

OUTCOME OF SACRAL NEUROMODULATION IN PAINFUL BLADDER SYNDROME/INTERSTITIAL CYSTITIS ASSOCIATED WITH IRRITABLE BOWEL SYNDROME

Hypothesis / aims of study:

Painful Bladder Syndrome/Interstitial Cystitis (PBS/IC) is a chronic bladder condition characterized by urinary frequency, urgency, nocturia, and supra-pubic pain related to bladder filling. Irritable Bowel Syndrome (IBS) is a functional gastrointestinal disorder characterized by abdominal pain and altered bowel habits in the absence of specific and unique organic pathology. Association between PBS/IC and IBS is in the range of 25-50% of cases. A common pathogenesis, that is the interaction of mast cells with nerve cells to produce neurogenic inflammation and pain, has been proposed for interstitial cystitis and irritable bowel syndrome. [1]. Another potential link between interstitial cystitis and irritable bowel syndrome involves serotonin which may have a role in suppressing voiding and the urge to void, is abundantly stored in enterochromaffin cells located throughout the gastrointestinal tract. Investigators have assumed that molecular defects in the human gut resulting in changes in serotonin receptor function may be responsible for symptoms of irritable bowel syndrome [2]. There is an experimental evidence of cross-neural talk and sensitization as a reasonable explanation of PBS and IBS overlap. [3]

There is no study on the impact of IBS on the outcome of PBS/IC treatment, this study was conducted to explore this effects.

Study design, materials and methods:

A retrospective chart review of patients who were diagnosed to have PBS/IC and referred for sacral neuromodulation therapy in our center from 2002-2009 was conducted. Demographic data, duration of symptoms, voiding parameters, pain score and association with IBS were retrieved from the charts. All patients underwent bilateral percutaneous nerve evaluation (PNE), and they consider candidates for permanent implantation if they showed improvement by 50% or more in their pain score and voiding parameters. Voiding diary and visual analog scale (VAS) were the tools used pre and post PNE to conclude the success or failure outcomes. Correlation and logistic regression analysis was done to evaluate the predictors that may affect the outcome of PNE and on long-term follow-up. Age, gender, duration of symptoms, pain score, association with IBS and frequency were used as predicting parameters.

Results:

79 female patients were diagnosed with PBS/IC refractory to oral and intervesical therapy and they were referred to our center for sacral neuromodulation therapy.

25 patients (32%), were confirmed to have IBS associated with their PBS/IC disease and they are on treatment and follow-up for that in GI clinic. 45 patients (57%) had 50% or more improvement in their voiding symptoms and pain score during their PNE stage, 43 patients underwent permanent implantation, 2 patients declined it. 34 patients (43%) didn't improved during PNE and were not candidates for permanent implantation.

Table (1):

outcome	n	age	Duration of symptoms	Frequency (voided/24hrs)	Pain score	IBS associated
success	45	41.8±11.6	5.3±3.1	18.7± 4.9	6.2±1.5	8
failure	34	44.2±12.2	7.4±6.1	18.7±4.1	8.1±1.2	17
P value		0.38	0.04	0.62	0.0001	0.002

