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Vagus nerve stimulation therapy in a developing country: A long term follow up study and cost utility analysis

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ABSTRACT

Purpose: To evaluate clinical outcomes, quality-adjusted life years (QALY), cost effectiveness and cost utility associated with VNS therapy in children with refractory epilepsy in a developing country.
Methods: Retrospective review of all children who underwent VNS implantation at King Abdullah University Hospital and Jordan University Hospital in Jordan.
Results: Twenty eight patients (16 males) had implantation of the VNS therapy system between the years 2007 and 2011. Mean age at implantation was 9.4 years. Mean duration of epilepsy prior to implantation was 6.5 years. The most common seizure type was generalized tonic clonic seizures. Fifteen patients showed a 50% or more reduction in seizure frequency. There was a significant reduction in total number of seizures ($p = 0.002$) and emergency room (ER) visits ($p = 0.042$) after VNS therapy. Atonic seizures were more likely to respond than generalized tonic clonic seizures, $p = 0.034$. Direct hospital costs prior to VNS implantation were analyzed in relation to ER visits and intensive care unit (ICU) admissions. Cost savings per patient did reduce the financial burden of the device by about 30%. There was a QALY gain per lifetime of 3.78 years for children and 1 year for adolescents.
Conclusion: Response to VNS implantation in Jordan was favorable and similar to what has been previously reported. QALY gain and cost per QALY analysis were encouraging. Cost savings were related to reduction in seizure severity. In circumstances of limited resources as in developing countries, targeting patients with frequent utilization of health services would improve cost effectiveness.

1. Introduction

From its approval by the FDA in 1997 for the treatment of refractory partial epilepsy, the vagus nerve stimulation (VNS) therapy system has been implanted in over 100,000 patients worldwide.[1] Numerous reports have established VNS therapy as a safe and effective treatment option for children and adults who have refractory epilepsy.[1–6] The cost effectiveness of VNS therapy has also been assessed and established in the developing world, [7,8] however there are very little reports on its use in developing countries,[9] and none that address cost related issues. In this report, we describe the experience with VNS therapy in children with refractory epilepsy from the two major university hospitals in Jordan, and perform an analysis of direct hospital costs and cost utility.

2. Materials and methods

This is a retrospective review of all children who underwent VNS implantation at King Abdullah University Hospital, and Jordan University Hospital. King Abdullah University Hospital is an urban, JCIA[a] accredited, tertiary referral hospital in the north of Jordan, and Jordan University Hospital is a JCIA accredited tertiary referral hospital in the capital Amman. Detailed clinical evaluation, brain magnetic resonance imaging results, and electroencephalography results were collected for all patients. Parents were instructed to keep seizure diaries for at least two months prior to implantation of the device, and to continue with the diaries after implantation.

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[a] JCIA: Joint Commission International Accreditation.

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Data regarding seizure frequency, seizure severity, and complications of VNS therapy were collected every visit, as was data regarding the child's behavior, alertness, and interaction. Seizure severity was assessed by duration of seizures, intensity of convulsive phenomena, loss of posture or injury during seizures, frequency of status epilepticus episodes, duration of postictal phenomena, and speed of recovery. The McHugh VNS specific outcome scale was utilized for assessment of seizure frequency and severity after implantation.[10]

Data regarding frequency of emergency room visits, ward admissions, and intensive care unit admissions pre and post VNS implantation was collected retrospectively from patients' medical records and from caregivers.

QALY was calculated as the product of age specific life expectancy and average utility scores. Utility scores utilized were determined using data from Forbes et al.[11] A utility score of 0.848 was assigned to the months where patients' seizure frequency was less than once a month, and a utility score of 0.681 was assigned to the months where patients' seizure frequency was more than once a month. A utility value of 0.285 was assigned to patients with more than 50% reduction in seizure frequency. QALY was calculated for the 6 months prior to VNS implantation and the total post VNS period. Cost per QALY was calculated by dividing net cost (total cost minus costs averted) by the number of QALYs gained over a six year period (assuming battery life of 6 years).

