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Literature Review

The Role of Topical Treatment on Vaginal Tightening

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ABSTRACT

Background: Physiological changes in a woman's life, such as labor, weight fluctuations, hormonal changes, aging, and menopause, cause changes in both appearance and function of the vagina. As estrogen deficiency continues, changes occur in the form of atrophy and dystrophy in the vaginal mucosa, vulva, and other structures in the urogenital tract which are called symptoms of vulvovaginal atrophy. It affects women's quality of life, self-confidence, and sexuality. As alternative modality for noninvasive therapy, topical therapy in vaginal rejuvenation is becoming available in the care of outpatients. This makes it increasingly important for dermatologists to be well-informed about these treatment options. **Purpose:** This review aims to assess the role of topical therapy in vaginal rejuvenation, especially in vulvovaginal atrophy cases. **Literature Review:** Vulvovaginal atrophy has a negative effect on interpersonal relationships, quality of life, daily activities, and sexual function. Topical hormone replacement therapy includes all preparations such as estradiol, estradiol valerate, or conjugated estrogen. considered in cases with vulvovaginal atrophy accompanied by atrophy of the urogenital system as well as the accompanying complaints because this therapy is intended to prevent systemic complications. The topical use of hyaluronic acid, lubricants, moisturizers, and herbs is a therapeutic choice in vulvovaginal atrophy patients contraindicated with estrogen therapy or in patients who do indeed choose nonhormonal therapy. **Conclusion:** Topical therapy of hormonal and non-hormonal rejuvenation in various studies has shown improvement in symptoms of vaginal dryness, vaginal itching, dyspareunia, cell maturity, and changes in vaginal pH toward acidity.

Keywords: *topical therapy, vaginal tightening, vulvovaginal atrophy, human and health.*

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BACKGROUND

Physiological changes in a woman's life, such as labor, weight fluctuations, hormonal changes, aging, and menopause, cause changes in both appearance and function of the vagina.[1] As estrogen deficiency continues, changes occur in the form of atrophy and dystrophy in the vaginal mucosa, vulva, and other structures in the urogenital tract which are called symptoms of vulvovaginal atrophy (VVA).[1,2] Condition of VVA affects women's quality of life, confidence, and sexuality.[1,3] As a choice for non-invasive therapy, topical therapy for vaginal rejuvenation has become available in outpatient settings, making it of utmost importance for dermatologist to have adequate knowledge regarding this choice of therapy.[1,4]

The purpose of VVA therapy includes to recover the function of vagina epithelial tissue, easing the complains and symptoms caused by estrogen decline, and to improve the quality of life, especially regarding sexual activity.[4,5] Despite VVA's negative impact on quality of life, only 25% of women with VVA seek professional healthcare. This might be caused by embarrassment to express the complaint and popular belief that VVA is a part of aging.[6,7] A survey in England of 2,045 women aged 55 to 85 years found that 34% of the population had dyspareunia and or dryness in vagina but did not seek medical attention, while 40% delayed until more than a year to seek professional healthcare.[7]

The advantage of topical therapy for vaginal rejuvenation includes lower dose in topical estrogen with reduced risk of endometrial hyperproliferation

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and adenocarcinoma as compared to systemic estrogen therapy.[1,5,6] Even with said advantage, vaginal rejuvenation therapy procedure using topical therapy is still deemed controversial as there is still no consensus about its terminology and a limited number of long-term studies that assess the safety and efficacy of this procedure. Moreover, multiple studies regarding VVA reported various results with less objective parameters, calling the need of further study regarding this subject.[1,2,5]

LITERATURE REVIEW

The vagina is a woman's external genital organ, comprised of several parts. The vulva is composed of structures including mons pubis, labia mayor, labia minor, the clitoris, vaginal introitus, and urethrae orificium (Figure 1).[1]

Blood supply to the vulva is primarily sourced from the branch of pudendal artery, while blood supply for the mons pubis is sourced from inferior epigastric artery, a branch of the external iliac artery. The vagina also receives vascularization from a branch of the pudendal artery (Figure 2).[1]

