Colostrum in menopause effects on vaginal cytology/symptoms

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Summary

The aim of this study was to assess the effects of three weeks of daily colostrum cream on vaginal cytology and local symptoms related to menopause. Genito-urinary symptoms and cell morphology were analyzed at time 0 (T0) and after three weeks (16 ± days since the end of treatment) at time 1 (T1). Dyspareunia, vaginal dryness, and maturation index (MI) reached a statistically significant difference between T0 and T1. The results proved to be an alternative treatment for vaginal distress caused by lack of hormones in patients in which hormonal treatment is contraindicated.

Key words: Colostrum; Menopause; Vaginal cytology.

Introduction

A normal vaginal epithelium is made of pluristratified cells; the basal cells lay on a basal membrane in the inner layer; the cells are rounded in shape, small (10-12 microns), with dense omogeneous and basofilic cytoplasm, and have a large centrally-located nucleous. They are typical of postmenopausal Papanicolau (Pap) smears characterized by intense atrophy [1]. Vaginal atrophy and related symptoms (vaginal dryness, soreness, and itching, dyspareunia, and dysuria) are caused by a drop in the estrogen level, as seen during menopause. Atrophy is characterized by several cell modifications resulting in a slower cellular turnover. In menopause, topical treatment based on estrogen and lubricant creams is the main remedy currently used. Literature reports many studies on local hormonal treatment, while studies on medication other than hormones are much less [2-4]. The aim of this study was to assess the effects of colostrum on vaginal cytology and local symptoms related to menopause.

Material and Methods

Between February 2010 and June 2010, 38 patients with physiological menopause with a negative Pap smear within one year, were enrolled at the Outer Gynaecology Department of Sapienza Faculty in Rome. Genito-urinary symptoms related to menopause (vaginal dryness, soreness, itching dyspareunia, and dysuria), and cell morphology were analyzed at time 0 (T0) and after three weeks of one daily application of a colostrum vaginal cream. Patients were evaluated 16 ± days since the end of treatment at time 1 (T1). Colostrum is what is actually called "first milk", a thick, yellowish serum that provides the newborn with the essential vital substances following delivery. Table 1 shows all the components derived from colostrum and its related activities.

Cytological assessment: scraping of the lateral vaginal wall at the fornix was made using an Ayre spatula; the samples were then fixed on a glass using a cytological fixative. An expert cytologist manually evaluated all samples previously inked with a Pap method. The main parameter for cytological evaluation was the cell maturation index (MI) corresponding to a rate between parabasal, intermediate, and superficial cell numbers. On 100 cell counts, the number of parabasal cells was multiplied by 0.0, while the number of intermediate cells was multiplied by 0.5, and the number of superficial cells was multiplied by 1.0. The total number was then divided by the total number of cells: a high total number corresponded to the most estrogenic effect on cells (maximum = 1.0). Clinical symptoms assessment: patients were asked to answer a questionnaire at T0 and after one daily treatment with a colostrum vaginal cream for three weeks. A score ranging from 0 to 3 was associated to severity of symptoms (0 = absent, 1 = mild, 2 = moderate, 3 = severe). Statistical assessment: Student's t-test was used to compare the results obtained at T0 and T1 either for cytological assessment or for clinical symptoms.

Table 1.

IgG, IgA, IgM, IgE infections	Protection against bacterial and mycotic
Cytokines (Interleukins 1,6,10; γ interferon, TNF, Lymphokine)	Immune messengers responsible for immune cells intercommunication
Growth factors (IGF1-2, TGFβ, EGF, VEGF, FGF)	Responsible for growth of the cells, repair of injured cells
Glycoproteins (PRP, α2, AP, α Lactoglobulin, etc.)	Regulatory, repair and transport activity

Results

Nine patients dropped out from follow-up; three patients had inflammation at T0 (two of them were not evaluated). Eight patients were evaluated just for symptoms because they had a high MI at T0. Three patients were excluded for side-effects (intense burning) and two for comorbidity (vulval intraepithelial neoplasia - VIN1, lichen sclerosus). All patients complaining of clinical symptoms at T0 improved after treatment. Dyspareunia and vaginal dryness reached a statistically significant difference between T0 and T1 results, respectively (p = 0.006358) Table 1 (p = 0.000683), and Tables 2 and 3.

MI reached a statistically significant difference between T0 and T1 results (p = 0.00195097) Table 4.

Interestingly, 78.5% of patients had cytological signs of aspecific inflammation on T1 samples (18% discrete, 45% mild, and 36% severe inflammation) (Table 5). Thirty-three percent of patients complained of symptoms besides a high MI at T0; in these patients an improvement in the severity of symptoms was also seen after treatment.

