Efficacy and Safety of Sacral Neuromodulation in Treatment of Refractory Overactive Bladder

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Abstract

Background*:* Overactive bladder syndrome is a urinary disorder that occurs more frequently in women and older people and is characterized by feeling an urge to urinate (sudden urge to urinate, with the feeling that you cannot get to the bathroom in time), doing it many times throughout the day (more than six) or having episodes of urinary incontinence (involuntary loss of urine) and nocturia (waking up several times during the night to urinate). In addition, other secondary symptoms may also occur, such as headache, dry mouth or blurred vision, among others. It is a problem that has a clear impact on the quality of life of those who suffer it and that can lead them to significantly reduce their social activity and negatively condition their work.

Overactive bladder (OAB) is defined as urinary urgency with or without urgency urinary incontinence, nocturia, and/or frequency in the absence of UTI or other obvious pathology. Sacral neuromodulation is a newer surgical therapy for refractory OAB.

Aim of Study*:* Is to assess the sacral neuromodulation (SN) safety and efficacy in refractory overactive bladder patients.

Patients and Methods: In the period from November 2015 to May 2017. the unit of neurogenic bladder and neuromodulation in (Gazi Al_Harriry) surgical specialty hospital, medical city complex 27 patient aged from (17—55) year old were complaining from refractory overactive bladder. All the 27 patients underwent stage1 & stage2 SNS devices implantation.

Results: Patients of urgency incontinence (group1) demonstrated that the number of leak was significantly reduced (p=0.01) after implantation of SN, (11.6_2.7) leak/day pre& post SN, numbers of pads (6.9 _ 0.8) pad/day pre&post SN. Patients with urgency frequency (group 2), numbers of voids/day pre & post SN implantation decreased significantly (p=0.01) (14.7 _ 6) voids /day. The voided volume increased significantly (p=0.02) from (136.4 _ 371.8) ml/void. The urgency episodes were decreased significantly (p=0.01) from (6.4 _ 2.1) episode/day. The complications occurred in 5 patients (18.5%). Two patients (7.4%) developed pain after trauma to the back, lead migration, lack of efficacy of device, treated by reprogramming the device, one patient (3.7%) get infection at the site of device implantation, SN was removed , there was one female patient (3.7%) got pregnancy and devise was deactivated. One patient (3.7%) complaining from pain and discomfort at the device site was treated conservatively.

Conclusion: Sacral neuromodulation is FDA approved as option for treatment of refractory OAB. There is expanding of utilizing of SN in the past two decades. According to multiple studies in addition to our study results. The sacral neuromodulation is safe and efficacious treatment option for refractory OAB.

Keyword: *Neuromodulation, OAB, UTI, incontinence*

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Introduction

Overactive bladder syndrome is a urinary disorder that occurs more frequently in women and older people and is characterized by feeling an urge to urinate (sudden

urge to urinate, with the feeling that you cannot get to the bathroom in time), doing it many times throughout the day (more than six) or having episodes of urinary incontinence (involuntary loss of urine) and nocturia (waking up several times during the night to urinate). In addition, other secondary symptoms may also occur, such as headache, dry mouth or blurred vision, among others. It is a problem that has a clear impact on the quality of life of those who suffer it and that can lead them to significantly reduce their social activity and negatively condition their work.

During the nineteens of the 20th century the Overactive bladder was described at the first as group of bladder storage symptoms consisting of urgency, frequency, nocturia, and urinary incontinence. (1) These grouping symptoms without diagnosis due to detrusor overexertion, which was an objective urodynamic detection of involuntary detrusor activity. (2) OB is defined as urgency of urination with incontinence or no seizures, night and / or frequency in the absence of IPS. Another obvious pathology. Wet OAB is defined as involuntary loss of urine associated with a strong desire to empty.3 Wet OABs have a huge gradient of severity and can have a significant negative impact on quality of life due to significant annoying symptoms and sudden loss of urinary control. (4)

OAB, specifically moist OAB, symptoms now disturb a significant rate of the population, and the overall prevalence of OAB has been shown to be comparable between men and women. A study conducted in the United States showed a prevalence of OAB in 16% of men and 16.9% of women.(4)