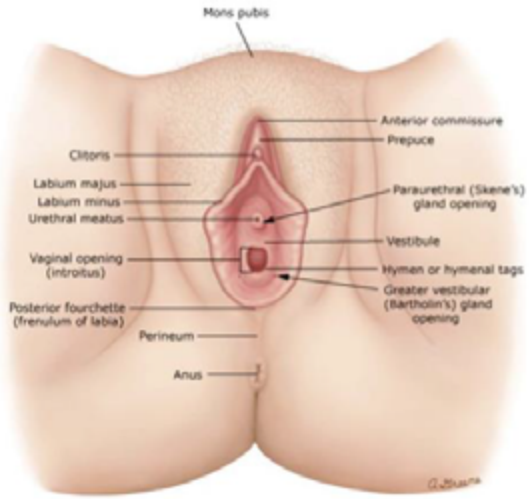

Figure 1. Anatomy of the vagina.[1]

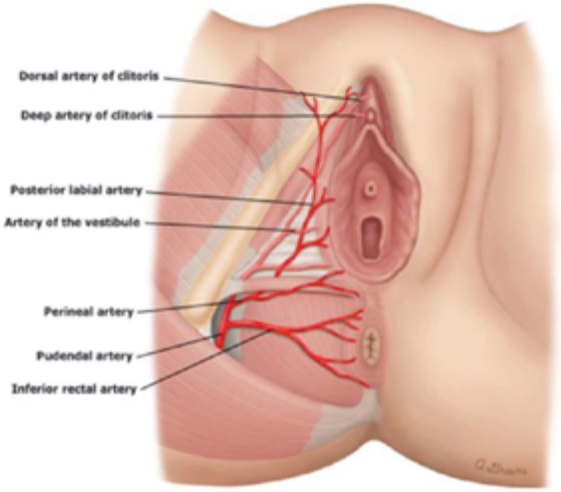

Figure 2. Illustration of vagina vascularization.[1]

Vaginal laxity is a symptom of pelvic floor dysfunction, with vaginal looseness being the most common complaint. The leading cause of vaginal looseness is unknown, but it is assumed that it is caused by pregnancy and the vaginal delivery process. Another symptom that may arise is reduced vaginal sensation during sexual intercourse.[8,9] Menopause is an inevitable phenomenon of a woman's life.[1,2,7] The average age where women develop menopause in Europe is 46.7 to 50.2 years. Menopause is caused by the loss of hormonal function of the ovary. In 7 to 10 years after the end of the menstrual cycle, atrophic change occurs to 50% of women, and as time goes on the number increases to 73 to 75%. Within those numbers, 70% women with atrophy symptom do not return to a medical facility due to the subject's view that the condition was normal.[7]

When estrogen level drops, vagina epithelial tissue becomes thinner, losing its barrier function and elasticity. Secretion of Bartholin gland also declines. These changes contribute to trauma and discomfort in vaginal mucous tissue (Figure 3).[1,7] Other condition induced by estrogen deficiency is the disturbance of vagina normal flora by fecal flora, dominated with Gram-negative bacteria, and other bacteria. This causes a change of vaginal pH from 5.5 to approximately 6.8.[7] In a study by Brotman et al., correlation between vaginal microbiota, low concentration of lactobacillus, and VVA symptom manifestation was established.[7]

Diagnosis of VVA is made based on history taking and clinical examination; however, other objective examination such as Vaginal Maturation Index (VMI), Vaginal Health Index (VHI), vaginal pH measurement, vaginal flora investigation, and laboratory examination can also be utilized.[1,10,11,12] Evaluation of vaginal health using VHI can be done at the end of therapy to evaluate the outcome or during the therapy with certain consideration. Besides history taking, clinical examination and other diagnostic modality, or follow-up using questionnaire could also be done to evaluate symptoms improvement and its effect on patients'quality of life such as improvements of libido and dyspareunia that contribute to improved quality of life for postmenopausal women.[13,14,15]

A novel questionnaire called Day-to-Day Impact of Vaginal Aging (DIVA) has been introduced in America. The questionnaire is used to evaluate the effect of vaginal atrophy symptoms in menopausal

women such as the sexual function and quality of life (QoL), where a lower score corresponds to greater urogenital atrophy.[16,17]

In response to hypoestrogenism as VVA etiology and the pathogenesis of VVA symptom manifestation, the most logical therapy for this condition is estrogen hormone replacement therapy.[12,13] Application of topical estrogen in symptomatic VVA in several clinical studies showed improvement of VVA symptoms, improving maturation index of vaginal cell, and lower vaginal pH.[14,15] Estrogen operates at molecular level by activating estrogen receptors (ER) - alpha and ER-beta.[11] ER-alpha is located in the uterus, ovary, hypothalamus, liver, fibroblast, and macrophage, while ER-beta can be found in ovary, central nervous system, circulation system, immune system, genitourinary system, and respiration system. Both estrogen receptors can be found in vaginal wall epithelium, where the distribution of the two receptors is affected by menstruation.[12]