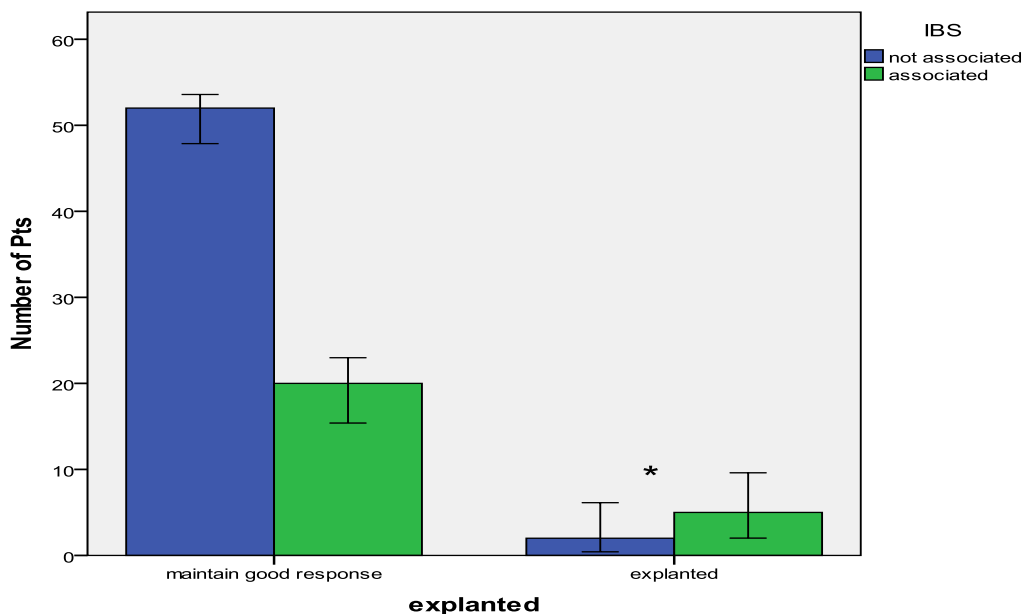
Pearson data analysis revealed a strong and moderate negative correlation ($r = -0.59, -0.34$) between the outcome and pre-implantation pain score and association with IBS respectively. On the other hand there is mild correlation with duration of symptoms ($r = -0.22$). There is a positive correlation between high pain score and association with IBS in patients with PBS/IC ($r = 0.26$) $p = 0.021$.

Logistic regression analysis, table (2).

Predicting factor	Log. regression coefficient	SE	sig	Odds Ratio (OR)	95% CI for OR	
					Lower	Upper
IBS	-1.41	0.69	0.04	0.24	0.063	0.94
Age	-0.01	0.03	0.75	0.99	0.94	1.05
Duration of Symptoms	-0.07	0.07	0.32	0.93	0.81	1.07
pain	-1.09	0.29	0.001	0.34	0.19	0.59

Average follow up was (5.1±2.6) yrs, during that period of follow-up, 7 patients underwent explantation, 5 (71%) due to pain at the site of IPG or ipsilateral limb, 2 patient explanted due to loss of efficacy. Correlation analysis revealed positive correlation between pre-implantation pain score and association with IBS with explantation on long term follow-up, ($r = 0.25, 0.27$), ($p = 0.024, 0.02$) respectively.

Fig. (1) Effect of IBS association on long term F/U



Interpretation of results:

PBS/IC and IBS are challenging conditions to be treated, due to our incomplete understanding of their pathogenesis. Sacral neuromodulation is a promising therapy in treating PBS/IC. This study suggests that simultaneous presence of PBS/IC and IBS forms a complex syndrome that affects pelvic organs and manifests predominantly as pain and associated with urinary symptoms or changing in bowel habits. Failure of SNM after long term follow-up is a clue for the possibility of progressive pathology, especially if pain is still the main symptom, though its location may have changed. Based on our analysis, it was not clear to us if bilateral permanent sacral neuromodulation could offer more control of pain in this subset of patients.

Concluding message:

Severity of pre-implantation pain and its association with IBS are factors affecting the long-term success of sacral neuromodulation in PBS/IC.

References

1. Theoharides TC, Cochrane DE. Critical role of mast cells in inflammatory diseases and the effect of acute stress. *J Neuroimmunol.* 2004 Jan;146(1-2):1-12.
2. Gershon MD. Review article: serotonin receptors and transporters -- roles in normal and abnormal gastrointestinal motility. *Aliment Pharmacol Ther.* 2004 Nov;20 Suppl 7:3-14.
3. Pezzone MA, Liang R, Fraser MO. A model of neural cross-talk and irritation in the pelvis: implications for the overlap of chronic pelvic pain disorders. *Gastroenterology.* 2005 Jun;128(7):1953-64.

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<i>What were the subjects in the study?</i>	HUMAN
<i>Was this study approved by an ethics committee?</i>	Yes
<i>Specify Name of Ethics Committee</i>	University Health Network Ethics Board
<i>Was the Declaration of Helsinki followed?</i>	Yes
<i>Was informed consent obtained from the patients?</i>	No