

## Study Protocol

**Comparative evaluation for the efficacy of collecting sample by using vaginal atrophy screening combistick (VAS combistick) as against the traditional method of collecting sample for screening of vaginal atrophy in perimenopausal women**

### Abstract

**Background:** Genitals and sexuality is an essential element of healthy and happily aging perimenopausal women with their partners. Vaginal atrophy (VA) of menopause is a condition associated to physiological, histological and anatomical changes noticed in the genital and urinary tracts in peri and postmenopausal women. Vaginal atrophy is the sequel of the decrease levels of estrogens in plasma, which are symptoms of menopause.

**Objectives:** **1.** To evaluate the baseline data for vaginal maturation index (VMI) & pH in perimenopausal women. **2.** To evaluate and compare the method of collecting sample by using VAS combistick & traditional method. **3.** To evaluate and compare the accuracy of VMI score & pH using VAS combistick & traditional method. **4.** To evaluate and compare the feasibility & acceptability using survey based analysis in VAS combistick method and traditional method.

**Methodology:** The study will be conducted after approval from the institutional ethics committee. This will be an interventional-cross sectional comparative study. This study will include women who will come to Acharya Vinobha Bhave Rural Hospital (Obstetric and Gynaecology) OPD with at least one symptoms of vaginal atrophy. These women will take self sampling by using VAS combistick will be included in 'sampling A' (self sampling group) while, samples of the same group of patients taken by the traditional method will be included in 'sampling B' (clinician sampling group).

**Results:** In this study we have hypothesized that vaginal sampling by vaginal atrophy screening (VAS) combistick may be better when compared to traditional method of sampling for screening of vaginal atrophy in terms of adequacy, feasibility and acceptability.

**Conclusion:** VAS combistick may be considered as an alternative and better examining strategy which may give a reproducible and equivalent result to screening of vaginal atrophy in comparison to that of traditional sampling methods.

**Keywords:** vaginal atrophy, perimenopausal women, screening, combistick, vaginal maturation index

### **Introduction:**

Genitals and sexuality is an essential element of healthy and happily aging perimenopausal women with their partners. One in two postmenopausal women experience a collection of symptoms and signs known as vaginal atrophy (VA) of menopause.<sup>1</sup> Vaginal atrophy (VA) of menopause is a condition associated to physiological, histological and anatomical changes noticed in the genital and urinary tracts in peri and postmenopausal women. Vaginal atrophy is the sequel of the decrease levels of estrogens in plasma, which are the symptoms of menopause.<sup>1,2</sup> Oestrogen levels play a primary role in helping to regulate the density and wetness of the urogenital region. The vaginal epithelium cells become thin, squamous & stratified. This is because of the hypo estrogenic nature of the vagina. This also causes the vagina to drop its elasticity and lower the blood flow. Additional changes are seen in the vaginal flora and the pH of the vagina increases by 5. Although these symptoms are annoying, they are often considered by the perimenopausal women as the normal effect of age and menopausal state. This fact is embarrassing for the women and demotivates them for consulting their health-care provider <sup>3-6</sup>. In present days, the screening method for vaginal atrophy in clinical research is limited. However, sampling requires an examination (vaginal speculum) with the help of a tool called spatula. Some doctors use a device called a cytobrush, which is a combination of brush and spatula. This sampling method requires specially trained

---

personnel and might be uncomfortable to the participants. This method of sampling is seen as an invasion of the women's privacy. This is the most important cause behind dropping of screening in India. Additionally, barriers to screening include shame and phobia, especially when it involves unnecessarily exposure of genital organ in front of male health care providers. This can negatively affect the women's self-assurance & confidence. In most of the clinical settings where resources are limited and women do not possess health care policy, health care expenses are usually paid out of pocket. This monetary concern is also a major factor for non compliance of screening (vaginal) in the women population. Manifestations of the genitourinary syndrome in menopause (GSM) are troublesome to perimenopausal women. It affects their quality life, sexual relations, and daily life activities. If left untreated, symptoms of vaginal atrophy can not only cause discomfort but can also negatively impact the quality of life of the women, including sexual relationship as well as emotional wellbeing<sup>7-10</sup>. Late detection of vaginal atrophy may affect the other quality-of-life aspects. This includes clothing choices, exercise options and general comfort of the pelvic floor<sup>11,14-20</sup>.

