Vagal Nerve Stimulation of 24 Iraqi Patients with Refractory Epilepsy

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Abstract:

Background: refractory epilepsy is a major problem for neurologists and epileptic patients; vagal nerve stimulation is one of the palliative **surgical** therapies.

Objective: to assess the effect of vagal nerve stimulation therapy on refractory epilepsy.

Patients and method: this study was conducted in the Neurosciences hospital for the period from February 2008 to January 2009.Twenty four patients with refractory epilepsy, eleven males, thirteen females were enrolled in this study, their age ranges from 14 years to 40 years with a mean age of 23 year, while two patients were below 12 years, seven with mixed type epilepsy (generalized tonic clonic, myoclonic and a tonic), six with generalized tonic clonic, six with focal and secondary generalized epilepsy, four with complex partial epilepsy, and one with Lennox Gastuat.

Results: Three of the patients developed no more attacks, twelve patients get benefit by a decrease of 50 %-90% in frequency of epilepsy, eight patients with the same frequency and one excluded because the patient got use to scratch the site and the device was removed.

Conclusion: VNS is a good surgical option in the absence of surgical resection, and easy to be done with a good team of neurologist and neurosurgeon.

Key wards: refractory epilepsy, vagal nerve stimulation.

Introduction:

Seizure is a paroxysmal event due to the abnormal excessive hypersynchronus discharge from an aggregate of the central nervous system .[1]

Epilepsy is a condition in which a person has recurrent seizures due to chronic underlying process. This distribution implies that a person with a single seizure or recurrent seizures due to controllable or avoidable circumstances does not necessarily have epilepsy. [1]

Refractory epilepsy remains somewhat controversial. After 2-3 generally effective AEDs have failed to render a patient seizure-free, the chances of that patient ever becoming seizure-free on any medication are only about 5-10%. In general, about 47% of patients will become seizure-free after the first AED. An additional 13% will become seizure-free after the second AED. On a third or multiple AEDs, the chance of seizure-freedom is about 1-3%. [2]

Vagal nerve stimulation is one of the palliative surgical therapies for refractory epilepsy. The European Community approved VNS therapy for epilepsy in 1994, and in 1997, the U.S. Food and Drug Administration (FDA) approved VNS therapy ''for use as an adjunctive therapy in reducing the frequency of seizures in adults and adolescents over 12 years of age with partial-onset seizures which are refractory to antiepileptic medications' [3]

Patients and method:

In this therapeutic trial (intervention study), twenty four patients with refractory epilepsy diagnosed and selected as a candidate for VNS therapy in epilepsy clinic in neurosciences hospital by taking thorough history and reevaluation of the epilepsy state with frequent admissions that help to prove the diagnosis and to try a third antiepileptic or starting the most appropriate drugs for the type of epilepsy. Routine biochemical and hematological investigations, EEG and brain CT for all the patients were carried out.

Eleven males and thirteen female were enrolled in the study. The first implant in the Neurosciences hospital in Iraq was at 24-2-2008 and the last one was in 5-1-2009.

Eight patients were on two drugs with full doses (tried before with three drugs with failure due to side effects), fifteen were on three drugs, one on four drugs. Age from 14 years to 40 years with a mean age of 23 year while two patients were below 12 years.

Vagal nerve device were implanted by a neurosurgeon assisted by biomedical engineer in Neurosciences hospital.

Statistical Analysis:

The following statistical data analysis approaches were used in order to analyze and assess the results of the study : ***1. Descriptive data analysis***: a. Tables (Frequencies, Percentages and Cumulative Percentages), mean value, standard deviation, (95%) confidence interval for population mean values, two extreme values (min. and max) respondents, graphical presentation by using: Bar- chart , Stem and leaf chart; ***2. Inferential data analysis:*** These were used to accept or reject the statistical hypotheses, which included the following: Chi – square test, Binomial test, Paired matched (t-test) for testing the difference between mean in periods .

