Introduction: Postmenopausal vaginal atrophy is a progressive clinical condition. Vaginal dryness, irritation; itching; burning; dysuria; dyspareunia and postcoital bleeding are the most common symptoms. Locally applied vaginal estrogen is widely used to treat this condition, but some women are still reluctant to estrogen treatment especially those with a personal or family history of malignant and cardiovascular diseases. Therefore it is important to find an alternative therapy to be used for treatment of postmenopausal urogenital atrophy. Material and methods: 64 postmenopausal women with vaginal atrophy were recruited for this study, including two treatment groups with 24 women in each group and 16 women in a placebo group. Vagitocin (oxytocin gel) in two different concentrations (100IU and 400IU/ml) or placebo gel, were topically administered once daily over 7 weeks. Vaginal biopsies were collected in 24 of the women. Three visits in the hospital were included and also one telephone contact two weeks after cessation of treatment. Clinical evaluation of the vaginal mucosa, recording of vaginal pH and vaginal mucosal cytology and histology were performed. The women reported their intensity of symptoms at all three visits. Also, the most bothersome symptom was reported. The doctor made an overall evaluation of the vaginal mucosal health. Results: The most bothersome symptom from vaginal atrophy was strongly reduced in the 400IU group vs placebo, p=0.0089. The percentage of the three cell layers in the vaginal mucosa were significantly changed within groups over time by 400 IU (p=0.0004, 0.05, 0.03 for parabasal, intermediate and superficial cells respectively). A significant increase of the maturation value was also observed in the 400IU group but not in the 100IU over time, p=0.0002 versus 0.11. Vaginal pH decreased significantly after 100IU and after 100+400IU together, P= 0.02 and 0.009. Score of vaginal atrophy according to histological evaluation was significantly reduced after administration of 100IU and after 100+400IU together (P= 0.03 and 0.0078). Conclusion: Vaginal application of oxytocin in women with vaginal atrophy gave rise to a major improvement in symptoms and physiological expressions of vaginal atrophy. The 400IU dose was in most cases more effective than the 100IU dose. Treatment with intravaginally applied oxytocin might be a good alternative to treatment with local estrogen in future.