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Research Article

Rigenase® and Polyhexanide Combination in a Hydrogel Formulation for the Treatment of Vaginosis Symptoms: The PMCF Survey

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Abstract

Background and Objectives: Signs and symptoms of vulvovaginitis, especially when recurrent, have a significant impact on women's quality of life. The aim of this study was to evaluate the efficacy of a novel vaginal hydrogel (Fitostimoline® Septagel) composed of wheat extracts (Rigenase®) and polyhexanide in reducing vulvovaginitis symptomatology. **Materials and Methods:** A nationwide analysis of a national survey performed on 1402 patients across Italy. Pre-and postmenopausal women with suspicion of vulvovaginitis due to at least four of the following symptoms (leucoxanthorrhea, bad odor from genitalia, vulvovaginal dryness, petechiae, burning, and pruritus) while waiting for microbiological swab analysis were included and treated with one hydrogel application every 3 days for 1 week. Primary endpoint was the complete resolution of the symptomatology by the hydrogel application. **Results:** Overall, 1402 (722 of fertile age and 680 in post-menopause) women were included in this study. At the 28th follow-up examination, complete resolution of symptomatology was achieved in 1380/1402 (95%; $p<0.001$) within 12.8+- 7 and 14 +- 8 days for those of fertile age and in post menopause, respectively ($p=0.342$). All of the evaluated symptoms were significantly reduced after treatment ($p=0.001$) without differences according to the patient's menopausal status. No patient reported side effects, adverse reactions, or discontinued therapy and the product was found to be in compliance with its indication and application. **Conclusions:** This pilot study showed that the hydrogel based on Rigenase® (wheat extract) and polyhexanide could be a promising treatment for the relief of vulvovaginitis symptoms.

Keywords: Vulvovaginitis; Hydrogel; Wheat extract; Bacterial vaginosis; Local therapy; Non-antibiotic treatments; Vaginal burning

Introduction

Vulvovaginitis is an inflammatory condition involving the vulva and the vagina [1]. While it is generally caused by infection, especially after menopause, may be the consequence of hormonal imbalance [2]. Typical symptoms are: burning, pruritus, dyspareunia, pain, leucoxanthorrhea, and vaginal discharge [3]. There are different types of vaginitis, which have other causes, symptoms, and treatments. The most common types are bacterial vaginosis, which affects approximately 22 to 50% of symptomatic women, Candida-species vulvovaginitis (17% to 39%), and *Trichomonas vaginalis* (4% to 35%) [4,5]. While each type of vulvovaginitis has its own specific treatment, according to national and international guidelines, diagnosis may sometimes be time-consuming, and alternative treatments that could alleviate symptoms while preventing the worsening of the causative factor may be useful [6,7]. Recent studies have confirmed that there is an unmet need to treat these cases of vaginitis where an immediate clinical diagnosis is unfeasible. Fitostimoline® Septagel (Damor Pharmaceuticals, Naples, Italy) is a novel medical device containing Rigenase®, a proprietary wheat extract from *Triticum vulgare*, plus polyhexanide, an antiseptic active on both bacteria and yeasts, in a novel vaginal hydrogel formulation with anti-inflammatory, antioxidant, and wound-healing properties [8]. Due to the adhesive properties of the novel hydrogel formulation, the device has a posology of one application every three days. For all of these reasons, this medical device seems an excellent candidate to be used as an alternative or adjuvant therapy to antimicrobic agents for relieving the symptoms of vulvovaginitis [9].

In this trial, we evaluated through a survey on a large population of patients, the efficacy and tolerability of the Fitostimoline® septagel formulation.

Materials and Methods

Survey design and participants

This survey (PMCF: post-marketing clinical follow-up) starts from the medical need to understand the best clinical practice in managing vulvovaginitis.

For this reason, in March 2023, we designed a questionnaire based on the national recommendations for the pharmacovigilance on medical devices. Our research group included 8 key opinion leaders belonging to different Italian Regions and a group of 88 physicians (please see appendix) who participated in actually administering the PMCF survey to patients. The questionnaire was revised by the key opinion leaders and shared with the general practitioners with the aim to enroll the highest number of patients.

The PMCF survey included two visits, one at the enrollment and one at the end of the follow-up. For the enrollment survey, the following evaluations were included and completed by the physicians: patient age, sex, product indication for the treatment of vulvovaginitis symptoms, posology prescribed and duration of the treatment.

The follow-up survey collected efficacy data by the physician (indication, dosage, effects and adverse reactions) and by asking the patients whether the product was painful or there was any side effect. Furthermore, patients were asked to indicate on a scale from 1 to 10 (where 1 is not satisfied at all, and 10 is completely satisfied) their satisfaction for the evolution of the vulvovaginitis after the treatment with septagel. During the follow-up visit, also safety and customer satisfaction data were collected by giving a judgement on the product itself considering the product indication, composition, formulation and improvement of the patient quality of life.

The survey was compiled by the physicians and administered to patients who had symptoms of vulvovaginitis. Each physician should enroll the same number of patients. The duration of treatment was of at least 14 days.