Result:

Table (1): Descriptive Statistics for some related studied variables with comparison significance

Variables	Groups	Freq.'s	%	Cum. %
Age Groups	> 10	1	4.2	4.2
	10 – 19	9	37.5	41.7
	20 – 29	8	33.3	75
	30 – 40	6	25	100
Gender	Male	11	45.8	45.8
	Female	13	54.2	100
Type of Epilepsy	Generalized tonic clonic	6	25	25
	Focal with second generalization	5	20.8	45.8
	Complex Partial	5	20.8	66.7
	Lennox Gas taut syndrome	1	4.2	70.8
	Multiple types	7	29.2	100
Side Effect	Nil	10	41.7	41.7
	Headache	3	12.5	54.2
	Hoarseness, Diff. in swallowing	1	4.2	58.3
	Cough	3	12.5	70.8
	Infection , Removed	1	4.2	75
	Dysphagia	2	8.3	83.3
	Hoarseness , Neck m. cont	1	4.2	87.5
	Hoarseness	3	12.5	100
Duration of Epilepsy (year)	< 10	4	16.7	16.7
	10 – 19	14	58.3	75
	20 >	6	25	100
Duration of implant (months)	< 5	8	33.3	33.3
	5 – 9	10	41.7	75
	10 >	6	25	100
Side effect	Nil	10	41.7	41.7
	Defectives	14	58.3	100

NS: Non Sig. at P>0.05; S: Sig. at P<0.05; HS: Highly Sig. at P<0.01

The above table shows that the vast majority of the study sample is within the last third category of age groups along the period (10–40) years and accounted for (95.8%), and also shows that the majority of the study sample (45.8%) is male and the remaining are female.

Relative to subjects type of Epilepsy, they were recorded asymptotically coincidence outcomes except with only one patient of Lennox Gas taut syndrome type within (4.2%)

With respect to the side effects, results indicate that highest percentage of the study sample were registered at (Headache, Cough, Hoarseness) with (64.3%) overall defective individuals of this indicator.

With respect to the Duration of Epilepsy (year) results indicate that highest percentage of the study sample were at the mid interval with (58.3%).

Regarding to the subjects Duration of implant (months), the majority of the sample were presented in the mid interval with (41.7 %) compared with the total sample.

Table (2): Summary Statistics for the two implant periods – per month

Implant period -Per month	Mean epileptic attacks	N	SD	SEM
frequency before implant-Per month	54.63	24	55.75	11.38
Frequency after implant-Per month	16.79	24	19.33	3.95

Table (2) showed the Summary Statistics for the two implant periods – per month before and after implantation process, the results indicating a highly improvements had been occurred regarded to statistics recorded in the two periods. According to the mean value statistics , the reduction in the studied criteria

arrived to more than 300 % . In addition to that the same results had been achieved with standard deviation statistic .

Table (3) : Comparison between the two implant repeated periods – per month

Paired Differences of epileptic attacks	Mean of epileptic attacks	Std. Dev.	Std. Error Mean	95% Confidence Interval of the Difference		t-test	d.f.	Sig. (2-tailed)
				Lower	Upper			
	37.83	60.62	12.37	12.24	63.43	3.057	23	P = 0.006 HS

HS: Highly Sig. at P<0.01

Table (3) showed the Comparison significant for the two implant repeated periods – per month , the test statistic proved within a non suspicion that a highly changeability occurred as a result or due to the implant process since a highly significant different at (p<0.01) recorded in testing the mean value of differences overall the total individuals of the study sample, For summarization to preceding, we can conclude that all readings of the studied samples had been showed a highly occurrences of changeability of positive direction of improvement .

