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THE EFFICACY OF VAGUS NERVE STIMULATION (VNS) ON OUTPATIENT DRUG RESISTANT EPILEPSY PATIENTS : A CASE – SERIES FROM THE JORDANIAN ROYAL MEDICAL SERVICE

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ABSTRACT

Background: Epilepsy affects up to 1% of the general population. it poses huge challenges for patients, their families, and the health sector.

Objective: To investigate the impact of VNS on lowering the number of seizures among patients with epilepsy.

Method: A total of 23 patients were included in this study. VNS was applied as a therapeutic model in these patients. The impact of VNS on lowering the number of seizures was measured. Data of patients included age, gender, and number of seizures pre-VNS and post-VNS.

Results: The main findings of the present study were that VNS significantly lowers the number of seizures per week. The improvement percentage was about 60%.

Conclusion: VNS is an effective therapeutic strategy to overcome seizure problems among patients with epilepsy.

KEYWORDS: Vagus nerve stimulation, Implantation, Complications, Outcome.

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INTRODUCTION

Epilepsy affects up to 1% of the general population [1], and it poses huge challenges for patients, their families,and the health sector. This includes psychological issues (e.g. depression and anxiety), social stigma and demarcation, physical injuries (e.g. fractures), permanent brain damage, early death, drug cost and their side effects, and gestation troubles on the mother and her child [1]. Refractory epilepsy is set up in at least 30% of all epileptic cases [2]. And despite 14 new AEDs entering the market in the last 15 years, the rate of refractory epilepsy has not been significantly reduced [3]. Approximately 75% of patients on AEDs discontinue therapy within 5 years, whereas only 20% of VNS patients discontinue therapy [4, 5]. Cost accounting for extra hospitalizations due to seizures suggests that the savings of VNS versus medicines are significant [5, 6]. The concept of using electricity for treating epilepsy goes back to 76 A.D.,when the Greek Pedanius supported seizure treatment with the electric torpedo ray [5]. Then the idea was tested through the ages including the trials that were conducted during the 11th century, by Ibn-Sina, who used the electric catfish on the brow of the afflicted [5]. The Electrical basis of seizures was noticed for the first time by Todd, in the 19th century [7], which was followed by great efforts that ended with recordings of the first human EEG via scalp by Burger, in 1929 [8]. Experiments on animals were first conducted in 1938, by Bailey & Bremer [9]. The first human vagal nerve stimulator was done by William Bell, a pediatric neurosurgeon, in 1988 [10]. Grounded on the following clinical trials, VNS was approved by the US Food and Drug Administration (FDA) in 1997, as an adjunct for the treatment of refractory epilepsy [1, 4, 6, 11]. Since 1999, several studies have proven the effectiveness and safety of VNS in both children & adults with different types of seizures [4, 11]. The exact mechanism(s) of VNS by which it reduces the frequency of epilepsy is still unclear [11, 12, 13], suppositions include de-synchronization of neuronal activity, changes in the limbic circuit, alteration of the levels of certain neuro mediators, alteration of the blood inflow to certain cortical and nuclear regions, and stimulation of the anti-inflammatory hypothalamic-pituitary-adrenal pathway [5, 11, 12, 13, 14, 15]. What remains sure is that the vagus nerve has diffuse central projections that ultimately enable seizure reduction by its stimulation. VNS is indicated for refractory seizures for ≥ 9 months which are either due to non-localizable focus or localizable lesion that fail or unsuitable for resection or with bilateral cortical localization [1, 2, 5]. Drug-resistant epilepsy is defined as failure of two AED regimens with appropriate type, dose, and duration to control seizure [10]. All of the contraindications are relatives and include cases who bear a full voice all the time e.g. teacher, requiring regular MRI in the exclusion zone, oppressively immune-compromised, with severe coagulopathy, or with severe cardiac arrhythmias [1]. Epilepsy patients who had tried ≤ 4 seizure medications or who were implanted with the VNS within 5 years of onset of the seizure were three times more likely to report no seizures after 3 months of treatment than those who had received the device after failing more medications or waiting > 5 years [5]. The side-effect profiles of VNS is very low and most of them occur only during stimulation and generally diminish over time [1]. The complications of VNS can be classified as early which is directly related to the operation and late which are related to the nerve stimulation and the device. Early complications include intraoperative brady-arrhythmias, hematoma, infection, and injury to the vagus nerve, inferior (recurrent) laryngeal nerve and thoracic duct. The most common late complications are infections and wound dystrophy. Late complications are linked to vagus stimulation and include bradyarrhythmias, laryngeal disorder(s), obstructive sleep apnea, irritation of the phrenic nerve, tonsillar pain like in glossopharyngeal neuralgia [15, 16]. Some of these complications (if not all) can be reversed by adjusting the stimulation parameters [15]. Laryngeal dysfunction is the most common complication, reported in about 50-60% of patients, occurs due to the stimulation of the inferior laryngeal nerve, and presented as transitory (uncommonly permanent) coughing, hoarseness of voice, and dyspnea [15, 17]. Other reported late complications include corrupt of the device e.g. in mentally retarded patients (twiddler's' syndrome), vagal nerve stretching due to short strain loop relief, and increased drooling and hyperactivity in pediatrics [18].