Lower dose of estrogen therapy might be considered if higher dose of estrogen increases risk of endometrial hyperproliferation and adenocarcinoma occurrence.[12,16] Topical estrogen therapy can rapidly reduce the symptoms of VVA; however, this therapy route could not improve vasomotor symptom or protect from osteoporosis.[17,18,19] According to the data gathered by North American Menopausal Community, topical estrogen therapy given to menopausal women can improve the number of Lactobacilli in vagina, repair vaginal and urethral epithelial tissue, and repair vaginal rugae structure.[12] Topical estrogen therapy preparations come in the form of cream, a vaginal ring containing estriol, conjugated estrogen, estradiol, or estrone.[12] According to a Cochrane review from 2006, all kinds of topical estrogen therapy in the vagina have similar efficacy to improve symptoms of vaginal atrophy such as vaginal dryness, dyspareunia, and itching. There was also no significant difference in endometrial thickening and endometrial hyperplasia incindence.[12]

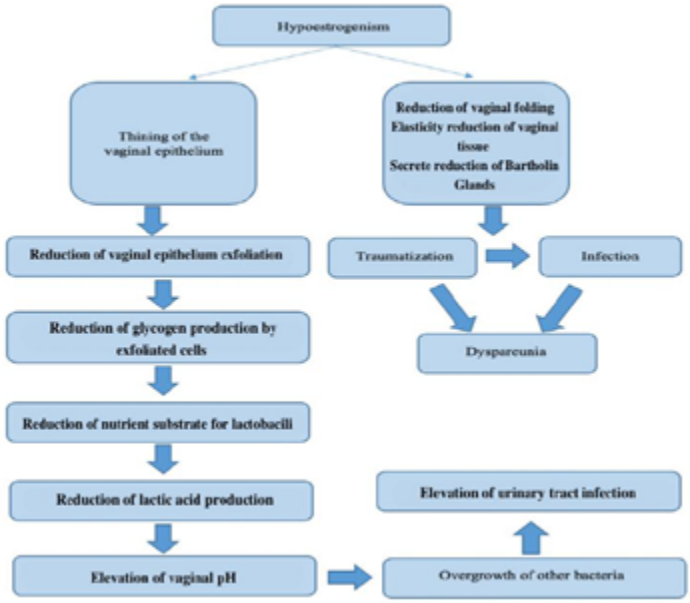

Figure 3. Vulvovaginal atrophy pathogenesis.[10]

Table 1. Vaginal health index scoring component[15]

Score	Overall Elasticity	Fluid secretion type and consistency	pH	Epithelial mucous	Moisture
1	None	None	6.1	Petechiae noted before contact	None, mucosa inflamed
2	Poor	Scant, thin yellow	5.6 – 6.0	Bleeds with light contact	None, mucosa not inflamed
3	Fair	Superficial, thin white	5.1 – 5.55	Bleeds with scraping	Minimal
4	Good	Moderate, thin white	4.7 – 5.0	Not friable, thin mucous	Moderate
5	Excellent	Normal (white flocculent)	< 4.6	Not friable, normal mucosa	Normal

Table 2. Day-to-day impact of vaginal aging questionnaire[17]

