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ORIGINAL RESEARCH—PHARMACOTHERAPY

Evaluation of the Effects of a New Intravaginal Gel, Containing Purified Bovine Colostrum, on Vaginal Blood Flow and Vaginal Atrophy in Ovariectomized Rat

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ABSTRACT

Introduction. Vaginal dryness due to vaginal atrophy is a common complaint of postmenopausal women, interfering with sexual function and quality of life. Hormone replacement therapy is the only effective therapy but with known risks that leave unmet medical needs. A new product, ZP-025 vaginal gel, containing purified (dialyzed lyophilized) bovine colostrum, has been developed for the treatment of vaginal dryness secondary to vaginal atrophy.
Aim. The study aims to investigate the effects of intravaginal application of ZP-025 on vaginal atrophy using an animal model.
Methods. Ovariectomized female Sprague-Dawley rats were used. Three weeks after surgery, rats were divided into four groups and treated for 4 weeks (twice a day) with placebo or ZP-025 at low (0.5%) or high (2.3%) concentrations of colostrum; in the control group, rats did not receive any treatment. Changes in vaginal blood flow due to pelvic nerve stimulation were assessed by laser Doppler flowmetry and vaginal tissue was collected for histological assay.
Main Outcome Measures. The main outcome measures were vaginal blood flow before and after pelvic nerve stimulation and histology of vaginal epithelium.
Results. Treatment with ZP-025 to ovariectomized rats induced an increase of vaginal blood flow parameters (vascular capacitance, amplitude and area under the curve of the response) in response to pelvic nerve stimulation compared with control group, statistically significant at 2.3%. Vaginal epithelium showed a physiological estrous cycle aspect in treated animals, with at least five cell layers vs. one or two cell layers in control rats. As expected from a topical formulation, systemic effects on body weights and uterine wet weights were not observed with application of ZP-025.
Conclusions. In this study, the new product ZP-025, containing purified colostrum, was shown to have beneficial effects on vaginal atrophy in ovariectomized rats, improving vaginal hemodynamics and thickness of vaginal epithelium. **Vailati S, Melloni E, Riscassi E, Behr Roussel D, and Sardina M. Evaluation of the effects of a new intravaginal gel, containing purified bovine colostrum, on vaginal blood flow and vaginal atrophy in ovariectomized rat. Sex Med 2013;1:35–43.**

Key Words. Vaginal Atrophy; Bovine Colostrum; Ovariectomized Rat; Vaginal Blood Flow

Introduction

Vaginal atrophy is caused by a decrease in oestrogen production and is a common complaint of postmenopausal women, interfering with sexual function and quality of life. In about 45% of menopausal women, vaginal atrophy can be clinically manifest as a syndrome of vaginal

dryness, itching, irritation, and dyspareunia [1,2].

The vaginal atrophy becomes clinically apparent 4–5 years after menopause and its hallmarks are thinning of vaginal epithelia layers, increased vaginal pH, decrease in the local blood flow, and diminished vaginal secretion. Clinical studies have shown that these signs significantly correlate with the decline in circulating ovarian hormones [3–6].

While systemic and local estrogen-based hormonal therapy is effective in treating symptoms of vaginal atrophy in postmenopausal women [3,7–9], these medications are contraindicated in some populations (women with unknown vaginal/uterine bleeding or those with a known or suspected ovary, endometrial cancer, and breast cancer) and other women choose not to take them for fear about their safety [10,11]. Because of these issues, recent work has focused on developing more specific, and in many cases nonhormonal, alternatives to traditional postmenopausal hormonal therapy to treat vaginal dryness in presence or in absence of vaginal atrophy [12].

Zambon SpA (Bresso, Milan, Italy) has developed a gel product (ZP-025 vaginal gel—Monurelle Biogel), containing purified bovine colostrum to be administrated topically, for the treatment of vaginal dryness also in presence of vaginal atrophy. Colostrum is a substance produced from female mammary gland during the first few hours postpartum, and numerous investigators have reported that the colostrum imparts many advantages for the development of the infants [13]. Thanks to its constituents, colostrum is able to help the local defense (immunoglobulin A); modulate the immunitary response (immunoglobulin E, M, G); promote antibacteric and antiviral action (lactoferrin and transferring); modulate the inflammation factors (cytokine, interleukine); promote normal cell growth, normal cell activities, cell migration and proliferation, and tissue repair (transforming growth factor alpha and beta; epidermal growth factor); stimulate the mucosal restore; and accelerate wound healing (insulin-like growth factors—IGF-1 and -2). In particular, IGF-1 is involved in the regulatory feedback of growth hormone [14] and interferes with insulin-like growth factor binding proteins [15]. To date, based on the best scientific knowledge available to us, no sexual hormones are directly present in bovine colostrum.

Because vaginal mucosa, because of its anatomic and physiologic features, is exposed to epithelium damage and to vaginal ecosystem and local defense factors alterations, colostrum can help in promoting the mucosal trophic restoration and preserving from bacteric and viral aggression. Our hypothesis is that topical application of colostrum could have a beneficial effect specifically on vaginal atrophy.

Besides purified colostrum, this vaginal gel contains other natural substances with humectants, hydrating, re-epithelizing, and antioxidant properties at concentrations <5%: betaine, sericin, panthenol, glycerin, tocopherol, *Lepidium meyenii* root extract.

The aim of the present study was to assess the effect of ZP-025 vaginal gel on vaginal blood flow and tissue morphology using ovariectomized (OVX) rats as an animal model for vaginal atrophy. This well-characterized experimental model is very useful to induce experimental menopause, as within a short period of time postovariectomy, female rats without ovarian hormone secretion mimic many human postmenopausal changes, including vaginal atrophy. It has been well documented also in this animal model that estrogen replacement increases pelvic blood flow and restores the structural and functional integrity of vaginal tissue [16–21], confirming that the loss of estrogens is the key factor leading to vaginal atrophy.

Materials and Methods

Animals and Treatments

Adult nonpregnant female Sprague-Dawley rats (Elevage Janvier, Le Genest-St-Isle, France, 8–10 weeks old, 200–225 g) were housed 7 days prior to the beginning of the experiments, with free access to standard chow and water and maintained on an inversed 12-hour dark/light cycle (10:00/22:00). All procedures were performed in accordance with the legislation on the use of laboratory animals (NIH publication N°85-23, revised 1996) and Animal Care Regulations in force in France as of 1988 (authorization from competent French Ministry of Agriculture—Agreement No. A91-471-109, May 2009).

After a 1-week acclimation period, all rats were bilaterally ovariectomized under 1–1.2% isoflurane anaesthesia (CSP, Cournon, France).

After 3 weeks of postsurgical period to induce artificial menopause, the rats were divided into four groups (n = 8/group) and received 50 L of the following intravaginal treatments, delivered via a micropipette twice a day (8–10 hours intervals) for 4 weeks: in the control group, rats did not receive any treatment but a micropipette tip was introduced into the vagina; in the placebo group,