Milsom et al. in their study agree with that mentioned by the population of Europe, with an estimated prevalence of OAB (15.6%) in male and 17.4% in female on reviews finished by patients with in age older than 40 years. A correlation has been found between increasing age and prevalence of OAB wet symptoms. (5) Stewart et al found that the prevalence of wet HF symptoms increases with age for both men and women, and increases significantly after age 44 for women and age 64. For men. Stress and mixed urinary incontinence are also more common in the elderly, but patients with purely moist OAB are more likely to need treatment. (4)

The US Food and Drug Administration approved CH in September 1997 to treat nausea incontinence for those patients who were unsuccessful in managing their symptoms with more conservative therapies. They later approved HF for urinary retention syndrome and urgency. (6)

SN uses electrical stimulation to stimulate the bladder pacemaker, which is the sacral nerves that supply the pelvic floor and lower urinary tract muscles. Using electrical stimulation, you can inhibit or excite neural reflexes. (7)

Aim of the Study: Is to assess the sacral neuromodulation (SN) safety and efficacy in refractory overactive bladder patients.

Patients and Methods

In the period from November 2015 to May 2017. the unit of neurogenic bladder and neuromodulation at (Gazi Al_Harriry) surgical specialty hospital, medical city complex 27 patient aged from (17_55) year old complaining from refractory over active bladder (Patients not responed or not tolerate conservative treatments for more than 3months). All patients undergone full detailed history with physical examination with emphasis on the genitourinary and neurologic examinations, voiding diaries, urodynamic Studies, lumbosacral MRI, and flexible cystoscopy.

Exclusion criteria: -

1. Mechanical bladder outlet obstruction, bladder anatomical abnormalities.

2. Patient's planning to undergo diathermy (shortwave; microwave; ultrasound) or MRI in the future.

3. Inadequate response during test stimulation intra op.

4. the patient unable to operate the device.

5. patient age less than 16 years.

6. Pregnancy.

7. Anatomical bony abnormalities of the sacrum, in which trans foraminal access could be difficult or impossible.

After that we divided these patients in two groups.

- (Group1(16 Patients with urgency incontinence.
- (Group2) 11 Patients with urgency frequency.

All the 27 patients underwent stage1 & stage2 SNS devices implantation. After taking the informed consent from the patients.

Patients are taught keep a bladder diary during the trial stage (2weeks) to assess if there is a significant and worthwhile improvement in OAB symptoms.

If the test stage success in reducing the symptoms of bladder overactivity by at least (50%) in at least one of the following then we can proceed to permanent pulse generator implantation[19]:

The advantage of the test stage is the ability to test out the SNS device over several days to see if it is suits the individual before committing to the treatment.

The patient and doctor decide together before the 2nd stage procedure if the SNS device has made enough of a difference to symptoms to proceed to the permanent pulse generator implantation.

All patients were reevaluated using voiding diary After two weeks , one month, three , six months and 1 year after the insertion of permanent SNS device and seeking for complication if found .

Statistical Analysis

SPSS version 23 was used for data entry and analysis. Mean and standard deviation were used to represent the numerical data while the frequency and percentage was used to represent the categorical data. Appropriate tests (chi square test, paired sample t test) were used to confirm significance where the significance level was set at p <0.05.

Results

The results showed that the mean age of group with urgency incontinence was significantly lower than that of group with urgency frequency syndrome (26.6 ±3.6 sd, 36.7±2.8 sd) respectively as well as the results revealed that male patients represented 68.8% of first group and 81.8 of later group but the difference was considered non-significant as seen in table 1.

Table.1: Sociodemographic characteristic of studied groups

		Groups				P-value
		urgency incontinence		urgency frequency		
		Mean	SD	Mean	SD	
Age/year		26.6	3.6	36.7	2.8	0.02
		No.	%	No.	%	
Gender	Female	5	31.3%	2	18.2%	0.4
	Male	11	68.8%	9	81.8%	

The results of patients (group1) of urgency incontinence demonstrated that the number of leak was significantly reduced (p=0.01) after implantation of sacral neuromodulation as the mean value of number of leaks was 11.6/day pre implantation of the device and become 2.7 leak/day post implantation of the device with mean difference of 8.9 leaks/day. The same significant difference was reported with mean value of number of pad as it was 6.9 pads/ day before implantation and become 0.8 pads/day after device implantation with mean difference of 6.1 pad/ day as displaced in table 2.

