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INCONTINENCE & INTIMATE PARTNERS: ASSESSING THE CONTRIBUTION OF TREATMENT

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INTRODUCTION

Urge urinary incontinence (UUI) is a socially debilitating disease due to its inherently unpredictable nature and sometimes large volumes of urine loss. Women with UUI may experience anxiety over public episodes of incontinence and concerns about odor and as a result, isolate themselves socially. This isolation affects both partners in the relationship and may be a source of discord. The impact of UUI also moves into personal relationships where fears or actual episodes of incontinence during physical intimacy, including but limited to intercourse, may result in limited interactions and changes in the relationship satisfaction for both partners. Few studies have examined the role of urinary incontinence, particularly UUI, in the dynamics of an intimate partner relationship and none have evaluated the impact of successful UUI treatment.

The long-term goal of our research is to understand the social and emotional impact of pelvic floor disorders, particularly UUI, on the well-being of an intimate relationship. Ultimately, we aim to evaluate the role that successful treatment plays in the alleviation of discord in intimate partner relationships that are affected by UUI and other pelvic floor disorders.

Our *objective* for this proposal is to characterize, using validated, quantifiable methods the quality of the relationship in couples affected by UUI and to identify the role that treatment plays in improving this relationship. Our *central hypothesis* is that UUI has a negative impact upon the emotional and physical well-being of a relationship and that effective treatment will result in improvement in areas of the relationship that have been detrimentally affected by UUI. Our *rationale* for this study is that an understanding of UUI in the context of a couple, particularly from the perspective of the male partner, will improve our ability to holistically treat UUI, thus improving patient outcomes and satisfaction.

To test our central hypothesis and complete the objective outlined in this proposal, we propose the following *specific aims*:

Specific Aim #1: To define the levels of relationship satisfaction and sexual function among couples with the female partner having primarily: UUI symptoms and mixed urinary incontinence (urge predominant).

Hypothesis 1: Couples with (female partner) UUI will have lower levels of relationship satisfaction and sexual function based upon validated measures of sexual function and relationship cohesion.

Specific Aim #2: To measure the impact of successful treatment of UUI on the relationship.

Hypothesis 1: Successful treatment with Vesicare will result in improvement in relationship satisfaction and sexual function for both male and female partners.

We expect that the results of this prospective study will allow us to objectively quantify the degree to which intimate relationships are affected by UUI thus filling a critical gap in our knowledge. We also expect to demonstrate that successful treatment of UUI leads to an improvement in relationship satisfaction and sexual function.

Significance of the Proposed Work

Chronic illness places emotional, physical, and financial burdens upon both the patient and her partner, and can be a significant source of stress in a relationship. The symptoms of UUI inherently pose greater social challenges than those faced by women other forms of pelvic floor disorders. For example, women with UUI may avoid social situations due to fear of having an accident or may be reluctant to participate in activities during which it may be difficult to find a bathroom. The resulting social isolation impacts both members of the dyad and may serve as a source of relationship discord. Changes in sexual function and perceived intimacy, including non-intercourse intimacy, as well as communication may be new sources of stress in a previously healthy relationship or may serve to amplify pre-existing relationship problems.

Sexual function is another area in which UUI may cause a negative impact. Studies of coital incontinence among incontinent clinic populations report prevalence ranging from 10%-56% with a median of 22% (1). The prevalence of coital incontinence may be related to the type of incontinence as well as the severity of symptoms. Stress incontinence has been associated with leakage of urine during intercourse, while detrusor instability and urge incontinence have been correlated with leakage during orgasm (2). A cross-sectional study of women with UUI and urinary incontinence found that among women reporting low sexual desire, stress incontinence was common (47%), while 46% of women reporting orgasmic phase dysfunction reported symptoms of urge incontinence (3). Qualitative data corroborates the negative impact of UUI on dyadic and sexual relations (4).

Another mechanism by which UUI may affect satisfaction with dyadic relations is through depressive symptomatology. Urinary incontinence is associated with a decrease in overall health-related quality of life and is positively correlated with depression, anxiety, and stress (5-7). Studies of other chronic illnesses demonstrate a correlation between the patient's level of depression and that of their spouse; level of depression shows an inverse relationship with degree of satisfaction with the relationship (8).

