

Epilepsy 2019: Vagus Nerve Stimulation (VNS) is an adjunctive treatment in Iraqi patients with drug resistant epilepsy – Anmar Oday Hatem - Baghdad Teaching Hospital

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Background: Despite the introduction of new antiepileptic drugs (AEDs) and advances in the surgical treatment of epilepsy, an important group of patients still remains uncontrolled by any of these methods. Vagus nerve stimulation (VNS) is an adjunctive treatment for those with drug resistant epilepsy. In addition to the reduction in seizure frequency, there is other variables need to be assessed for better determination of VNS efficacy like quality of life (QOL) improvement.

Aims of the study: Evaluate the effectiveness of VNS, for Iraqi patients with drug resistant epilepsy, in reducing seizure frequency and improving QOL of these patients.

Method and Patients: Forty-six patients of drug resistant epilepsy were retrospectively examined. They underwent implantation of a stimulator in Baghdad medical city during 2015, and with a follow-up of one year. They were 25 male and 21 females, and their ages at VNS implantation was ≥ 18 year old for 28 patients and between 11-17 year old for 18 patients. Analysis of seizure reduction (using McHugh classification) with the effect of demographic and clinical variables on it, and assessment of QOL (using QOLIE-35 and QOLIE-AD 48 scales) were done in this study. SPSS v.22 was used for the statistical analysis.

Results: The total well response rate (including class I and II and equal to reduction in seizure frequency $\geq 50\%$) was 58.7 % (27/46 patients), 6 cases became seizure free, and 6 cases reported no improvement, we also found that the factors of gender, age and predominant seizure type had clinical outcome effects. The mean seizure frequency and number of AEDs that used by the patients reduced. The mean of all domains and overall score of QOL scales improved and some domains had statistically significant improvement.

Conclusion: VNS is a safe, well-tolerated and effective treatment in reducing seizure frequency and improving QOL for patients with drug resistant epilepsy.

Patients and Methods: This study is designed as a retrospective study to analyze the efficacy and tolerability of VNS Therapy in patients with drug resistant epilepsy. The study conducted at medical city in Baghdad/ Iraq. The surgical procedure performed during 2015 and all data are collected retrospectively during the follow up visits at 2016 in the epilepsy clinic of Baghdad Teaching Hospital, these data are

collected from the patients, their families and their available medical records from baseline to 12 months after VNS implantation. Forty-six patients diagnosed as drug resistant epilepsy, according to ILAE criteria (6), and on VNS Therapy were interviewed and enrolled in this study. Detailed demographic and clinical data can be seen in table (1).

VARIABLE	DATA
Gender	
Male	25(54.35%)
Female	21(45.65%)
Age at VNS implantation	
Adolescent (11-17 years)	18(39.1%)
Adult (≥ 18 years)	28(60.9%)
Age at seizure onset(year)	8.283 \pm 7.1854
Type of epilepsy	
Focal	27(58.7%)
Generalized	19(41.3%)
Age at VNS Implantation(years)	24.130 \pm 11.3169
Duration of epilepsy (years) prior to VNS implantation	15.674 \pm 9.5127
No. of AEDs	
Prior to VNS	2.957 \pm 0.7588
After one year of VNS	2.652 \pm 0.6739
Seizure frequency (per week)	
prior to VNS (baseline)	7.696 \pm 3.8173
after one year of VNS	3.978 \pm 4.5680

The QOL assessed through a standard scale for each age groups. The QOLIE-31 scale used as a survey of health related QOL for adult patients (≥ 18 year-old), while the QOLIE-AD-48 designed for adolescent patients (11-17 year-old) (7,8,9).

The Results:

The seizure frequency outcomes after one year of follow up according to the McHugh classification is shown in table (2).

