

# Comparison of the Effects of Vaginal Royal Jelly and Vaginal Estrogen on Quality of Life, Sexual and Urinary Function in Postmenopausal Women

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## ABSTRACT

**Introduction:** Several causes can disturb the quality of life in postmenopausal women. Stress, urinary incontinence is one of the factors that can influence the quality of life of women, since they evade social activities and limit their behavior. Vulvovaginal disorders adversely impacts sexual action, psychosocial health, and partner relationships.

**Aim:** The aim of this study was to examine the therapeutic properties of vaginal cream of royal jelly and estrogen on quality of life, sexual and urinary problems in postmenopausal women.

**Materials and Methods:** This study was a randomized controlled clinical trial that was done on 90 married postmenopausal women 50 to 65-year-old. A total of 90 women were randomly distributed to three groups and were treated with vaginal cream of royal jelly 15%, lubricant, and conjugated

estrogens for three months. Before and after intervention, quality of life and vaginal cytology were evaluated. Data was analysed by SPSS 16 using ANOVA and Tukey tests.

**Results:** The results expressed that vaginal royal jelly is considerably more effective than conjugated estrogens and lubricant in the improvement of quality of life, sexual and urinary function in postmenopausal women ( $p < 0.05$ ). Results of Pap smear showed that improvement of vaginal atrophy in conjugated estrogens group was better than other groups ( $p < 0.001$ ), and there was no significant difference between lubricant and royal jelly groups ( $p = 0.89$ ).

**Conclusion:** The effectiveness of vaginal royal jelly in treatment of sexual and urinary problems of postmenopausal women is related to its estrogenic properties and could be suitable in promotion of life quality in postmenopausal women.

**Keywords:** Conjugated estrogens, Menopause, Vulvovaginal atrophy

## INTRODUCTION

More than 80% of the women face physical and psychological problems when they approach menopause leading to a reduction in the quality of life [1]. World Health Organization (WHO) described quality of life as an individual's insight of their situation in life in the base of the culture and value systems in which they habit and in relation to their aims, expectancies, standards and concerns. Studies have revealed that menopause might have an adverse impact on quality of life of women [2].

Several causes can disturb the quality of life in postmenopausal women. Stress, urinary incontinence is one of the factors that can influence the quality of life of women, since they evade social activities and limit their behavior [3]. Vulvovaginal disorders adversely impact sexual activity, psychosocial health and partner relationships [4]. More than 56% of postmenopausal women undergo dyspareunia affected by vaginal dryness [5], and the dyspareunia is correlated with reduced libido [6] and ultimately disturbed quality of life. The commonest urogenital symptoms related to menopause are vaginal dryness, followed by irritation or itching, discharge, and dysuria. These problems are the outcome of vaginal atrophy which is caused by decreased transudation through the vaginal epithelium and decreased cervical gland secretions due to post-menopausal estrogen reduction. Vaginal dryness is the commonest symptom of urogenital disorders in menopause. Vaginal atrophy is strongly associated with sexual disorder and lower urinary tract problems, such as frequency, nocturia and dysuria, also incontinence and recurring infection are reported more often in the existence of vaginal atrophy. These problems, apart from being troublesome also negatively influence their quality of life. Thus, before irreversible alterations occur, quick detection and treatment of vaginal atrophy should be performed [4].

Postmenopausal women frequently suffer from urinary incontinence caused by an increase in intra-abdominal pressure such as sneezing, coughing, jumping, laughing and or sexual intercourse [7]. Stress incontinence influences sexual activity as well [8,9].

To reduce vulvovaginal atrophy (VVA) symptoms, primary therapies were suggested as non-hormonal vaginal lubricants, moisturizers and regular sexual function [10]. For women who do not improve by lubricants and moisturizers, estrogen therapy was recommended as a therapeutic standard [11]. Various vaginal estrogen compounds such as conjugated equine estrogens, estradiol and estriol vaginal creams, a sustained release intra-vaginal estradiol ring and a little dose estradiol and estriol pills are useful therapeutic choices in the treatment of this problem [10].

## AIM

The present study aimed to compare the therapeutic effects of vaginal cream of royal jelly and estrogen on quality of life, sexual and urinary function in postmenopausal women.

