who did not become seizure-free despite treatment with various combinations of AEDs. All of them were unsuitable candidates for resective surgery, there were subsequently treated with VNS.

VNS is a simple surgical therapy of choice because it need a routine electro-encephalography EEG, brain computed tomographic (CT) scan or MRI that can be easily done in comparison to surgical resection which need more sophisticated investigations like functional magnetic resonance imaging (FMRI), video EEG monitoring, intraoperative EEG, positron emission tomography (PET) scan and Single photon emission computerized tomography (SPECT) which are not available now in Iraq.

In the present study, the severity of the attacks was decreased in our patients, which agree with other international studies [6,9-11]. Moreover, in 26.5% of cases the severity of the attacks improved by more than 50% and totally in 26.5%, a finding that is also reported by Cramer [12].

The attacks frequencies per month were decreased. The mean duration from the time of implantation of the device till the end of the study was 1.8 year. This finding was very compatible with those reported by DeGiorgio and coworkers [13]. Moreover, the frequency of the attacks were improved by more than 50% in 38% of the patients and totally in 26.5% of the patients improved, which agree with the results of DeGiorgio and associates [6].

In present study, the VNS were well tolerated by the patients apart from some side effects of the device that was also reported by others [14,15].

Four patients not included in the statistical analysis of the study, because of the following reasons: Patient with myoclonic epilepsy with generalized tonic clonic seizure came for follow up only four visits then lost contact till now. The second patient with multiple types of epilepsy, died from aspiration pneumonia. The third patient with partial complex seizure, the device is removed because of infection of the device the patient used to scratch the area. The last patient also the device was removed because of infection and unfortunately died after removal of the device (suicide).

In conclusion, vagal nerve stimulation is a good adjunctive tool of therapy added on drug therapy for patient with refractory epilepsy. It is effective safe and well tolerated in our patient.

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