Factor	Item	All women	Sexually active
Activities of daily living	During the past 4 weeks, how much have vaginal symptoms such as dryness, soreness, irritation, or itching made it uncomfortable for you to or interfered with your ability to…		
	… walk at your usual speed?	0.71	0.69
	… wear the clothing or underwear you want?	0.68	0.64
	… use the toilet or wipe yourself after using the toilet?	0.63	0.58
	… sit for more than an hour?	0.76	0.75
	… get a good night/s sleep?	0.59	0.61
Emotional wellbeing	During the past 4 weeks, how often have vaginal symptoms such as dryness, soreness, irritation or itching caused you to feel…		
	… depressed or down?	0.81	0.79
	… embarrassed?	0.76	0.78
	…frustrated or resentful?	0.76	0.73
	… bad about yourself?	0.75	0.75
Sexual functioning	The following questions ask about the impact of your vaginal symptoms on vaginal sexual intercourse as well as other types of sexual activity such as self-stimulation or masturbation. During the past 4 weeks, have vaginal symptoms such as dryness, soreness, irritation, or itching affected…		
	…your desire or interest in having vaginal sexual intercourse or other types of sexual activity (including self-stimulation or masturbation)?	0.73	0.77
	…how frequently you had sexual intercourse or other type of sexual activity (including self-stimulation or masturbation)?	0.52	0.57
	…your desire or interest in being in a sexual relationship?	0.88	0.83
	…your confidence that you could sexually satisfy a partner?	0.82	0.73
	…your overall satisfaction with your sex life?	0.82	0.82
	…your ability to become aroused during sexual activity (including self-stimulation or masturbation)?	NA	0.71
	…your ability to be spontaneous about sexual activity (including self-stimulation or masturbation)?	NA	0.85
	…your ability to relax and enjoy sexual activity (including self-stimulation or masturbation)?	NA	0.90
	…the amount of pleasure you experience during sexual activity (including self-stimulation or masturbation)?	NA	0.88
Self-concept and body image	The following statements describe ways in which your vaginal symptoms may have affected your feelings about yourself and your body. Please indicate how true each of the following statements has been for you during the past 4 weeks.		
	My vaginal symptoms make me feel like I'm getting old.	0.74	0.72
	I feel undesirable because of my vaginal symptoms.	0.79	0.79
	When I think about my vaginal symptoms I feel like I have lost something.	0.85	0.83
	My vaginal symptoms make me feel like my body is deteriorating.	0.81	0.78
	I feel less sexy because of my vaginal symptoms	0.86	0.85

NA, not applicable

Consideration for choosing the kind of topical estrogen depends on patient preference. Available preparation included vaginal cream, vaginal ring, and vaginal capsules (Table 3). [1,4,12,20] Vaginal cream containing conjugated equine estrogen and vaginal cream containing estradiol are the most frequently used preparations, as both of the creams have decent moisturizing property.[12] The amount of cream applied needs to be monitored, as application of cream more than the recommended daily dose poses a risk of side effect.[12] Based on data gathered by Kingsberg et al., women who use vaginal cream may feel discomfort in the vaginal area.[11] Vaginal cream containing 0.5-1 g of estrogen is used daily in the first two weeks, three times a week in the third week, and two times a week in the fourth week (Table 3).[12] Topical estrogen may minimize systemic estrogen exposure and the potential side effect it might cause. [7,10,12] Local estrogen application using topical estrogen therapy should be chosen if vaginal symptoms are the only complaints.[1,12,19]

Table 3. Hormone topical therapy for vulvovaginal atrophy [7]

Route of administration	Medication	Pharmacological preparations	Initial dosage	Maintenance dosage
Vaginal cream	Estradiol-17b	Estrace 0.01%	0.5 – 1 g daily for the first 2 weeks	0.5 – 1 g one to three times weekly
	Conjugated estrogens	Premarin 0.625mg/g	0.5 – 1 g daily for the first 2 weeks	0.5 – 1 one to three times weekly
Vaginal capsules	Estradiol-17b softgel capsules	TX-005HR	4/10/25 µg daily for 2 weeks	One or two times per week
Vaginal ring	Estradiol-17b	Estring	2 mg (releases 7.5 µg daily)	Insert for 90 days
	Estradiol acetate	Femring	12.4/24.8 mg (releases 0.05/0.1 µg daily)	Insert for 90 days

Various studies have shown that hyaluronic acid compound is safe with low odds of adverse effect. [19] Hyaluronic can be given to VVA patients with contraindication toward estrogen therapy, or patients who prefer non-hormonal therapy to improve vaginal surface integrity and mucosal restoration. [4,5,20,21]

Lubricant application is recommended in vaginal dryness. Lubricant improves vaginal wetness during penetration, thus improving sexual satisfaction.[22,23] Lubricant is chosen as a therapy for women with estrogen therapy contraindication.[10,12,23] Lubricant may reduce dryness symptoms and discomfort during sexual intercourse by providing short-term symptom alleviation.[22]

Moisturizer for vagina rehydrate dry mucosal tissue mimics natural vaginal secretion.[1,22] The frequency of moisturizer application should be adjusted to the severity of vaginal atrophy (in more severe atrophy, moisturizer application should be more frequent). Effect of moisturizer lasts longer compared to lubricant effect.[1,18,22]