## MATERIALS AND METHODS

This study was a double-blind randomized controlled clinical trial that was done on 90 married postmenopausal women aged between 50 to 65-year-old referred to Women Clinics of Hajar Hospital, from January 2013 to January 2014. After approving the research by the Ethics Committee of Shahrekord University of Medical Sciences, the interested women were requested to contribute in this clinical trial, the aims and process of the study were elucidated to them. All of women who signed the consent were included. Then, women entered their information in a questionnaire containing demographic characteristics, medical history, pregnancy information and Contraceptive method. Finally, the participants were assigned and divided into three therapeutic

groups based on simple sampling, 27 subjects in group of lubricant, 22 subjects in group of conjugated estrogen, 24 subjects in group of royal jelly: Vaginal estrogen 0.625 mg (Conjugated estrogens: manufacturing Pharmaceutical Company: Aboreihan Bironi company, Tehran, Iran), Placebo (KY jelly manufacturing ABURAIHAN Pharmaceutical Company), and vaginal cream of royal jelly 15% in lubricant base. Total number of patients was 90 at the beginning of the study but 73 patients were remained at the final. The flow diagram of participants and the allocation into various groups have been shown in [Table/Fig-1].

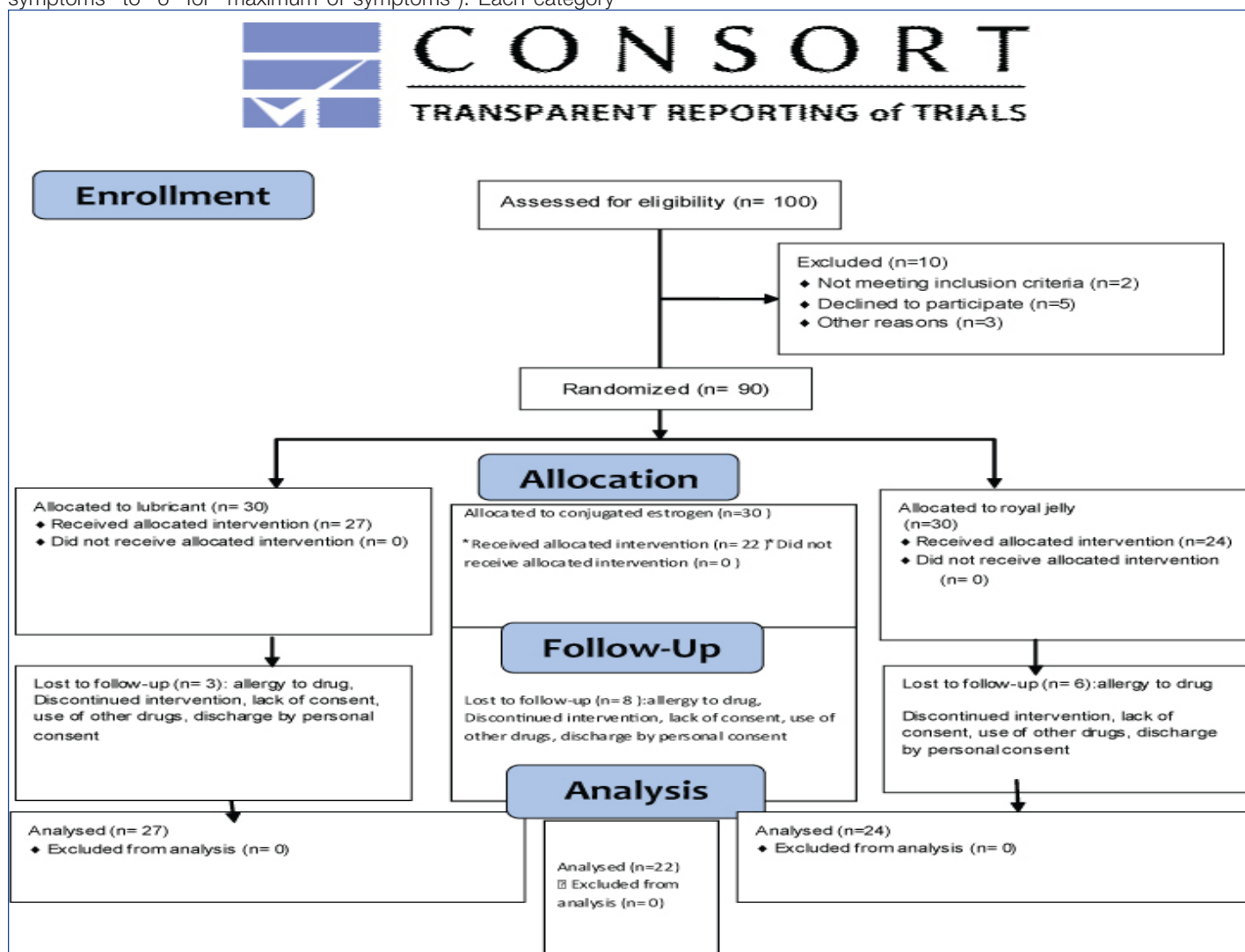
Inclusion criteria were age 50 to 65-year-old, normal Pap smear within the last 3 years, at least 12 months of amenorrhea and or having FSH test more than 40 IU, vaginal pH>5, symptoms of vaginal atrophy, having sexual activity, naturally menopause.

