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Urogynecology Digest

Presented by Fiona M. Lindo

Are there changes in symptoms of pelvic floor disorders after bariatric surgery?

Cuicchi D, Lombardi R, Cariani S, Leuratti L, Lecce F, Cola B. Clinical and instrumental evaluation of pelvic floor disorders before and after bariatric surgery in obese women. Surg Obes Relat Dis. 2013 Jan;9(1):69–75.

Cuicchi et al. performed a prospective study aiming to identify the frequency, severity, and effect on quality of life (QOL) of pelvic floor disorders (PFD) relative to obesity. In addition, it relates the effect that surgically induced weight loss has on pelvic floor anatomy and dysfunction. One hundred obese women [body mass index (BMI)≥30 kg/m^2] were evaluated by physical exam, endoanal ultrasound, rectal balloon distension test, and dynamic magnetic resonance imaging (MRI). They also completed six validated specific and QOL questionnaires regarding PFD. The questionnaires were repeated at 6 and 12 months. Of the 100 patients, 87 were reassessed by physical exam at 12 months after bariatric surgery utilizing the Roux-en Y gastric bypass. Chi-square test was used to compare the prevalence of PFD symptoms by degree of obesity. McNemar test and nonparametric repeated measures analysis of variance (ANOVA) were used to measure changes from baseline to 6 and 12 months of follow-up. Overall PFD frequency decreased from 79.3 % to 48.3 % (P<0.0001). Urinary incontinence (UI) was the most common symptom (61 %), with associated risk factors that included BMI (P=0.04) and history of chronic bronchitis (P=0.04). With an increase in the degree of obesity (moderate, severe, morbid), there was a significant increase (P=0.04) in UI frequency (22.2 %, 63.6 %, and 65 %, respectively). Postoperative UI incidence decreased from 58.6 % to 9.2 %. Fecal Incontinence (FI) was reported in 24 % of patients, which decreased postoperatively to 5.7 %. Pelvic organ prolapse (POP) symptoms significantly reduced, from 54 % to 18.4 % 12 months postoperatively (P=0.0001).

The study further reiterates the profound effect obesity has on UI that has been shown in previous studies. In addition, it emphasizes how decreasing BMI can affect other PFDs, such as FI and POP, which have been studied less systematically. It is important when treating obese patients with PFDs that we counsel appropriate weight-loss intervention that can be achieved by conservative or surgical treatments and that can help improve symptoms and QOL.

Interstitial cystitis/bladder pain syndrome: Has an associated gene been identified?

Reeder JE, Byler TK, Foster DC, Landas SK, Okafor H, Stearns G, Wood RW, Zhang Y, Mayer RD. Polymorphism in the SCN9A voltage-gated sodium channel gene associated with interstitial cystitis/bladder pain syndrome. Urology. 2013 Jan;81(1):210.e1–4

Previous studies identified a nonsynonymous single nucleotide polymorphism (SNP) in the *SCN9A* voltage-gated sodium channel gene related to the A allele of SNP rs6746030 that is associated with enhanced pain perception and has been located in chronic pain syndromes. In their pilot basic science experiment, Reeder et al. attempted to establish whether an association exists between interstitial cystitis/bladder pain syndrome (IC/BPS) and this polymorphism in the *SCN9A* gene. They hypothesize that pain perception in patients with IC/BPS might be influenced by sequence variations in gene. Germline DNA was sampled from bladder biopsy specimens from diagnosed IC/BPS patients and from hysterectomy specimens, which served as controls. The IC/BPS group was compared with the control group by contingency analysis of genotyping data using Pearson's chi-square test and Fisher's exact test. Using polymerase chain reaction (PCR), the SNP rs6746030 was amplified and analyzed with gel electrophoresis. Of the 26 controls, only three (11.5 %) were AG; all others were GG (88.5 %). Of the 53 IC/BPS patients, 21 (39.6 %) had AA or AG genotypes (P=0.036). In addition, the A allele was seen more frequently in the IC/BPS group than in the hysterectomy control group (P=0.009).