Adverse effects/surgical complications	n (%)
change of voice (hoarseness)	26(56.5%)
Cough	20(43.7%)
Temporary difficulty in swallowing	12(26%)
Throat tangling/ tightness sensation	4(8%)
Throat pain	4(8%)
Shortness of breath	4(8%)

For all patients, the mean frequency of seizure prior to VNS implantation was 7.69 ± 3.81 per week, while after 1 year of VNS was 3.97 ± 4.56 per week, the p-value was significant for this reduction (0.002).

Regarding the age at VNS implantation, there was significant response to VNS therapy in both age groups, with more response rate among those with 11-17 year-old, and according to the seizure type, the response was well in both groups but it was significant in patient with predominant focal seizure type.

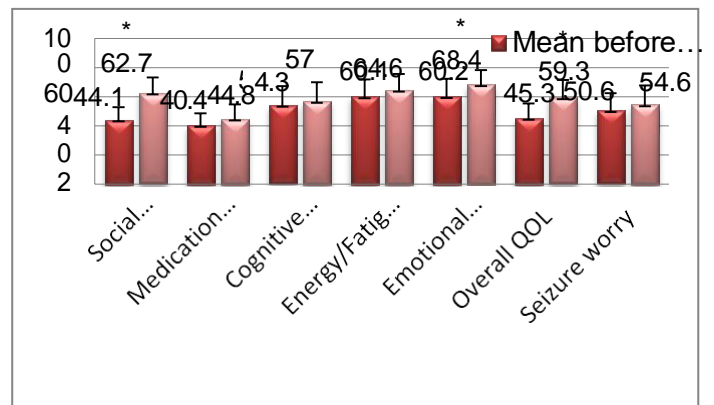
The mean number of AEDs taken by our patients was 3.13 ± 0.45 for the pre-VNS period while this number decreased to 2.739 ± 0.53 in the post-VNS period. So, there was significant reduction in AEDs number after VNS therapy.

The side effects and complications that are considered to be related to VNS were analyzed in our study as shown in table (3).

Table (3): Side effects and complications following VNS implantation in 46 patients with treatment-resistant epilepsy.

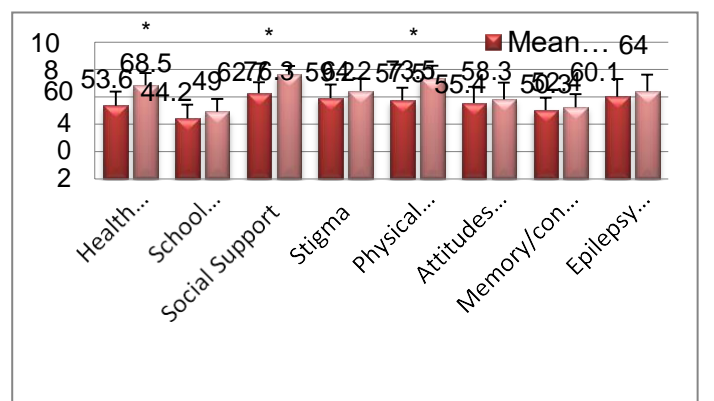
Adverse effects/surgical complications	n (%)
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Cough	20(43.7%)
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According to the QOLIE-31 data for ≥ 18 -year-old patients, all domains showed improvement, but not all were statistically significant. Domains with higher impact (statistically significant) from VNS therapy were social functioning, scoring 44.1 ± 8.8 before VNS therapy and 62.7 ± 10.5 after therapy; emotional well-being, scoring 60.2 ± 12.1 before treatment and 68.4 ± 9.9 after treatment; and overall quality of life, scoring 45.3 ± 10.3 before treatment and 59.3 ± 12.1 after treatment (Figure 1).



(*) significant p-value < 0.05

For those between 11-17 year-old and according to the QOLIE-AD-48 data, all domains showed improvement, but not all were statistically significant. Domains with higher impact (statistically significant) from VNS Therapy were health perception, scoring 53.6 ± 10.1 before and 68.5 ± 8.9 after VNS Therapy; social support, scoring 62.7 ± 7.9 before and 76.3 ± 6.2 after treatment; and Physical Functioning, scoring 57.5 ± 9.1 before treatment and 73.5 ± 9.3 after treatment (Figure 2).