Exclusion criteria were dissatisfaction to participate in the study, history of sexual problems, chronic or systemic disease (e.g., diabetes, personal and family (first degree family) history of breast or endometrial cancer, prolapse grade 2 and above of bladder and uterus, history of endometriosis, surgery of anterior posterior repair (APR), personal and family (first degree family) history of thromboembolism, chronic liver disease, migraine, optic nerve disease, epilepsy and hereditary dyslipidaemia), use of hormones, allergy to honey, Sensitivity to estrogenic compounds and its products and not sexually active women viz divorced/unmarried/widowed.

Data were collected using the quality of life questionnaire and laboratory observations. The Menopause-specific Quality of Life (MENQOL) questionnaire is self-administered and consists of a total of 29 items in a 7 point Likert-scale format (ranging from "0" for "no symptoms" to "6" for "maximum of symptoms"). Each category

investigate the effect of each of these menopausal problems during the last month: vasomotor (items 1–3), psychosocial (items 4–10), physical (items 11–26), and sexual (items 27–29). Higher scores indicate better quality of life in every area and lower scores indicate poor quality of life. This questionnaire has been used in various studies in Iran and has been standardized and validated [12].

The questionnaire was completed pre- and post-intervention period by women's Resident as personal interview. In addition, questions related to sexual and urinary problems (5 questions) were considered and evaluated in this questionnaire. Cytological examination of the cervix and vagina was also done pre- and post-intervention period. So that the Pap smear sampling of patients was done before and after the study, with the following conditions: Avoid having sex 24 hours before Pap smear, Lack of douching in the past 48 hours, Non-use of vaginal creams in the past week, No spotting. The sampling was performed from ectocervical and endocervical regions by spatula. The samples were drawn on the separate sections of Lam. The Lams were fixed immediately with 96% alcohol. At the end of the day, the samples were sent to pathology and were interpreted by a pathologist. The percentage of parabasal cells observed in Pap smear was the classification criteria of vaginal atrophy severity. The increased parabasal cells and decreased superficial cells showed more severe atrophy [13]. Collaborator pathologist who was unaware of the study groups, classified severity of atrophy based on the percentage of parabasal cells in the smears of patients: Score 1; the lack of parabasal cells (no atrophy), Score 2; 1-20% parabasal cells (mild atrophy), Score 3; 20-50% parabasal cells (moderate atrophy), Score 4; >50% parabasal cells (sever atrophy).



[Table/Fig-1]: Flow diagram of participating of three groups during study.

The creams were prepared in the same tube. Patients, physicians and pathologists were unaware of the type of medication prescribed. At the beginning of the study, Patients were instructed how to use the vaginal creams: First and second week; one applicator per night, third and fourth week; an applicator as four nights a week, the fifth week until the end of the twelfth week; an applicator as two nights a week. The intervention period was three months.

The antioxidant activity of Royal jelly was evaluated by DPPH (2, 2-diphenyl-1-picrylhydrazyl) assay [8].

## STATISTICAL ANALYSIS

Data were analysed by SPSS 16 software. Descriptive statistics were obtained for all variables. The normality of variables was tested by the Kolmogorov-Smirnov test and results were reported using frequency, mean, standard deviation. Also, data analysis was performed using ANOVA and Tukey tests.

## RESULTS

In this study, 90 postmenopausal women were divided into three groups consisting of 27 subjects in group of lubricant, 22 subjects in group of conjugated estrogen, 24 subjects in group of royal jelly.