The debilitating effects IC/BPS have on patients, the multiple proposed etiologies, and the lack of effective treatment makes it an important disease process on which to focus study. Association studies looking at SNPs can be misleading due to chance equilibriums in allelic distributions. However, similar observations are made in studies that focus on other syndromes

that express both decreased and increased pain perception. Reeder et al. suggest that individuals carrying the A allele of the identified SNP in the *SCN9A* gene are at increased risk of developing IC/BPS. Although this translational research is a small pilot study, it has the potential of laying the foundation for innovative treatment for IC/BPS, such as developing targeted pharmacotherapy directed at the voltage-gated sodium channel gene. It may also provide a way to selectively identify and screen patients most at risk of enhanced pain syndromes.

Is the long awaited new OAB drug mirabegron efficacious and safe?

Chapple CR, Kaplan SA, Mitcheson D, Klecka J, Cummings J, Drogendijk T, Dorrepaal C, Martin N. Randomized double-blind, active-controlled phase 3 study to assess 12-month safety and efficacy of mirabegron, a β(3)-adrenoceptor agonist, in overactive bladder. Eur Urol. 2013 Feb;63(2):296–305.

Mirabegron, a β_3-adrenoceptor agonist, is a new class of agents with a distinct mechanism of action. β_3- adrenoreceptors are located predominantly in the detrusor muscle of the bladder and facilitate urine storage by inducing detrusor relaxation. The double-blinded randomized control trial reported by Chapple et al. and conducted in 306 sites worldwide enrolled 2,444 patients with symptoms of overactive bladder (OAB) with or without urge urinary incontinence (UUI) >3 months. The aim of the study was to assess the safety and tolerability of 12 months of treatment with once-daily mirabegron (50 mg and 100 mg) and assess the efficacy and safety of the drug compared with tolterodine, an orally administered antimuscarinic agent that represents the class of current pharmacotherapy treatment for OAB. Demographic and OAB-related baseline characteristics were similar across all groups. The primary safety indicator was the incidence and severity of treatment-related emergent adverse events (TEAEs), which were similar in all treatment groups: mirabegron 50 mg (59.7 %), mirabegron 100 mg (61.3 %), and tolterodine extended release (ER) 4 mg (62.6 %). TEAEs most frequently identified were mild or moderate in severity and included hypertension, dry mouth, constipation, and headache, with incidence similar across all treatment groups except for dry mouth, which was higher in the tolterodine group (8.6 % vs 2.8 % and 2.3 % for mirabegron 50 mg and 100 mg, respectively). Discontinuation of medication due to AEs were comparable across treatment groups: 6.4 %, 5.9 %, and 6.0 % of patients on mirabegron 50 mg, 100 mg, and tolterodine, respectively, as well as serious adverse events (SAE): 5.2 %, 6.2 %, and 5.4 %, respectively. No SAE of urinary retention was reported. Adjusted mean changes from baseline to 12 months in morning systolic blood pressure in mirabegron 50 mg and 100 mg and tolterodine ER 4 mg were 0.2 mmHg, 0.4 mmHg, and −0.5 mmHg, respectively. Improved treatment efficacy was observed in adjusted mean change within 1 month of therapy and was maintained throughout 12 months in each treatment group, including a reduced number of voids (−1.27 for mirabegron 50 mg, −1.41 mirabegron 100 mg, and −1.39 for tolterodine ER 4 mg) and incontinence episodes (−1.01, −1.24, and −1.26, respectively) per 24-h period.

Overall data of the study shows that mirabegron is a viable and safe treatment option to offer patients with OAB symptoms, with efficacy after 1 month of use. Patients should have lower symptoms of dry mouth compared with antimuscarinics such as tolterodine, which was three fold higher in the study. However, when using mirabegron 50 mg and 100 mg, there is a risk of having increased systolic blood pressure, which should be taken into consideration when treating hypertensive patients. Interestingly, mirabegron use did not result in more cardiovascular AEs compared with tolterodine. The safety profile of mirabegron after 12 months of use is consistent with that seen in the phase III studies conducted previously. This β_3-adrenoceptor agonist showed 12 months' safety, tolerability, and continuous effect in patients with OAB.

Conflicts of interests None.

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