(*) significant p-value < 0.05

Figure (2): Overall results from QOLIE-AD-48by score subscales before and after VNS (n = 18).

The overall score for both QOL scales are derived from weighting and summing the domains score according to specific formula. It is found that there was significant improvement in overall score after 1 year of VNS Therapy for both scales in both age groups as shown in table (3.11).

Overall score	Before	After	p-value
QOLIE-31	51.5	60.2	0.007*
QOLIE-AD-48	54.9	61.6	0.003*

(*) significant p-value< 0.05

Discussion:

Based on clinical observations, the effects of VNS treatment vary from one patient to other. In our study, we investigated the efficacy of VNS Therapy in 46 Iraqi patients with drug resistant epilepsy. The VNS was shown to be an effective add-on treatment for these patients as 58.7% of patients had a good (McHugh class I, II) outcome ($\geq 50\%$ reduction in seizure frequency after one year of VNS therapy) and these results is agreed with many studies like Kamelet al (2013)(10),García-Navarrete et al(2013)(11), Arcos et al(2014)(12),Mengetal (2015)(13) and Englot et al., (2016)(1).

The results from different case series have shown an extremely variable reduction in seizure frequency after VNS (between 11% - 70%), e.g. only 11.3% (5/44) of patients had more than 50% reduction in seizure frequency according to Pakdamanetal (2016) (14). This variability in the results may be due to differences in patients' selection criteria and outcome assessment as the efficacy increased with increasing of the duration after VNS Therapy. Englot et al (2016) (1) reported progressive increase in the rate of seizure freedom, rate of

response to treatment, and median decrease in seizure frequency were observed over time.

Also in our study, there was a significant reduction in the average number of seizures per week in response to VNS and this is agreed with Kamelet al (2013)(10).

By analysis of our results, we found that there is significant response in both age group (adult and adolescence), but higher among adolescent patients, and there was significant value for this variable, this is agreed with Colicchio et al (2012)(15). Although there was well response for both patient groups with generalized or focal predominant seizure, but the response was significant in patients with predominant focal type, this results is agreed with Alonso-Vanegas et al(2010)(16). Also, there was significant reduction in number of drugs used by the patients and these results are compatible with Kamelet al (2013) (10). The side effects of VNS are widely variable and reported with different percentage in other studies. Other benefits from VNS, in spite of seizure control, should be evaluated as the improved QOL might be an alternative significance of VNS Therapy in drug resistant epilepsy. Regarding QOLIE-35 scale, all domains improved. The highest post VNS mean score was in emotional well-being domain, and lowest one was in medication effect domain, this may be due to that all patients remain on AEDs and most of them take same number of medication after VNS.

The significant improvement seen in social functioning, emotional well-being, and overall quality of life domains and this is agreed with Alonso-Vanegas et al(2010)(16) who reported also significant improvement in energy domain, but it isn't agreed with McLachlan et al(2003)(3), which reported significant improvement in cognitive domains.

Regarding QOLIE-AD 48 scale, all domains also improved. The highest mean score was in social support, and the lowest one was in school behavior domain, this may be due to lack of special school for these patients or because of the priority for the patients and their relatives was to control the seizure and to improve social integration rather than school performance. The

significant improvement was seen in health perception, social support, and physical functioning domains. The difference in the results of QOL assessment between studies may be due to the reason that different countries have different cultures beliefs and socioeconomic factors which in turn can affect QOL measures.

Also, these results were subjective, since they based on communications with the patients or their relatives, and not on objective standards or measurable physiological responses.

Conclusion:

In patients with drug resistant epilepsy, VNS is a safe, well-tolerated and effective treatment, but it is not considered as a first line therapy and instead is considered only after medical therapy has failed and a patient has been unsuitable for resection or is unwilling to accept the risks of surgery. the VNS is effective in reducing seizure frequency and improving of QOL in patients with drug resistant epilepsy after VNS Therapy.

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