The mean age of participants was 53.57±4.89-year-old, and the mean age of onset of menopause in women was estimated 48.33±4.97-year-old in the age range 45 to 57. The mean BMI of samples was 28.5±4.17 in the range of 19 to 41%.

Most of the participants (54.4%) were illiterate. Average number of delivery was 5.21±2.66, and 95.8% of women were housekeepers. The mean age of participants, age at menopause, education, body mass index, career status and mean number of delivery in the three groups were not significantly different [Table/Fig-2].

In addition, at the beginning of the study, the severity of vaginal atrophy and the mean quality of life of women in the three groups were similar and, therefore, the groups were matched [Table/Fig-3].

ANOVA test showed significant differences of all aspects of life quality and vaginal cytology (vaginal atrophy) between three groups at the end of intervention ( $p < .001$ ). Tukey test showed that vaginal royal jelly and conjugated estrogen are more effective than vaginal lubricant in improving the quality of life and sexual and urinary problems in postmenopausal women ( $p < .05$ ). Effectiveness of royal jelly in improving the quality of life was more than Premarin, but the difference between two groups was not significant ( $p > .05$ ).

The results of Pap smear showed that the group of conjugated estrogens had the most reduction in the parabasal cells of the vagina and improvement of vaginal atrophy. Tukey test showed that there were significant differences between the groups receiving lubricant

		lubricant group	Premarin group	Royal jelly group	p-value
Age, year		54.37±4.75	53.72±5.12	52.79±4.88	0.52
Menopause age, y		49.16±3.81	49.44±2.52	46.42±6.98	0.09
Body mass index, kg/m <sup>2</sup>		29.43±3.95	26.97±4.16	28.98±4.17	0.10
Number of delivery		5.92±2.49	5.04±2.47	4.66±2.92	0.23
Employment status	Housekeeper	26	20	21	0.14
	Employee	0	1	3	
Education	Illiterate	13	11	13	0.34
	Elementary	8	4	3	
	Secondary school	3	2	1	
	High School and Diploma	1	1	4	
	College	0	1	3	

**[Table/Fig-2]:** Demographic Characteristics of the Participants in three groups<sup>a</sup>  
<sup>a</sup> Data are presented as Mean ± SD.

and conjugated estrogens and the group receiving conjugated estrogen had lower parabasal cells ( $p = 0.004$ ). However, there was no significant difference between royal jelly group and lubricant group, ( $p = 0.89$ ). Also, significant differences were observed between the groups receiving royal jelly and Conjugated estrogens ( $p = .02$ ), and status of vaginal atrophy in patients taking conjugated estrogens was better than royal jelly group [Table/Fig-4].

The amounts of phenols, flavonoid and flavonols of Royal jelly measured 12.2 mg/g, 45.62 mg/g and 60.47 mg/g, respectively. Antioxidant activity of Royal jelly by DPPH method was determined 15%.

	lubricant group	Premarin group	Royal jelly group	p-value
Vasomotor problems	8.88±5.45	8.45±5.08	10.37±5.60	0.44
Psychosocial problems	14.03±8.64	17.54±8.79	18.54±9.90	0.18
Physical Problems	41.77±18.54	41.31±14.84	50.41±17.52	0.12
Sexual Problems	11.37±5.85	12.00±5.30	12.91±5.83	0.62
Quality of life	76.07±29.20	79.31±26.24	92.25±30.56	0.12
Vaginal atrophy	2.26±1.25	2.27±1.31	2.12±1.19	0.89

**[Table/Fig-3]:** Comparison of quality of life and severity of vaginal atrophy in the three groups, at the beginning of the study<sup>a</sup>  
<sup>a</sup> Data are presented as Mean ± SD.

	lubricant group	Royal jelly group	Premarin group	p-value
Quality of life	-3.18±9.37	-30.36±14.39	-35.29±20.29	<.001
Sexual Function	-.81±3.06	-4.45±2.93	-4.83±4.17	<.001
Urinary problems	-.59±2.04	-2.50±2.57	-3.95±3.68	<.001
Vaginal atrophy	-.38±.63	-1.23±1.26	-.51±.67	0.004

**[Table/Fig-4]:** Comparison of changes in quality of life and vaginal atrophy in groups<sup>a</sup>  
<sup>a</sup> Data are presented as Mean ± SD.