Table.2; mean difference for no. of leak, no. of pad pre and post sacral neuromodulation

	Mean	SD	Mean difference	P-value
No . of leaks /day pre	11.6	3.4	8.9	0.01
No. of leaks /day post	2.7	1.6		
No. of pads/day pre	6.9	2.4	6.1	0.01
No. of pads/day post	0.8	1.1		

The findings of current study of patients with urgency frequency (group 2) showed that the numbers of voids/ day pre & post SN implantation was decreased significantly (p=0.01) from a mean of 14.7 voids/day to 6 voids /day with mean difference of 8.7 voids/day. The voided volume increased significantly (p=0.02) from a mean of 136.4 ml/void to 371.8 ml/void with mean difference of 235.4 ml/void of voided volume. The urgency episodes decreased significantly (p=0.01) from 6.4 episode/day prior to implantation to 2.1episode/day after implantation of the device with mean difference of 4.2 urgency episodes/day as displaced in table 3.

Table.3; mean difference in mean value of void, volume void and urgency episodes pre and post implantation of sacral neuromodulator device

	Mean	SD	Mean difference	p-value
No. of voids/day pre	14.7	2.9	8.7	0.01
No. of voids/day post	6.0	1.5		
volume/void pre	136.4	30.7	-235.4	0.02
volume/void post	371.8	84.7		
urgency episodes pre	6.4	2.2	4.2	0.01
urgency episodes post	2.1	1.3		

Our data indicated that complications were reported with three cases of (group1) with urgency incontinence.1st one device was deactivated after pt. discovered pregnancy, 2nd one; patient developed pain & discomfort at device site that treated conservatively and 3rd one; patient got pain after trauma to the back, lead migration and lack of device efficacy treated by reprogramming the device .

While complication reported with two cases of (group2) with urgency frequency ,1st case developed pain after trauma to the back, lead migration and lack of device efficacy treated by reprogramming the device, and 2nd case developed pain due to surgical site infection where device was removed. as seen in table 4.

Table.4; Incidence rate of complications with two groups

Complications	Groups			
	urgency incontinence		urgency frequency	
	No.	%	No.	%
device deactivated after pregnancy	1	6.3%	0	0.0%
pain & discomfort at device site treated conservatively	1	6.3%	0	0.0%
Pain after trauma to the back ,lead migration. reprogramming the device	1	6.3%	1	9.1%
Infection at the site of device implantation of device.SN was removed	0	0.0%	1	9.1%
Non	13	81.3%	9	81.8%

When we evaluate the percentage of complication in all patients of OAB included group1 and group 2 underwent SN implantation. We found the complications occurred in five patients (18.5%). Of these complication, 2(7.4%) patients developed pain after trauma to the back, lead migration, lack of efficacy of device. Treated by reprogramming the device , one patient (3.7%) get infection at the site of device implantation, SN was removed , there was one female patient (3.7%) got pregnancy and devise was deactivated. And One patient (3.7%) complaining from pain and discomfort at the device site was treated conservatively .

Discussion

Many studies were carried to determine the effectiveness of sacral neuromodulation. Latini et al had seen its effects on 41 patients with urgency incontinence; and discovered that 90% of patients had a more than 50% improvement in signs and symptoms of urgency incontinence as noticed by voiding diaries and number of pads. [8]

The frequency of incontinent episodes for the patients in his study declined significantly from a mean of 8.8 /day to 2.3 / day for 6-month follow-up duration, numbers of pads were also reduced in patients undergone neuromodulator implantation, the mean number of patients' diapers changed from 4.7 diapers per day to 0.8 diapers/day in follow-up period.[8]

Our results after 1 year of SN. implantation, (group1) patients with urgency incontinence demonstrated that the number of leak was significantly reduced (p=0.01) after implantation of sacral neuromodulation as the mean value of number of leaks was 11.6/day pre implantation of the device and become 2.7 leak/day post implantation of the device with mean difference of 8.9 leaks/day. The same significant difference was reported with mean value of number of pad, as it was 6.9 pads/day before implantation and become 0.8 pads/day after device implantation with mean difference of 6.1 pad/ day.