MATERIALS AND METHODS:

All patients, who underwent VNS implantation at our center, were obtained from operating room records. King Hussein Medical City's (KHMC) ethical committee gave the study its approval. Those with drug-resistant epilepsy (focal or generalized) of various ages were included. Three separate neurosurgeons implanted the VNS devices, and in every case, the devices were programmed in the operating room by accepted medical practices. The initial stimulation settings were (Output current = mA, frequency = Hz, pulse width = ms, signal on-time = s, and off-time = min). Clinic visits for follow-upand adjustment of the device occurred at every 2 months for the 6 months and every 6 months thereafter. Within the 1-2 months before to surgery, each patient underwent at least one baseline evaluation. Data on the frequency of seizures was then collected from patients' routine follow-up appointments.

RESULTS:

As seen in Table (1), the general characteristics of participants are described. Male participants were predominant (approximately 60%). Regarding age group, most participants were pediatrics (about 83%).

Table 1: General characteristics of participants

Gender (N, %): - **Male** - **Female**	 **14 (60.1%)** **9 (39.1%)**
Age groups (N, %): - **Pediatric** - **Adult**	 **19 (82.6%)** **4 (17.4%)**
No. of seizures pre-VNS per week (M±SD)	**27.22±26.93**
No. of seizures post-VNS per week (M±SD)	**9.04±10.80**
Seizure severity (N, %): - **Mild** - **Severe**	 **23 (100%)** **0 (0%)**
No. of AED (M±SD)	**2.83±0.49**
Improvement percent (M±SD)	**61.04±20.37**

As indicated by Table (2), the percent improvement was not impacted by the study variables including "Number of seizures pre-VNS per week" (p=0.432), "Number of seizures post VNS per week" (p=0.178), and "Number of AED" (p=0.930).

Table (2): The relationship between the percent improvement and study variables

		Sum of Squares	df	Mean Square	F	Sig.
Number of seizures pre-VNS per week	Between Groups	8393.613	11	763.056	1.111	0.432
	Within Groups	7556.300	11	686.936		
	Total	15949.913	22			
Number of seizures post VNS per week	Between Groups	1640.490	11	149.135	1.775	0.178
	Within Groups	924.467	11	84.042		
	Total	2564.957	22			
Number of AED	Between Groups	1.504	11	.137	.396	0.930
	Within Groups	3.800	11	.345		
	Total	5.304	22			

The impact of VNS on the number of seizures among patients

As shown in Table (3), VNS was able to significantly lower the number of seizures from 27.21±26.93 per week to 9.04±10.98 per week (p=0.000).

Table (3): The impact of VNS on the number of seizures among patients

	Mean	N	Std. Deviation	Significance
Number of seizures pre-VNS per week	27.2174	23	26.92575	0.000
Number of seizures post -VNS per week	9.0435	23	10.79764	

The relationship between the gender and study variables

As illustrated in Table (4), there was no any significant relationship between the gender and study variables such as "Number of seizures pre-VNS per week" (p=0.511), "Number of seizures post-VNS per week" (p=0.825), "Number of AED" (p=0.4436), and "Improvement percent" (p=0.389).

Table 4: The relationship between the gender and study variables

Variable	Significance
Number of seizures pre-VNS per week	0.511
Number of seizures post-VNS per week	0.825
Number of AED	0.436
Improvement percent	0.389

The relationship between age and study variables

As shown in Table (5), there was no any significant relationship between age and study variables (p>0.05).

Table 5: The relationship between age and study variables

Variable	Significance
Number of seizures pre-VNS per week	0.826
Number of seizures post-VNS per week	0.261
No of AED	0.426
improvement percent	0.052
Gender	0.483

DISCUSSION:

The results of the present study showed that VNS was able to significantly lower the number of seizures per week (p=0.000).

Vagus nerve stimulation can dramatically reduce the frequency of seizures per week. VNS therapy is utilized when conventional medicinal interventions for epilepsy are ineffective in achieving seizure management [19].

Individuals with epilepsy must prioritize reducing the frequency of their seizures to enhance their overall quality of life. Seizures have a detrimental and disruptive impact on multiple facets of everyday life, such as social interactions, occupational performance, and personal safety [20]. Vagus Nerve Stimulation (VNS) has the potential to greatly decrease the occurrence of seizures in patients weekly, leading to significant respite and improvement in their overall quality of life [21].

The results offer evidence for the practical effectiveness of VNS in managing epilepsy. This finding is consistent with prior research and real-world patient data that confirm the effectiveness of VNS when used alongside pharmacological treatments for epilepsy that do not respond to drugs [22]. The vagus nerve is stimulated by VNS, which causes changes in brain activity and decreases the chances of having a seizure [23].

Practitioners may utilize Vagus Nerve Stimulation (VNS) as a treatment for individuals with drug-resistant epilepsy who continue to have seizures even after taking medication. Before implementing VNS, it is important to take into account the individual needs, preferences, and therapeutic goals of each patient. It is advisable to have a consultation with a neurologist or epileptologist [24].

While the current study offers strong evidence for the benefits of VNSs, more research is needed to investigate other aspects such as the long-term effects, appropriate amounts of stimulation, and factors that determine treatment outcomes. Comparative study can provide insights into the effectiveness of VNS compared to other treatments for drug-resistant epilepsy [25].

CONCLUSION:

The finding that VNS significantly decreased the frequency of seizures weekly highlights the promise of this technology as an effective treatment option for medication-resistant epilepsy. Nevertheless, the determination of targeted therapy must be backed by a thorough clinical assessment and individualized patient attributes.

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