One of the two studies in the published literature that use quantitative methods to evaluate the impact of urodynamic stress incontinence and detrusor overactivity on the marital relationship concluded that both sexual function and marital relationships are negatively affected by incontinence (9). This study, like others, is based upon the perspective of the female partner. A recent study of Swedish women with urinary incontinence and urgency is the only study which includes the perspective of the male partner to examine the impact of UUI on the relationship (10). It concludes that, "Female urinary incontinence, urgency and frequency significantly impair the quality of life in both younger and older women, and also have negative effects on the partner relationship and the partner's life".

The perspective of intimate partners of women with UUI and other forms of PFD is largely missing from the literature. Any analysis of the role of UUI in intimate partner relationships is incomplete without this perspective.

Methodology

All women presenting with a chief complaint of UUI or MUI urge predominant with three months of symptoms presenting to the Division of Female Pelvic Medicine & Reconstructive Surgery at Loyola University Medical Center who meet the inclusion criteria will be invited to participate in this prospective study.

For the purposes of the study, women with UUI predominance will be defined as those women with an urge symptom index of $\geq$ 50% on the MESA who are not planning to undergo surgical correction of pelvic organ prolapse or stress urinary incontinence.

Following informed consent the following information will be extracted from their medical records (all obtained as part of routine gynecologic care):

- Demographics: age, self-reported race and ethnicity, vaginal parity, marital status, years with current partner, BMI, menopausal and hormone replacement status, prior treatment for pelvic floor disorders, prior medical and surgical history
- The Pelvic Floor Distress Inventory-Short Form 20 (PFDI-20) (11), a validated, condition-specific pelvic symptom questionnaire
- The Medical, Epidemiological, and Social Aspects of Aging (MESA) (12)
- The patient's goals for her treatment

As part of the study, women enrolled in this study will complete the following validated questionnaires:

- The Pelvic Organ Prolapse/Urinary Incontinence Sexual Function Questionnaire (PISQ-12) (13) and the Pelvic Floor Impact Questionnaire-Short Form 7 (PFIQ-7) (11), validated questionnaires measuring the impact of pelvic floor dysfunction, including urinary incontinence, on sexual function and general quality of life, respectively.
- The Golombok-Rust Inventory of Sexual Satisfaction (GRISS) (14).
- The Dyadic Adjustment Scale (DAS) (15).

Consenting male partners of women enrolled in this study will complete a questionnaire that includes information on:

- Demographics: age, BMI, and general health status.
- The Golombok-Rust Inventory of Sexual Satisfaction (GRISS)
- The Dyadic Adjustment Scale (DAS)

- Their goals for their partner's treatment

The Golombok-Rust Inventory of Sexual Satisfaction (GRISS) is a 28-item self-administered questionnaire that was developed by sex therapists to assess the quality of the sexual relationship of a heterosexual couple. The survey, which takes approximately 15 minutes to complete, evaluates 12 domains, 5 of which are female-specific, 5 male-specific, and 2 non-gender specific. The GRISS receives a Grade A recommendation from the International Continence Society for its appropriateness as a tool for evaluating sexual function as a dimension of overall health-related quality of life among patients with pelvic floor disorders.

The female version produces a Total GRISS Female Score as well as subscales of:

- *Anorgasmia* - the extent to which a woman is able to attain orgasm.
- *Vaginismus* - the extent of any tightness around the vagina that interferes with sex.
- *Non-communication* - The extent to which a couple are able to talk about any sexual problems.
- *Infrequency* - The number of times a week (or less) on which sexual intercourse takes place.
- *Female Avoidance* - The extent to which a female partner is actively avoiding having sex.
- *Female Non-sensuality* - The extent to which a female partner gains pleasure from touching and caressing.
- *Female Dissatisfaction* - The extent to which a woman is dissatisfied with their sexual partner.