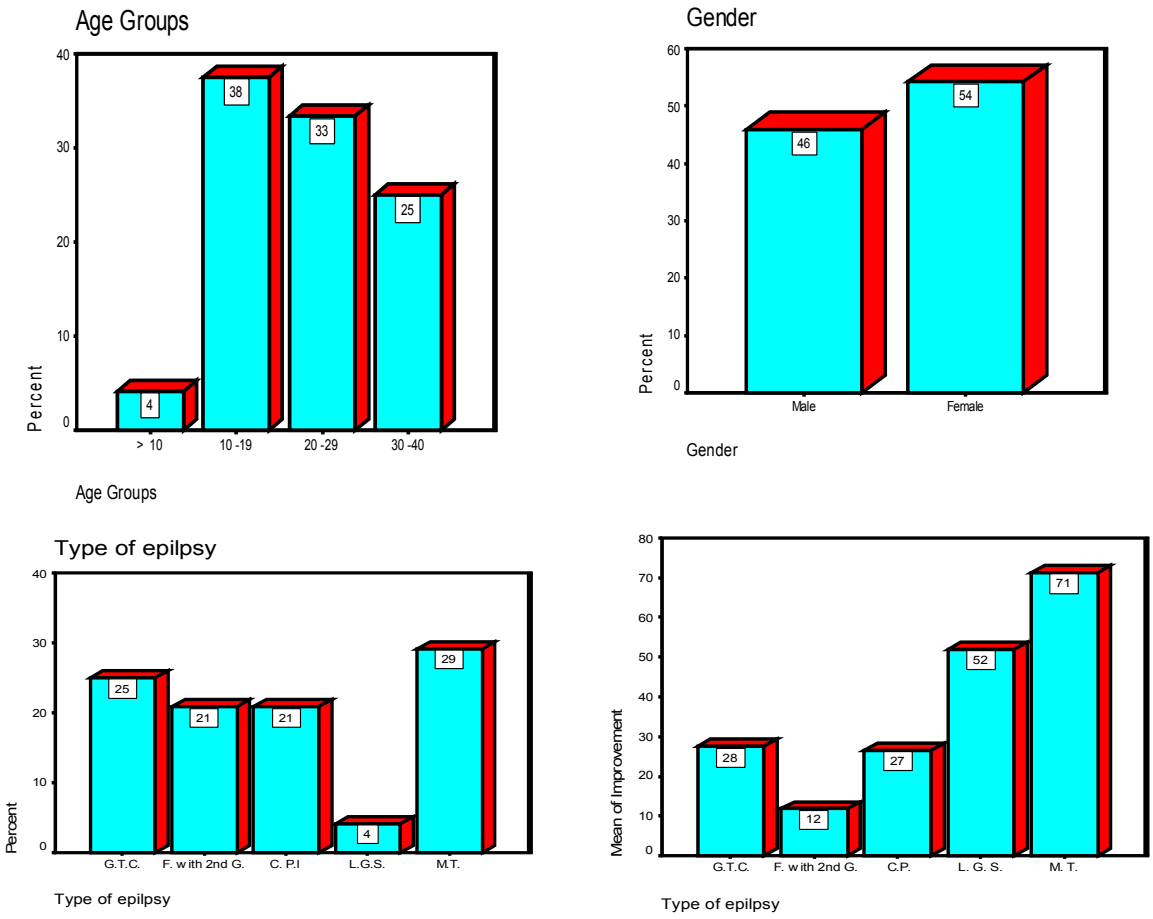
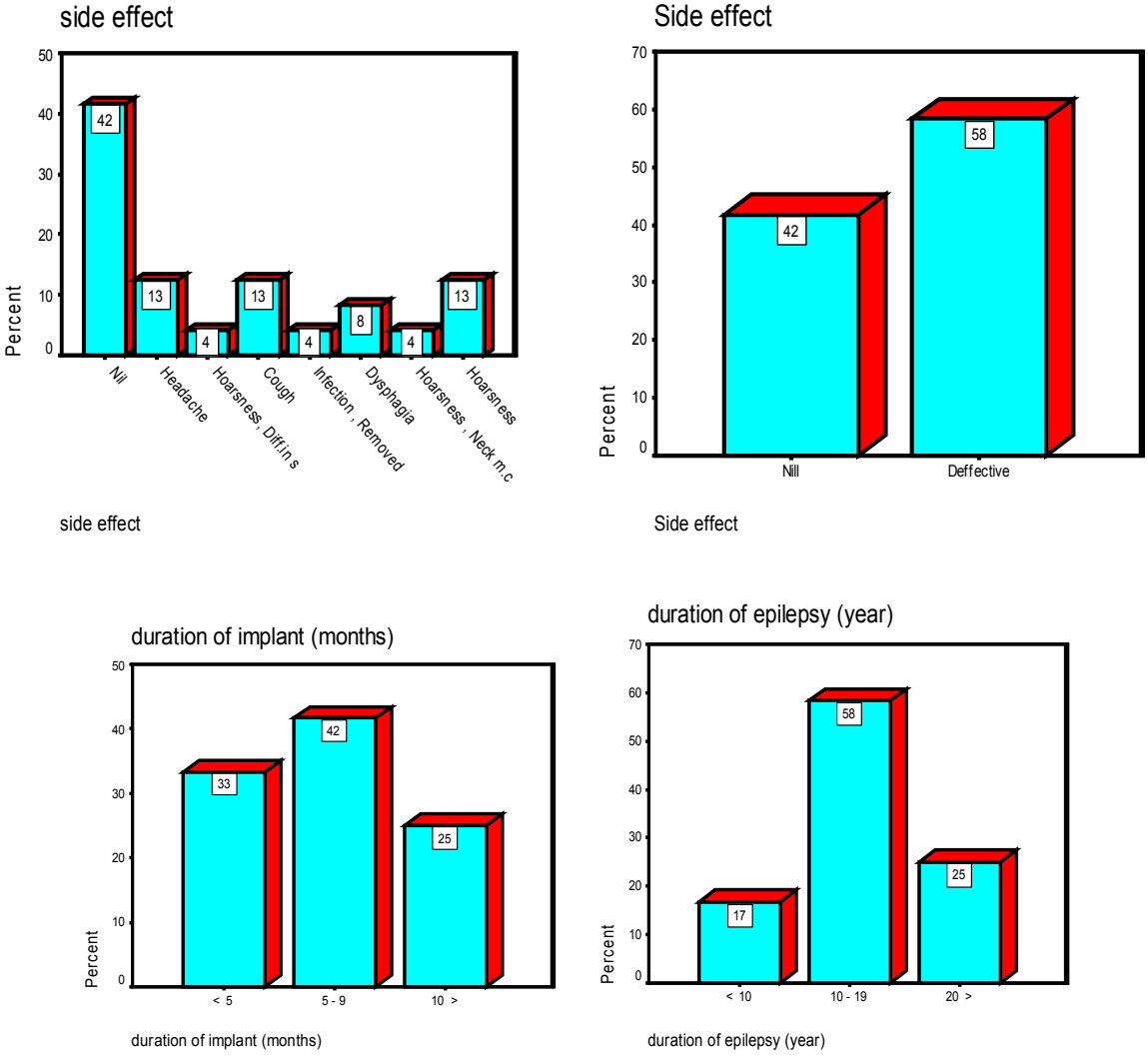