## DISCUSSION

Finding of the study showed that vaginal cream of royal jelly is significantly more effective than vaginal cream of conjugated estrogens and lubricant in improvement of quality of life and sexual and urinary problems in postmenopausal women. In addition, the conjugated estrogens was more effective than the lubricant in improving various aspects of quality of life, and the rate of vaginal atrophy in the group receiving conjugated estrogens compared to the other two groups significantly reduced.

In Bachmann et al., study, the estrogenic properties of RJ were examined using various approaches. This study reported evidence that RJ has estrogenic activities via interaction with estrogen receptors after endogenous gene expressions [13] that is consistent with our results.

Nakaya et al., found that royal jelly have an anti-environmental estrogen property. Royal jelly inhibits the stimulatory effect of growth of Bisphenol A on MCF-7 cells. Bisphenol A is an environmental estrogen that increases proliferation of MCF-7 cells of human breast cancer [14].

Antioxidant activities of RJ were investigated in several studies: it was shown that the antioxidative activities and ROS activities against active oxygen species of RJ were high in the sample with a low protein concentration. It was indicated that royal jelly possesses much higher antioxidative activity and ROS activity [15]. In a study by Cavusoglu, Royal jelly was shown to have antioxidant activity against cadmium-induced non toxicity and oxidative stress in albino mice [16].

Koc et al., found that RJ supplementation enhanced considerably glutathione peroxidase activities and erythrocyte superoxide dismutase and considerably decreased Malondialdehyde levels [17].



It has been demonstrated earlier that RJ reduced intracellular oxidation in a dose dependent manner. It also influences metabolic activity in a growth phase dependent manner [18]. Analysis of Protein profile indicated that royal jelly in the cell does not possess only ROS activity, but it influence protein expression as well [19].

In a study by Sinha and her colleague, it was shown that Local estrogen also is highly effective in relieving symptoms of urogenital atrophy and enhanced libido, and in improving sexual function in symptomatic postmenopausal women [20] that is in accordance with our findings.

In a meta-analysis study by Cardozo et al., ten randomized clinical trials were evaluated and it was indicated that estrogen therapy was an efficient treatment against vaginal disorders, and there was greater improvement in vaginal problems and cytological results with vaginal estrogen therapy compared to oral estrogen [21] that is consistent with our study.

Similar to our findings, the results of Long et al., study suggested that estrogen therapy alone enhances the vaginal blood stream and improves some sexual activities in postmenopausal women. Compared with systemic therapy, topical vaginal compounds were shown to associate with enhanced symptom relief [22]. Raymundo et al., showed that vaginal treatment with vaginal cream of conjugated equine estrogens resulted favourable changes in the vaginal tissues [23].

Besides, Al-Baghdadi et al., showed that topical vaginal estrogen compounds reverse atrophic alterations and relieve the symptoms, and prevent systemic effects [24]. In a study by Sinha et al., it was suggested that Lubricants are frequently used during intercourse to provide temporary alleviation from vaginal dryness and dyspareunia [25].

In addition, Nachtigall showed that moisturizers recover vaginal dryness, itching, dyspareunia, but their impacts are lesser than estrogen therapy [26] that is again consistent with our findings. Supporting our result, Raghunandan et al., study investigated the effects of local estrogen with or without local testosterone on sexual and urogenital health in postmenopausal women. They found that local estrogen either alone or with androgen is effective in recovery of urogenital atrophy symptoms and sexual activity in postmenopausal women without any side effects [27].

Ko et al., found that Stress urinary incontinence is frequently associated with adverse effects on quality of life of patients. Severity of incontinence, one's response to problems and physical image of oneself are among the factors affecting the quality of life [28]. The study by Perrotta suggested that topical estrogen therapy decreases the symptoms and prevent urinary tract infections [29].

Investigating natural products affecting quality of life and health of postmenopausal women is essential [30]. Royal jelly is one of the natural products that has several useful properties. RJ has been demonstrated to possess abundant functional properties such as anti-inflammatory activity, antibacterial activity, vasodilative and hypotensive activities, antioxidant activity, disinfectant action, antitumour activity and antihyper cholesterolemic activity [18].

## CONCLUSION

In this study, vaginal royal jelly was effective in improving symptoms of sexual and urinary problems and quality of life in postmenopausal women. Given to the various properties of royal jelly and its effectiveness on quality of life in postmenopausal women, further studies are recommended for use of royal jelly in improving menopausal symptoms.

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