The proposed VAS combistick device may help women to collect samples of their own for the screening of vaginal cytology. The combistick may help women to check their vaginal pH.

### **Rationale:**

This study has been selected along with the title because this study will be the first study of self collected sampling for screening of vaginal atrophy. This study is also proposed because of the success of other studies (in other settings) which included screening of sexually transmitted disease and cervical cancer and where women were able to collect self vaginal samples. These previous studies were feasible to implement and were accepted by the women population. Visiting a physician for a pelvic examination is usually sensitive. Therefore, self-sampling can allow for screening without undergoing pelvic examination. Hence, we aim to conduct this study in order to determine the efficacy, feasibility and acceptability of the vaginal atrophy screening (VAS) combistick in comparison to the traditional method.

## **Methods:**

This study will be an interventional cross sectional comparative study. It will be performed on cases that will come to Acharya Vinobha Bhave Rural Hospital (Obstetrics and Gynaecology) OPD with at least one complaint of vaginal atrophy. The study subject will be oriented to use VAS combistick to collect self sample. The sample of study subjects will be collected by clinician as per traditional method. The two samples from the subjects will be sent to pathology lab for evaluation of VMI and hormonal level. The pH recorded by the VAS combistick during self collection of sample will be compared with the clinician collected pH value. The findings will be compared and evaluated on the basis of feasibility, adequacy and acceptability. The inclusion criteria will be:

1. Perimenopausal women (45-60 years of age).
2. Women reporting at least one vulvo-vaginal atrophy symptom (itching, burning and pain during sex).

The Exclusion Criteria will be:

1. Vaginal infection.
2. Intercourse history of last 2 days.

The data will be calculated using Pearson's correlation coefficient to test the linear relationship between the samples and Cronbach's  $\alpha$  to assess consistency between the samples.

## **Expected Results:**

In this study we have hypothesized that vaginal sampling by vaginal atrophy screening (VAS) combistick may be better when compared to traditional method of sampling for screening of vaginal atrophy in terms of adequacy, feasibility and acceptability. The indicators for accuracy and feasibility will be a standardised questionnaire (Likert scale). The adequacy of the samples will be measured in the pathology lab by the pathologist (who will be blinded for the samples).

## **Discussion:**

Self-sampling might encourage in screening participation in the under diagnosed population. Some of the other benefits of self-sampling (as seen with other studies<sup>2,3,12,13</sup>) includes a superior clinical performance and cost effective than clinician collected sampling. Self-

sampling can be used as an alternative to other screening programs for prevention of vaginal atrophy.

### **Conclusion:**

Some of the barriers to screening include shame and phobia, especially when it involves unnecessarily exposure of genital organ. This can negatively affect the women's self-assurance & confidence. Hence, the VAS combistick may be considered as a better alternative (than the traditional method) to counter these barriers and improve screening though self sampling. The VAS combistick may be a better examining strategy which may give a reproducible and equivalent result to screening of vaginal atrophy in comparison to that of traditional sampling methods.

### **References:**

1. Alvisi S, Gava G, Orsili I, Giacomelli G, Baldassarre M, Seracchioli R, Meriggiola MC. Vaginal Health in Menopausal Women. *Medicina (Kaunas)*. 2019 Sep 20;55(10):615.
2. Di Pace R, Portuesi R. Vaginal health index score and urogenital syndrome of menopause. *Gazz Med Ital - Arch Sci Med* 2018;177:741-4.
3. Petridis, E. Vaginal problems diminish quality of life but often go unreported. *The North American Menopause Society*. 2018;1(1): 1-2.
4. Moral, E. The impact of genitourinary syndrome of menopause on well-being, functioning, and quality of life in postmenopausal women. *Pubmed*. 2021;1(1): 1-2.
5. Mercier J, Morin M, Reichetzer B, Lemieux MC, Khalifé S, Dumoulin C. Genitourinary syndrome of menopause symptom severity and impact outcome measures: are they reliable and correlated? *Menopause*. 2018 Dec 28;26(6):659-664.
6. Panda S, Das A, Singh AS, Pala S. Vaginal pH: A marker for menopause. *J Midlife Health*. 2014 Jan;5(1):34-7.
7. Hess R, Austin RM, Dillon S, Chang CC, Ness RB. Vaginal maturation index self-sample collection in mid-life women: acceptability and correlation with physician-collected samples. *Menopause*. 2008 Jul-Aug;15(4 Pt 1):726-9.