Figure (1) : Bar – charts for studied variables according to their different groups



Bar – charts for studied variables according to their different groups

Discussion:

In this study, the first impressive result is that two brothers from two different families have no more attacks of epilepsy although they had multiple types of seizures, long duration of epilepsy, two implant 10months and the second brothers 8 months duration of implant, which is not present in other studies to compare.

17.39%of patients get full benefit, 47.82% get good benefit (96.6%-- 42.8%), while 34.81%of patients have the same frequency off attacks, within one year of implantation, although the patients with the same attacks may get benefit within the second year, which with other studies that conclude efficacy of VNS appears over the first year [(4)], the efficacy of VNS therapy increased with time with maximal effect at 18-24 months[5].

Gender is not related to the efficacy of VNS, while patients with age above twenty five years old have more benefits than younger age group which agree the study of STeven[(6)] that said interestingly patients whose epilepsy began at older ages and with higher seizures rates at base line had the most favorable response to VNS therapy.

In our study we found that the patients with prolong epilepsy history get more benefit than others which disagree with other study done by J.Ben[(7)] who said earlier identification of appropriate candidates for VNS therapy (after two or three antiepileptic drugs and duration of epilepsy less than two years)would enhance seizure control and subsequent quality of life, this disagreement may be due to low number of patient in

our study notifying that VNS done in Iraq for the first time at 24-2-2008.

Patients with generalized tonic clonic epilepsy, myoclonic and tonic clonic,and complex seizure have more benefit than focal with secondary generalization, which may needs a resective surgery rather than VNS, although all types gets some form of decreasing frequency of seizure, which agree with all studies that said at least of patients with refractory epilepsy get benefit from VNS, there is now strong level 1 that VNS is an effective treatment for patients with partial onset seizure ,there is level 2 evidence that VNS is effective in most seizure types from large open studies with long term follow up indicating a broad range of activity, currently VNS devices are being implanted in patients with refractory seizures who cannot have resective surgery or have had surgery with poor results.[8]

A 6year old child with Lennox Gastaut syndrome on four drugs get benefit 86.6% decreased attacks frequency which agree with Frost[9] Helmers[10]VNS therapy appears to be particularly effective in treatment drop attacks in patients with Lennox Gastauat patient.

We found in our study that the VNS is safe and well tolerated by patients and the side effects were mild and easy to manage, that goes with studies in which most of acute complication of VNS implantation have been common infections vocal cord paresis lower facial weakness and in few cases bradycardia and a systole [11], the most common adverse side effect are stimulus relating coughing ,throat pain and hoarseness, all of which to improve with time[5].

***Conclusion &* Recommendations:**

1. Vagal nerve stimulation is a good adjunctive palliative therapy for patient with refractory epilepsy as alternative to resective surgery.
2. It is effective safe and well tolerated. we can use vagal nerve stimulation as an adjuvant therapy for patients with refractory epilepsy rather than doing many trials with many drugs consuming time and side effect of drugs for the patients.

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