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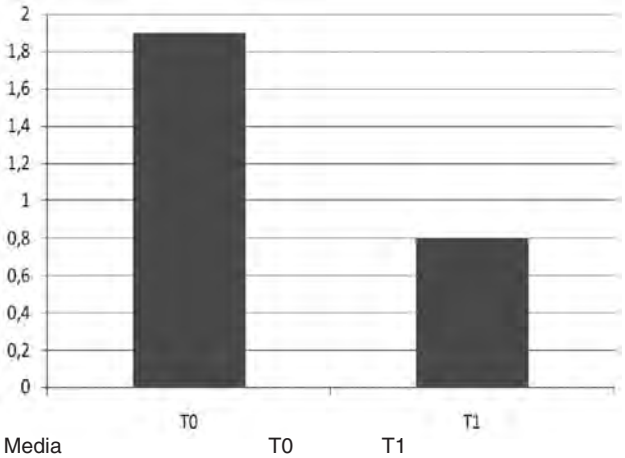
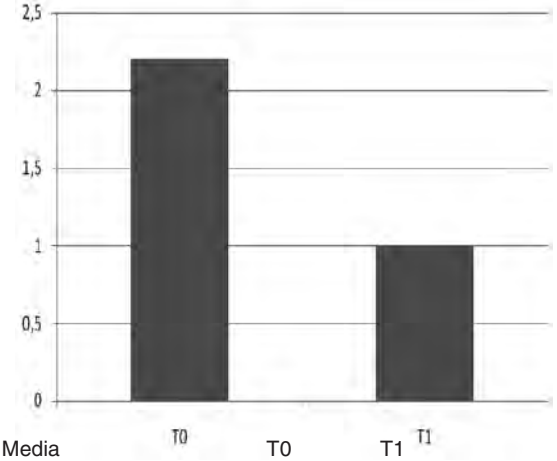
Table 2. — *Vaginal dryness*.



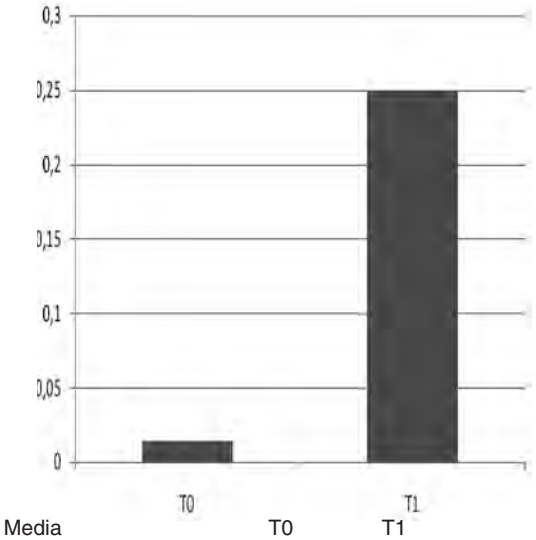
Media	T0	T1
Vaginal dryness	1.9	0.8

Table 3. — *Dyspareunia*.



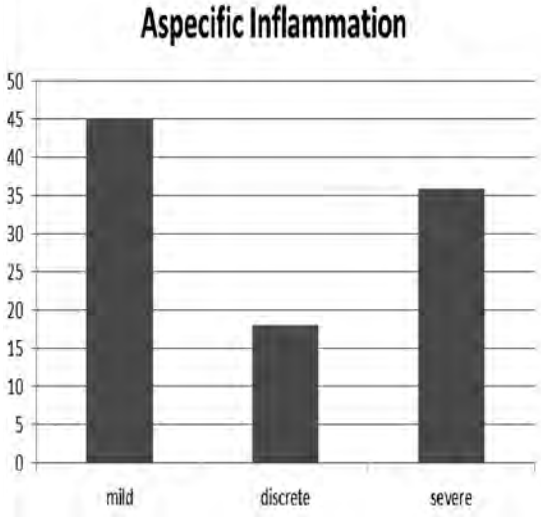
Media	T0	T1
Dyspareunia	2.2	1

Table 4. — *MI*.



Media	T0	T1
MI	0.014286	0.25

Table 5.