The male version produces a Total GRISS Male Score as well as subscales of:

- *Impotence* - the extent of any failure by a man to achieve an erection.
- *Premature ejaculation* - the extent to which a man has the tendency to ejaculate too soon.
- *Male Avoidance* - The extent to which a male partner is actively avoiding having sex.
- *Male Non-sensuality* - The extent to which a male partner gains pleasure from touching and caressing.
- *Male Dissatisfaction* - The extent to which a man is dissatisfied with their sexual partner.
- *Non-communication* & *Infrequency* – Same as the female version

The Dyadic Adjustment Score is a validated instrument for evaluation of adjustment in relationships between either married or unmarried cohabiting couples. It may be used at baseline to obtain a comprehensive description of the relationship and as an objective measure of change in the interaction between partners after an intervention The DAS consists of a 32-item self administered questionnaire that is not gender specific. It has fours subscales: relationship satisfaction, cohesion, consensus, and affectional expression. The DAS takes 5-10 minutes to complete.

All women presenting with a chief complaint of 3 months of UUI or mixed urinary incontinence (MUI) with urge predominance to the Division of Female Pelvic Medicine & Reconstructive Surgery at Loyola University Medical Center who meet inclusion criteria will be approached for study participation. Women will receive a thorough explanation of the study, including the risks, benefits, and potential side effects of the study drug, and their questions will be answered. Women of childbearing age will be counseled that they should be using an effective method of birth control during the study. They will sign an informed consent document. They will also be given a 3 day voiding diary to be completed at home. Prior to completing the 3 day voiding diary, patients currently taking an anticholinergic medication will undergo a 2 week wash out period during which

they will not take any drug. They will also be given a letter describing the study to give to their partner.

Women with a diagnosis of UUI or MUI, urge predominant, who have consented to participate and whose partners consent to participate will return to the clinic with completed study questionnaires (PISQ-12, PFIQ-7, MESA, GRISS, and DAS).
They will be given Vesicare 5mg with instructions for use. After 4 weeks of use, we anticipate that 50% of patients will note improvement. Those who do not feel that their symptoms are adequately controlled will have the option of increasing to 10 mg per day for the remaining 8 weeks of the study. After 12 weeks of medication use, patients will have a follow up visit, they will be asked to again complete all of the PISQ-12, PFIQ-7, MESA, GRISS, and DAS as well as the Overall Quality of Life Related to Urinary Incontinence Questionnaire. Male partners will also complete a second set of questionnaires either in the clinic or at home after their partner has undergone 12 weeks of treatment. Patients will be given a total of 16 weeks of Vesicare to allow for some variation in scheduling follow up and to ensure that they are currently taking Vesicare at the time that they complete their follow up questionnaires.

Subjects and Recruitment
Loyola's clinical research team is well-suited to successfully recruit women to this study. Our division has four clinical faculty members, all of whom are NIH funded investigators who participate in large clinical and surgical trials through the Urinary Incontinence Treatment Network and the Pelvic Floor Disorders Network. In addition, we have 4 full-time research nurses and a data entry manager. The entire group is fully supportive of this research.

Recruitment of men for studies on female urinary incontinence is a new area of research. This study would be the first to exam relationship dynamics from the perspective of the male partner using validated methods. Based upon a small pilot study of male partners that was conducted at our center, we believe that the recruitment of male partners is a feasible goal. Because there is no direct benefit to the male partner and given the personal nature of the data collected, compensation of the male partners (travel and parking) is reasonable and likely to give a more representative sample.

Subjects will be recruited from all racial and ethnic groups. Race and ethnicity will be determined by self-reporting according to the guidelines of The Office of Management and Budget Directive No. 15. On the screening questionnaire, subjects will be allowed to choose from 2 ethnic categories, "Hispanic or Latina" and "Not Hispanic or Latina". They will also choose from 5 racial categories: American Indian or Alaska Native; Asian; Black or African American; Native Hawaiian or Other Pacific Islander; and White. Appropriate definitions will be included on the questionnaire.

Women will eligible for ***inclusion*** in the study if they are:

- Age $\geq$ 18 years, and
- In a relationship with a male partner for at least 3 months, and
- Not pregnant (pregnancy test will be done at study enrollment) or planning to become pregnant, and

- Have a diagnosis of UUI or MUI, urge predominant, based on recall
- Are interested in medical management of their symptoms and are candidates for Vesicare, and
- Able to provide informed consent and complete the written questionnaires.