Inclusion and exclusion criteria

Eligible patients were women who were at least 18-year-old, screened by applying the following eligibility criteria:

Inclusion criteria

Presence of symptoms of vulvovaginitis.

Exclusion criteria

- Refusal to participate
- History of intolerance to *Triticum vulgare* extract or polyhexanide

Ethical aspects

A clear and informative description of the survey and an explanation of how collected data would have been used were given to respondents; participation was voluntary. According to the Italian regulatory framework, all of the data were anonymized and aggregated, and no personally identifiable information was collected.

Statistical analysis

The main characteristics of the participants are reported as mean ±SD or percentage. Statistical significance was determined by a p value <0.05. In the statistical analysis, differences for continuous variables were evaluated using two-sample t-test for approximately normally distributed variables and Mann-Whitney U test for severely skewed variables. Chi-square or Fisher tests

were used to measure associations between dichotomous and categorical variables. All analyses were performed using SPSS 26.0.

Results

2000 patients were initially enrolled, and 1402 fulfilled the eligibility criteria and successfully completed the survey, as shown in the flow chart in Figure 1.

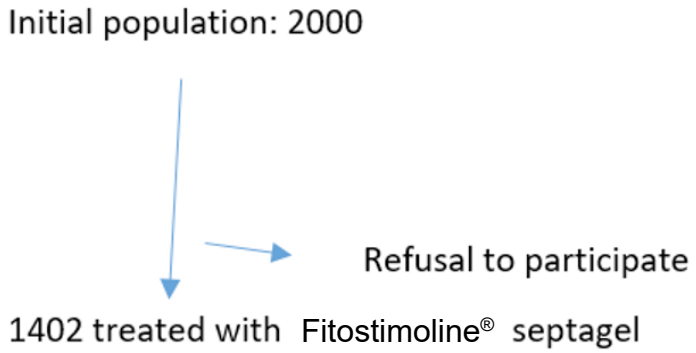

Figure 1: Flow chart of the study population enrollment.

There were no significant differences in terms of age in the women treated with the hydrogel formulation (Table 1). Following a 14-day treatment with Fitostimoline® Septagel, the survey revealed that 95% of patients had a complete symptom relief (Table 2). Coherently, the satisfaction score expressed by the patients was 9 or more probably on account a high percentage of complete symptom relief, the occurrence of pain is trivial, and very low incidence of side effects.

	Fitostimoline® septagel	p-value
N	1402	-
18-34 years %	358	-
35-50 years %	400	-
51-64 years %	380	-
65-80 years %	268	-

Table 1: Main characteristics of the examined population.

Efficacy	Fitostimoline® plus cream	p
Symptoms %	90	-
Pain%	0	-
Satisfaction score	9.5	-
Side effects No	2	-

Table 2: PMCF Efficacy results.

The safety was assessed by asking the patients two items: 1) if with the use of the medical device there was a sense of relief absent, mild, moderate, strong or very strong; 2) the indications contained in the leaflet of the formulation were clear. The answers to both these question were highly positive thus allowing the conclusion that the safety was optimal. (Table 3).

	Fitostimoline® septagel	p
Leaflet Indications clarity %	90	-
Safety %	98	-

Table 3: PMCF safety results.

Overall, the medical device was considered by the patients effective both in its formulation and in its ability to improve the patient's quality of life (Table 4).

	Fitostimoline® septagel	p
Product texture	good	-
Product grade	good	-
Product improvement of the quality of life (QoL) %	95%	-

Table 4: Customer satisfaction.

Discussion

The type of vulvovaginitis must be considered in the choice of any product, but particularly in the choice of antibiotics. Their effectiveness could be compromised in case of antibiotic resistance. Abusing the antibiotic application could lead to misfunction of the therapy without an effective symptom relief. In order to solve all these questions it is required that physician are well aware of the characteristics of novel devices in order to avoid topical antibiotic resistance in specific cases of vulvovaginitis.

Thus, the present study was aimed to obtain such information for an hydrogel based on Rigenase® and Polyhexanide. The formulation was considered efficacious in its indications. These results are in accordance with the type of administration of the medical device which is indicated for the vulvovaginitis symptoms relief as an ex-adiuvantibus therapy. In fact, the patients were overall satisfied by the treatment both because of its efficacy and also for the way through which the product is formulated and studied. Finally, the medical device was considered also to be safe for the indicated treatment.

Study Limitations

We do reckon that our research is not exempt from limitations. We recognize that therapeutic indications should be based on placebo-controlled randomized trial more than on the results of a survey, but strengths of this survey include the large population enrolled and the fact that the questionnaires were administered in multiple centers throughout Italy. Furthermore, albeit we do

not have full clinical data for all patients, our conclusions are corroborated by the fact that patients were enrolled by physicians who had prescribed the medical device on the basis of a complete knowledge of the clinical characteristics of their patients. Further dedicated interventional studies are warranted to endorse our findings.

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