Postmenopausal Pessary Users: Estrogen versus Trimosan

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IRB Protocol

Protocol Title: Postmenopausal Pessary Users: Estrogen versus Trimosan

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Population: Postmenopausal female new pessary users

Number of sites: Harris Health Clinics. Ben Taub Clinics. UT Houston Clinics

Study Duration: 6 months – 1 yr

Subject Duration: 3 months

General information:

Pelvic organ prolapse is seen in close to 96% of postmenopausal women (1). A pessary, which is a device placed into the vagina to support the prolapsing vaginal walls or to provide urinary continence, is commonly used to treat pelvic organ prolapse.

A common complication noted in pessary users is bothersome vaginal discharge. Vaginal discharge complication rates vary in different publications, ranging from 2.5% to 25% (2, 3). This complication may not cause pessary users to discontinue use (4); however, from clinical experience, it can be a source of embarrassment for the patient and a deterrent for family members to aid in self-care.

Little is known about the vaginal discharge in pessary users. In studies of vaginal discharge in pessary users, the symptomatic vaginal discharge is commonly attributable to bacterial vaginosis (5).

It is uncertain how vaginal pH is primarily established, but multiple factors are thought to contribute to establishing the acidic vaginal pH. Lactobacilli bacteria produce lactic acid, which is the primary acid in vaginal in normal vaginal secretions. The vaginal mucosa is also known to be an important source of lactic acid (12--6). While pH is known to alter the vaginal microbial environment, it has been shown that a pessary itself does not alter the microbial environment. (9)

The microbial composition between postmenopausal non pessary and pessary users have shown to be essentially similar (9).

Background Information:

Current popular creams used as an adjunct to pessary use are estrogen and trimo-san. Vaginally applied estrogen promotes epithelial cell growth and cellular maturation, decreases vaginal pH to premenopausal levels, and decreases severity of vulvovaginal symptoms (7)

Trimosan is a vaginal gel, with a pH of 4, marketed to help restore and maintain the normal vaginal acidity and coats the walls of the vagina with a lubricating film that helps reduce odor causing bacteria (8). There are not yet any published trials regarding Trimo-San's efficacy.

Bacterial vaginosis occurs in a setting of vaginal pH > 4.5, with peak adherence to vaginal mucosa occurring at pH 5 -6 (6).

There are previous papers which suggest that acidifying gels have been able to treat BV and prevent recurrence compared to placebo in its ability to acidify the vaginal pH. (Successful treatment of bacterial vaginosis with a policarbophil-carbopol acidic vaginal gel; recurrent bacterial vaginosis: the use of maintenance acidic vaginal gel following treatment). Given these suggestive findings, it goes to follow that Trimo-san may also be effective in decreasing pH and bacterial vaginosis infections.

In one study, vaginal pH of 6.0 to 7.5 is strongly suggestive of menopause (13). While it is known that estrogen can reduce vaginal pH and that Trimo-san may potentially do the same, these creams have never been studied in the context of pessary users.

Objectives:

Study hypothesis: In postmenopausal pessary users, estrogen users will have a more acidic pH, less complaints of vaginal discharge/odor, and decreased rates of bacterial vaginosis, than trimosan users.

Primary objective: vaginal pH with both treatment arms, as measured by pH test strips

Secondary objective: to see difference of patient satisfaction between treatment arms as measured by an unvalidated vaginal symptoms questionnaire.

Tertiary objective: rate of bacterial vaginosis infection (to be diagnosed either by gram stain (Nugent Score) or BV Affirm.

Study Design:

1) Randomized controlled
2) Study duration: 1 year – 3 years.
3) Subject duration: 3 months
4) Assessment of efficacy: Cost savings, future increase in compliance as less medication may be needed overall, possible decrease in bacterial vaginosis infection
5) Assessment of safety: Estrogen Side effects – abnormal vaginal bleeding, nausea, breast tenderness, bloating. Otherwise, low risk study.

Study Population:

6) Number of subjects to be enrolled? 34. 17 in each arm. Power 80%. P value: 0.05 P value 0.5. Power 80%. Sample size calculated with the expectation that estrogen will drop vaginal pH to 5.5 and Trimosan will decrease vaginal pH to 4.5.