The study was approved by the ethics committee.

3. Statistics

Statistical summaries were used to describe dependent and predictor variables. An ordinal logistic regression was utilized when dependent variables were counts, and was fitted for comparisons between the pre and post VNS periods regarding number of seizures and ER visits. ANOVA and correlations were utilized when the dependent variables were continuous; ANOVA was fitted for evaluating the effect of gender and seizure type on seizure frequency reduction, and correlations with confidence intervals of 95% were calculated to evaluate the effect of age of epilepsy onset, age at VNS surgery, and duration of epilepsy on seizure frequency reduction. When multiple comparisons were needed (e.g. effect of different seizure types on seizure frequency reduction) Tukey HD method was used. JMP software was utilized for analysis with $\alpha = 0.05$.

4. Results

4.1. Patient characteristics

Twenty eight patients (16 males) had implantation of the VNS therapy system between the years 2007 and 2011, Table 1. One

Table 1
Clinical characteristics of children who underwent VNS implantation.

Pt	Seizures	Etiology	Epilepsy duration[a]	VNS age[a]	Follow up[a]	Seizure frequency reduction	Seizure frequency after VNS	Seizure severity reduction
1	FS	Cerebral calcifications	5	9	5.5	100%	None	
2	FS	Unknown	9	15	6.5	>90%	Once/few months	Rapid recovery Shorter seizures
3	A	Perinatal insult	6	6	5	>90%	Once monthly	Abolished drops
4	FS	Unknown	3	8.5	5	>90%	<once monthly	Rapid recovery
5	A	PVL	3	4	6	>90%	<once monthly	
6	GTC	Unknown	9	16	6.5	70–90%	Twice/month	Rapid recovery No status
7	FS	Bilateral MTS/Dravet	2	2.5	4.5	70–90%	<once monthly	Rapid recovery No status
8	GTC, M,A	Pachygyria	16	16	5	70%	Twice/week	Abolished drops
9	FS	Unknown	5	9	3	70%	Once/10 days	
10	GTC, A	Dravet	5	6	4	70%	4 sz/week	Abolished drops Non convulsive, rapid recovery
11	FS	Unknown	5	13	5	50%	Weekly	Rapid recovery
12	GTC, M,A	Unknown	2	3	5	50%	Daily brief	Abolished drops, shorter GTC, rapid recovery
13	GTC	Unknown	9	11	5	50%	Twice/week	Rapid recovery
14	FS	Unknown	9	10	5.5	50%	Twice/week	Abolished daytime seizures
15	GTC,A	Dravet	1	2	5	50%	Weekly	Abolished drops, rapid recovery
16	FS,M	Ischemic stroke	3	9	4.5	50%	Once/week	Shorter seizures
17	FS,GTC	Unknown	5	6	6	30%	Once/week	Rapid recovery, nonconvulsive
18	GTC	Unknown	8	9	5	30%	4 sz/week	
19	GTC	Unknown	3	5	6	30%	Twice/week	Abolished daytime seizures
20	GTC,FS	Brain RTX	10	13	5.5	None	Daily	
21	GTC,A	Unknown	3	5	6	None	Once/week	Device removed
22	GTC,A	Brain atrophy	7	8	5.5	None	Daily	
23	GTC,A	Unknown	14	15	5.5	None	Twice/month	
24	FS	CD/postop	11	12	5	None	Daily	Device removed
25	FS	CD	13	19	6.5	None	Daily	
26	FS	Unknown	2	11	4.5	None	Once/week	Device turned off
27	GTC	Unknown	5	9	3.5	None	Once/week	

[a] In years.
FS: focal seizures, A: atonic, GTC: generalized tonic clonic, M: myoclonic, PVL: periventricular leukomalacia, MTS: mesial temporal sclerosis, RTX: radiotherapy, CD: cortical dysplasia.