A Randomized, Single Center Pilot Study Comparing Hyaluronic Acid to Vaginal Estrogen for Treatment of Genitourinary Syndrome of Menopause

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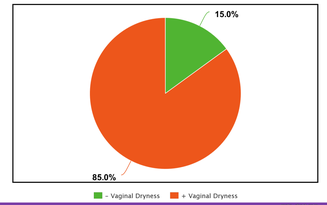
Introduction

Genitourinary syndrome of menopause (GSM) is a chronic condition resulting from a decrease in estrogen (1). It yields an array of vulvovaginal and urinary signs and symptoms in menopausal women including dryness, dyspareunia, burning and urinary incontinence (2). These symptoms are extremely prevalent amongst menopausal women and 85% of women over the age of 40 suffer from vaginal dryness (Figure 1)(3). In addition, over 50% of women who suffer from these symptoms report that they negatively affect their quality of life (4). Topical estrogen therapy has been the gold standard treatment for GSM, as it replaces depleted estrogen in post-menopausal women (5). However, due to both medical contraindications and patient preference, non-hormonal alternatives are important to explore for this extremely prevalent condition.

Figure 1: Vaginal Dryness in Women Over Age 40



Objectives

Primary	Secondary
Hyaluronic Acid (HLA) Vs. vaginal estrogen	Hyaluronic Acid (HLA) Vs. vaginal estrogen
↓	↓
Treatment of GSM	Improvement of physical attributes of GSM

Background

Topical estrogen therapy is utilized after over-the-counter vaginal moisturizers and lubricants have failed and has been the standard of care for GSM for many years (5).

Patient preference, along with instances of medical contraindication, even in topical form, exposes the need-gap to explore non-hormonal alternatives for GSM treatment.

HLA's role as a potential non-hormonal treatment for GSM has recently been identified but needs to be further studied.

Mouse studies on HLA show reversal of atrophy and suggests it has no effect on uterine weight (proxy for endometrial lining), which is a feared complication of systemic estrogen therapy (6). Human studies have also suggested improvement in vaginal symptoms as a result of HLA therapy (7).

Figure 2: Study Drugs (Topical Vaginal Estrogen & HLA Insert)

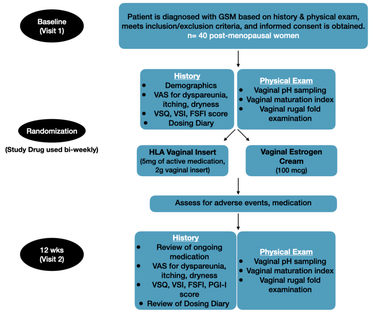
Study Enrollment

Inclusion Criteria
To participate in this study, individuals must meet the following criteria:
1. Postmenopausal status as defined by amenorrhea for ≥12 months or history of bilateral salpingo-oophrectomy or if the patient has had a hysterectomy and menopausal symptoms for >1 year or FSH > 40
2. Symptoms of GSM
3. Pap smear screening as per ASCCP (American Society of Colposcopy and Cervical Pathology) guidelines. If Pap smear was indicated in last three to five years, it must be negative.
4. Capable of giving informed consent
5. Ambulatory
6. Capable and willing to follow all study-relation procedures

Exclusion Criteria
Individuals who meet any of the following criteria are excluded from the study:
1. Use of any HRT (systemic or local) or raloxifene within six weeks of proposed start date
2. History of estrogen-sensitive tumor
3. Undiagnosed vaginal bleeding in the past 12 months
4. History of thromboembolic event
5. Currently have or have had liver problem
6. Bleeding disorder
7. Impaired mental status
8. Prior pelvic irradiation
9. Active vaginal infection
10. Any medical reason the investigator deems incompatible with treatment with vaginal estrogen

Methods

Study Design: A randomized, controlled, parallel trial



Assessment of Objectives

Primary Objective	Secondary Objective
Vulvovaginal System Questionnaire (VSQ)	Female Sexual Function Index (FSFI) changes
Visual Analog Scale (VAS)	Vaginal Symptom Index (VSI) score changes (baseline-12 week visit)
Vaginal Maturation Index (VMI)	Changes in % of superficial squamous cells in VMI
	Vaginal pH changes
	Rugal Fold Appearance changes
	VAS scoring changes for dyspareunia, vaginal itching & dryness

Analysis

Primary and secondary outcome measures will be summarized overall and by treatment group

Analysis will focus on the quality of life and objective measures of vaginal health improvement obtained in the HLA group, rather than hypothesis testing, to compare outcomes to those receiving estrogen

Compliance and retention will be similarly described overall and by treatment group

Figure 3: Study Schedule

Limitations

1.) Sample Size
- n=40 post-menopausal women who met inclusion criteria

2.) Study only included english-speaking patients
- Excludes major population of post-menopausal women who suffer from GSM symptoms

3.) Study conducted in a single center setting
- Limitations on diversity of patient population and external validity

Discussion

Results for this study are not available, as it is still in the recruitment phase. However, the implications the results could have on advocating for menopausal and post-menopausal health are significant. If it is found that HLA is equally efficacious in improving GSM symptoms in comparison to vaginal estrogen therapy, it could receive FDA approval as a non-hormonal alternative form of treatment for GSM. This ultimately has the ability to increase patient autonomy and improve post-menopausal health care.

Bibliography

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