Recent studies revealed that hormonal therapy is correlated with the increased risk of breast cancer and endometrial cancer, thus the researcher community and the population are taking interest in herbal medicine as safer alternatives.[22,23] Oak gall extract, isoflavone, and *Calendula officinalis* might reduce VVA symptoms by significantly improving sexual satisfaction and orgasm, tighter vaginal sensation during intercourse, vaginal lubrication, and reduced vaginal dryness.[23-25]

Table 4. Recommendation for healthcare professionals on vaginal lubricant and moisturizer based on vulvovaginal atrophy complaints and symptoms[22]

Symptom or situation	Recommendation	Rationale
Urogenital atrophy, elevated vaginal pH, experiencing pain in daily life due to extreme dryness	Use a vaginal moisturizer with acidic pH and osmolality below the WHO ideal recommendation of 380 mOsm/kg	Rehydrate vaginal tissues and lower vaginal pH to minimize infection (e.g. bacterial vaginosis)

Symptom or situation	Recommendation	Rationale
Dyspareunia (painful intercourse) caused by urogenital atrophy	Use a vaginal lubricant with acidic pH matched to vaginal pH and with osmolality below the WHO ideal recommendation of 380 mOsm/kg	Lubricate dry vaginal tissues without causing irritation and maintain or lower vaginal pH
Urogenital atrophy as a result of cancer treatment when HRT is contraindicated, or in combination with topical estrogen if still experiencing discomfort from atrophy	For daily comfort, use a paraben-free vaginal moisturizer with acidic pH and osmolality below the WHO ideal recommendation of 380 mOsm/kg For sexual intercourse or for use with vaginal dilators, use a paraben-free vaginal lubricant with acidic pH matched to vaginal pH and osmolality below the WHO ideal recommendation of 380 mOsm/kg	Rehydrate vaginal tissues and lower vaginal pH to minimize infection Lubricate dry vaginal tissues without causing irritation and maintain or lower vaginal pH Avoid potential endocrine disruptors (i.e. paraben preservatives)
Trying to conceive and needing a lubricant	At ovulation, use a sperm-friendly lubricant	Lubricant is pH-matched and iso-osmotic to semen
Rectal/anal sex	Use a rectal lubricant that is condom-compatible with osmolality below the WHO ideal recommendation of 380 mOsm/kg and a pH matched to rectal pH	Reduce the risk of condom damage and resulting pathogen transmission, without irritating/damaging the rectal epithelium
Vaginal or rectal examination	Use a lubricant that is pH-matched for the vagina or rectum and has osmolality below the WHO ideal recommendation of 380 mOsm/kg	Reduce the risk of irritating/damaging the vaginal or rectal epithelium.

HRT, hormone replacement therapy; WHO, World Health Organization; VVA, vulvovaginal atrophy.

CONCLUSION

Vulvovaginal atrophy is a "silent epidemic" affecting 50-60% of menopausal women's life. Symptoms of VVA including vaginal dryness, burning effect, itch, and pain during sexual intercourse may affect a patient's quality of life. The purpose of VVA therapy is to recover the function of vaginal epithelial tissue, reduce complaints and symptoms caused by estrogen decline and improve quality of life, especially related to sexual activity.

In response to hypoestrogenism as VVA etiology and the pathogenesis of VVA symptom manifestation, the most logical therapy for this condition is estrogen hormone replacement therapy.[12,13] Application of topical estrogen in symptomatic VVA in several clinical studies showed improvement of VVA symptoms, improving maturation index of vaginal cell, and lower vaginal pH.[14,15] According to a Cochrane review from 2006, any kind of topical estrogen therapy in vagina has a similar efficacy to improve symptoms of vaginal atrophy such as vaginal dryness, dyspareunia, and itching. There was also no significant difference in endometrial thickening and endometrial hyperplasia incidence.[12]

Various studies showed that hyaluronic acid compound is safe with low odds of adverse effect.[19] Hyaluronic can be given to VVA patients with contraindication toward estrogen therapy, or patients who prefer non-hormonal therapy.[4,5,10,21] Lubricant application is recommended in vaginal dryness. Lubricant improves vaginal wetness during penetration, thus improving sexual satisfaction.[22,23] Oak gall extract, isoflavone, and *Calendula officinalis* might reduce VVA symptoms by significantly improving sexual satisfaction and orgasm, tighter vaginal sensation during intercourse, vaginal lubrication, and reduced vaginal dryness.[23-25]

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