7) Recruitment: Will recruit 44 patients (assuming 15% non enrollment, and 15% drop out) This study will be open to all clinic patients at Harris Health (LBJ, Aldine, BT Clinics), UT Houston clinics (Memorial Hermann, Sugarland, Memorial City),
8) All participants will read and sign The Certificate of Informed Consent when they arrive at the designated testing site, prior to their participation in the research procedure. After the participants have finished their participation in the study, or once they have decided to withdraw from the study, they will be given a verbal and written debriefing statement.
9) Inclusion:
    - Postmenopausal female pessary user (ring with support pessaries only) 18 years and older. Postmenopausal defined as: 1) amenorrhea for a year 2) 3 months after surgical bilateral salpingo-oophorectomy
    - Is a new pessary user, or has not had a pessary for a year
10) Exclusion:
    - Pregnancy
    - Persistent Bacterial Vaginosis infection in the first two clinic encounters
    - Currently on hormone replacement therapy
    - Previously on hormone replacement therapy in the past 6 months
    - Currently on antibiotics
    - Patients with existing vaginal erosions/ulcerations

Study Procedures:

Estrogen Treatment Arm: Will use either Premarin or Estrace cream (dependent on patient's insurance). Premarin 1 gram every night for the first 7 days, then 0.5 grams twice weekly. Estrace cream – 2 grams daily for first 7 days, then 1 gram twice-weekly.

Trimosan Treatment Arm: ½ applicator for three times a week for 1st week, then ½ applicator for 2 times a week.

The procedures are different because of funding/resources differences at Harris Health Clinics versus UT clinics. At Harris Health, they can be fitted for a pessary, but they must then take a prescription to an outside pharmacy in order to buy their personal pessary, and must come back to have it placed. At UT clinics, they have a ready stock of pessaries that the patients may purchase at the time of their fitting.

For Harris Health and BT Clinics:
1st encounter - Clinic visit to fit pessary from kit, pessary will be ordered, vaginal pH collected, vaginal gram stain collected, pt will fill out questionnaire, and be randomized to a treatment arm.

2nd encounter – Clinic visit to have their own pessary inserted, and be advised treatment according to which treatment arm they were randomized to.

3rd encounter – Clinic visit in 2 weeks after pessary fitting to evaluate vaginal tissue and symptoms.

4th encounter – Telephone call (6 weeks after personal pessary fitting) – to remind patient of their next visit and compliance with treatment.

5th encounter - 3 month clinic visit – vaginal pH to be collected, vaginal gram stain, will fill out questionnaire. Exit process explained and standard of care for pessary users will be continued.

For UT clinics:
1st encounter: Patients will be fitted for a pessary, and their own pessary will be placed, consented, fill out questionnaire, vaginal pH collected, BV affirm collected, randomized to a treatment arm, cream will be prescribed.

2nd encounter: Clinic visit in 2 weeks after pessary fitting to evaluate vaginal tissue and symptoms.

3rd encounter – telephone call – 6 weeks after initial pessary fitting to remind patients of next visit and compliance with creams

4th encounter – 3 month clinic visit: vaginal pH to be collected, BV affirm to be collected, will fill out questionnaire. Exit process explained and standard of care for pessary users will be continued.

Data and Safety Monitoring:

11) No adverse events expected
12) Plans for reporting unanticipated problems: ***
13) Safety monitoring plan – periodic review by research team

Statistics: Level of significance p 0.5

Ethics

- IRB approval will be sought from CPHS.

The PI will see the patient. If the PI thinks that the patient may qualify for a study, she will communicate basic information to the patient and will inform the patient that the research coordinator will talk to her. The research coordinator will gather the pertinent information and will talk to the patient. If the patient agrees to hear about the study, the patient will be moved to a private room, if applicable. The PI will explain the consent form in the patient's native language provided that language is either English or Spanish. Other languages will require a consent form translated into the patient's native language. The PI will explain the study through the consent form page by page and will give the patient plenty of time to read the form and ask questions. If the patient agrees to participate then both the patient and the PI will sign the ICF and a copy will be given to the patient. Then in accordance with the protocol, the INC/EXC criteria will be revised and the screening test will be scheduled at the patient's convenience.

Data handling and record keeping

The research team will keep all the information confidential and locked in the research office at MSB 3.114. The computer recording all the data is password protected.

Quality control and assurance

All information will be kept in clinic. It will be collected weekly and verified by EMR.

Publication Plan

- Plan to publish in an urogynecology journal.

- Results will not be returned to research subjects.

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