Women will ***excluded*** from participation in the study if they have:

- PVR > 200 ml at initial visit
- Significant outflow obstruction
- Persistent/recurrent UTI
- Bladder stones
- A diagnosis of chronic interstitial cystitis
- Undergone pelvic irradiation
- Current pelvic malignancy
- Narrow angle glaucoma
- Urinary or gastric retention
- Current use of a tricyclic antidepressant
- A neurologic diagnosis that could affect bladder function (MS)
- A diagnosis of chronic pelvic pain
- An active psychotic disorder

Women will also be ***ineligible*** for participation if they:

- Or their partner is non-English speaking
- Decline permission for the study team to approach their partner regarding participation

Statistical Analysis

Power Analysis

While the change in the overall GRISS score is the primary outcome in this study, the sample size for this study is based upon published research utilizing the DAS (i.e., which also measures relationship satisfaction).

A prior study of the relative effectiveness of two behavioral interventions in the treatment of marital discord randomized 45 couples to a known intervention, an experimental intervention, or a wait list (control group)(16). This sample size was adequate to demonstrate a significant change in DAS score in response to the study intervention. Similarly, a study of 36 couples detected significant changes in DAS scores following an intervention that consisted of several variants of marital therapy (17). Similar sample sizes have been used in the published literature of studies using the DAS as an indicator of improvement in marital quality (18, 19). This study will recruit 100 couples (200 subjects) with the assumption of a 50% response rate to the study drug (Vesicare). This will allow for a final sample size of 40-50 couples, consistent with that of other studies in the published literature.

Statistical Analysis Plan

In this study, the Global Impression of Improvement (GII) score is used to indicate response to therapy following three months of treatment, where response to treatment comprises those who rate their Global Impression of Improvement (GII) as "a little better", "much better", or "very much better". Conversely, non-response to treatment comprises those who rate their GII as "no change", "a little worse", "much worse", or "very much worse".

Participants' baseline characteristics will be stratified by sex and compared between responders and non-responders using Pearson chi-square tests. For females, this includes comparisons between responders and non-responders on age (i.e., >=60 versus < 60), race, marital status, education attainment, years living with a partner (i.e., >=30 versus < 30), body mass index (i.e., >=30 versus < 30 kg/m^2), menstrual cycle, vaginal parity, prior treatment for pelvic floor disorders, prior surgery, and prior treatment for overactive bladder treatment. For males, this includes comparisons between responders and non-responders on age (as specified above), current sexual activity, general health, and medical history of hypertension, erectile dysfunction, arthritis, diabetes, cancer, heart disease, and depression. For these baseline comparisons, expected frequencies will be monitored and Fisher's exact tests will be used when such values are sparse.

For Aim 1, baseline Golombok Rust Inventory of Sexual Satisfaction (GRISS) scores will be compared between matched male and female partners using a paired samples *t*-test. The difference between female and male responses will be assessed for normality using a QQ plot and for outliers using a boxplot. If parametric assumptions are violated, conclusions may be confirmed using a Wilcoxon signed-rank test.

For Aim 2 we will subtract participants' overall 3-month GRISS score from their overall baseline score and compare this change in GRISS between those who respond and do not respond to solifenacin using an independent samples *t*-test. As before, the normal distribution of the change score in each response group will be assessed graphically using a QQ plot and for outliers using a box-plot. If parametric assumptions are violated, conclusions may be confirmed using a non-parametric Wilcoxon rank-sum test.

Finally, healthy male partners of female participants also complete the GRISS at baseline and after their female partner completes approximately 12-16 weeks of solifenacin treatment for UUI symptoms. For these male partners, a change score will be calculated by subtracting their baseline score from the follow-up score. This change score will be compared between male partners of female participants who respond to solifenacin versus male partners of female participants who do not respond to solifenacin.

All statistical analysis will be conducted using SAS Version 9.4 (SAS Institutes, Cary, NC) with the input of a Biostatistician.

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