Urgency & frequency symptoms get similar benefits for those with urgency incontinence. Charter_Kastler et al, in his study to evaluate the efficacy of SN for 9 patients with urinary frequency and found the voids/ day decreased from (16.1 void/day to 8.2 void/day). And increase in max.bladder capacity from 244 mL to 377 mL. and increase in the ability of patient to hold a greater volume between voids and over active bladder episodes [9]

Worldwide clinical study in seventeen centers van Kerrebroeck el la. 25 patient with urgency-frequency

underwent SN implantation ,mean number of voids/day decreased significantly from 19.3 to 14.8, with (40%) clinically success after five years. Volume voided per void also increased (92.3 ml to 165.2 ml) with clinical success (56%) after five years. The clinical success rate in decreasing episodes of urgency (56%). An important finding in this study is the high correlation between success rates for treated patients for one and five year; indicating durable response with SN [10]

Our study's results of patients with urgency frequency (group 2) showed that the numbers of voids/ day pre & post SN implantation decreased significantly (p=0.01) from a mean of 14.7 voids/day to 6 voids / day with mean difference of 8.7 voids/day. The volume voids increased significantly(p=0.02) from a mean of 136.4 ml/void to 371.8 ml/void with mean difference of 235.4 ml/void of voided volume. The urgency episodes were decreased significantly (p=0.01) from 6.4 episodes/ day prior to implantation to 2.1 episodes/day after implantation of the device with mean difference of 4.2 urgency episodes/day

Hassouna et al. take of 51 patients post SN implantation from 12 centers underwent baseline assessment, including a detailed voiding diary, urodynamic evaluation that was showed improvements in cystometry study and life quality according Health Survey. It was shown that the effects were attributed to SN because of when SN were deactivated their patients symptoms returned to baseline. after reactivate the stimulator the benefits were returned again [11]

There were numbers of complications that occurred in some patients who underwent SN implantation like any surgical intervention .

At a mean follow-up of ~3 years, White et al followed up 221 patients for 3 years and found that 30.3% developed complication that required surgical intervention. These complications such as pain; infection; device malfunction; hematoma and lead migration. Of these complications (3.5% surgical site infection),(2.7% pain which was related to the device)and(5.9% lead migration).. According this classification, they found the total complications rate (30.3%) and suspect that would represent the upper percentage end of complication .[12]

In our study; when we evaluate the percentage of complication in all patients of OAB included group1 and group 2 underwent SN implantation. We found the complications occurred in 5 patients (18.5%). Of these complication, One patient (3.7%) got infection at the site of device implantation, SN device was removed , And One patient (3.7%) complaining from pain and discomfort at the device site was treated conservatively by simple analgesia. Two patients (7.4%) developed pain after trauma to the back, lead migration, lack of efficacy, treated by reprograming the device. Lead migration is usually resolved by reprogramming and usually does not require a new lead to be inserted. This can also define the problem at each electrode and is handled by reprogramming to move the circuit of stimulation away from the broken or migrated electrode.[13]

During follow up of our patient there was a female patient (3.7%) who got pregnancy. Device was deactivated to be activated after delivery .it is unclear whether SN is safe in pregnant patients or not. Also, it's unclear whether it is teratogenic or not; especially in the first trimester. Wiseman et al looked at six pregnant patients with SN that didn't deactivated in the first trimester of pregnancy. This study shows that one of the six cases delivered a premature baby by 6 months but with no fetal abnormalities seen in any of these cases. This result promising that SN has no harmful effects to the pregnant women and her fetus. However, the manufacturers recommend that the pulse generator should be deactivated in female patient getting pregnancy.[14]

Conclusion

Sacral neuromodulation is FDA approved as option for treatment of refractory OAB. There is expanding of utilizing of SN in the past two decades.

According to multiple studies in addition to our study results, sacral neuromodulation is safe and efficacious treatment option for refractory OAB.

Conflicts of Interest: No

Source of funding: Self

Ethical Clearance: was taken from the scientific committee of the Iraqi Ministry of health

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