Discussion

In menopause, the vaginal epithelium shows a prevalence of basal cells and almost an absence of superficial cells resulting in a thinner epithelium. This fact leads to a lower exfoliation process of vaginal cells; usually during apoptosis, cells release glycogen that is hydrolyzed to glucose. Lactobacillus found in the vagina converts glucose to lactic acid. The conclusion is that in menopause, there is a change in vaginal pH resulting in a more basic vaginal pH value. This condition can lead to inflammation and infection caused by an imbalance of the vaginal flora. When estrogen levels drop, as seen during menopause, there is also lack of water tissue content, decreased blood tissue supply, and increased connective tissue despite of elastin. Cell atrophy can correspond to physical symptoms related to the genitourinary system. In this pilot study, besides the small numbers provided, the authors found a statistically significant difference in dyspareunia, vaginal dryness, and in MI, in patients treated with a daily application of colostrum vaginal cream for three weeks. The authors could not find a direct association between physical symptoms and cytological assessment; in fact even when the MI was high, patients would complain of symptoms as well. On the other hand, in 33% of these patients, the authors observed improvement of symptoms after treatment suggesting a placebo effect. This evidence strengthens the contribution of physician in explaining and supporting the transition process of finding a new balance after menopause. In this study, 78.5% of patients showed cytological signs of aspecific inflammation without symptoms after treatment. This finding did not correlate with MI improvement in the specific case but did correlate in the overall media samples, signifying that inflammation could represent the explanation key for interpreting the results. As stated, cytological signs of aspecific inflammation in T1 samples of this study, did not have a negative correspondence in terms of symptoms related to menopause. It must be taken in account that there is a physiological role of inflammatory cytokines that are

mandatory for many important conditions (i.e. follicle rupture, relaxation of the birth canal at term, etc.) [5-7]. This is the perspective from which the authors portray their results. In a study of Greendale *et al*., a relationship between examination characteristics believed to represent inflammation and inflammation biomarkers was not upheld [8]. Triggers of inflammation are a result of infectious agents, trauma, immune system activation, etc. The authors documented the presence of granulocytes, macrophages, and lymphocytes in 78.5% of T1 samples that appears to be independent of infection. Many factors can instead either stimulate or modulate synthesis of inflammatory mediators (i.e. hypoxia, environmental pollutants, exercise, etc.). Emerging literature highlights the active role of tissue recovery through biochemical activation triggered by irritative stimuli, against the old concept that a regained tissue homeostasis is only due to exhaustion of the inflammatory process. The authors focused their attention on some colostrum constituents (epidermal growth factor (EGF), immunoglobulin, and cytokines) involved in inflammation cascade [9]. The role of EGF in the skin process of repair is well known, otherwise different studies discuss its role on mucosal cell as well. Chao *et al*. reported that oral administration of EGF (60 mg/kg/day) can increase EGF content in the duodenal mucosa and promote the healing of rats with duodenal ulcer by its mitogenic action [10]. Immune mediators included in colostrum could elicit a receptor-mediated signal favoring inflammation through immune system activation and synergistically work with growth factors to promote cell maturation. The epithelium of barrier organs (respiratory tract, oral cavity, vagina, etc.) works constantly with the immune system to guarantee protection from the outside environment. This complex network of cells not only monitors and regulates immune homeostasis, but also has a role in epithelial homeostasis, development, and cell integrity. Particularly, many studies highlight the interaction between epithelial cells (EC) and intraepithelial lymphocytes (IELs) in maintaining epithelial integrity. Local γδ T cells are necessary for the differentiation and maintenance of intestinal crypt epithelia [11]. Some effector peptides produced by ECs and leukocytes can induce chemotaxis of neutrophils as well as stimulate epithelial wound closure [12, 13]. Leukocytes sensing any kind of cell injury create a PGE2 rich environment that favors proliferation of colonic epithelial progenitors [14]. As discussed above, colostrum components could have raised a local process involving inflammation that brought vaginal epithelial cells into the beginning of a new cell cycle that resulted in a MI improvement. Mitosis is a process developing in hours, as shown in Mori experiment, whereas the mitotic rate can change based on different hormonal cell status and cell age [15]. The hormonal topical treatment for genito-urinary symptoms was recently confirmed in a meta-analysis including 19 randomized clinical trials that enrolled 4,162 women [2]. The problem arises when women treated for estrogen-related cancer in premenopause, like breast cancer, complain of the same symptoms. Research should direct to find alternative treatments for this type of patient.

Conclusions

In this pilot study, besides the small numbers provided, the authors found a statistically significant difference in dyspareunia, vaginal dryness, and in MI, in patients treated with a daily application of colostrum vaginal cream for three weeks. These results proved to be an alternative treatment for vaginal distress caused by lack of hormones that can include patients in which hormonal treatment is contraindicated.

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