8. Cheryl Karcher, Neil Sadick, Vaginal rejuvenation using energy-based devices, *International Journal of Women's Dermatology*, Volume 2, Issue 3, 2016, Pages 85-88, ISSN 2352-6475
9. Wysocki, S. Management of Vaginal Atrophy: Implications from the review survey. *Clinical medicine insight*. 2014;1(1)
10. Rahn DD, Carberry C, Sanses TV, Mamik MM, Ward RM, Meriwether KV, Olivera CK, Abed H, Balk EM, Murphy M; Society of Gynecologic Surgeons Systematic Review Group. Vaginal estrogen for genitourinary syndrome of menopause: a systematic review. *Obstet Gynecol*. 2014 Dec;124(6):1147-1156.
11. Jha S, Wyld L, Krishnaswamy PH. The Impact of Vaginal Laser Treatment for Genitourinary Syndrome of Menopause in Breast Cancer Survivors: A Systematic Review and Meta-analysis. *Clin Breast Cancer*. 2019 Aug;19(4):e556-e562.
12. Paraiso MFR, Ferrando CA, Sokol ER, Rardin CR, Matthews CA, Karram MM, Iglesia CB. A randomized clinical trial comparing vaginal laser therapy to vaginal estrogen therapy in women with genitourinary syndrome of menopause: The VeLVET Trial. *Menopause*. 2020 Jan;27(1):50-56.
13. Sritonchai C, Manonai J, Sophonsritsuk A, Cherdshewasart W. Comparison of the effects of Pueraria mirifica gel and of placebo gel on the vaginal microenvironment of postmenopausal women with Genitourinary Syndrome of Menopause (GSM). *Maturitas*. 2020 Oct;140:49-54.
14. Matarazzo MG, Caruso S, Giunta G, Valenti G, Sarpietro G, Cianci A. Does vaginal estriol make urodynamic changes in women with overactive bladder syndrome and genitourinary syndrome of menopause? *Eur J Obstet Gynecol Reprod Biol*. 2018 Mar;222:75-79
15. Simon, James A. MD, CCD, NCMP, IF; Druckman, René MD Non-Hormonal Treatment of Perimenopausal and Menopausal Climacteric Symptoms [1A], *Obstetrics & Gynecology*: May 2016 - Volume 127 - Issue - p 12S
16. Politano CA, Costa-Paiva L, Aguiar LB, Machado HC, Baccaro LF. Fractional CO2 laser versus promestriene and lubricant in genitourinary syndrome of menopause: a randomized clinical trial. *Menopause*. 2019 Aug;26(8):833-840.

17. Kozma B, Póka R, Sipos A, Ács N, Takács P. A hüvelyi CO<sub>2</sub>-lézer-kezelés rövid távú hatásai a menopausalis genitourinalis szindróma tüneteire [Short-term efficacy of vaginal CO<sub>2</sub> laser therapy as a treatment modality for genitourinary syndrome of menopause]. *Orv Hetil.* 2019 Oct;160(41):1617-1622. Hungarian.
18. Gambacciani M, Levancini M. Short-term effect of vaginal erbium laser on the genitourinary syndrome of menopause. *Minerva Ginecol.* 2015 Apr;67(2):97-102. PMID: 25763800.
19. Quick AM, Dockter T, Le-Rademacher J, Salani R, Hudson C, Hundley A, Terstriep S, Streicher L, Faubion S, Loprinzi CL, Coleman JS, Wang KC, Lustberg M. Pilot study of fractional CO<sub>2</sub> laser therapy for genitourinary syndrome of menopause in gynecologic cancer survivors. *Maturitas.* 2021 Feb;144:37-44.
20. Sokol ER, Karram MM. Use of a novel fractional CO<sub>2</sub> laser for the treatment of genitourinary syndrome of menopause: 1-year outcomes. *Menopause.* 2017 Jul;24(7):810-814.
21. Schiavi MC, Di Tucci C, Colagiovanni V, Faiano P, Giannini A, D'Oria O, Prata G, Perniola G, Monti M, Zullo MA, Muzii L, Benedetti Panici P. A medical device containing purified bovine colostrum (Monurelle Biogel) in the treatment of vulvovaginal atrophy in postmenopausal women: Retrospective analysis of urinary symptoms, sexual function, and quality of life. *Low Urin Tract Symptoms.* 2019 Apr;11(2):11-15.