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Research Article

Rigenase® and Polyhexanide Combination in a Hydrogel Formulation: The PMCF Survey 2024

Marco Battistello[1], Filippo Ninni[2], Lucia Ricci Maccarini[3], Annunziata Carlea[4], Francesco Paolo Improda[5], Carmela Mancuso[6], Giulia Chairello[7], Lorenda Zingaro[8], Anna Maria Spiga[9*]

[1]Unità Operativa di Ostetricia e Ginecologia ASST Vimercate, Italy

[2]Specialista in Ginecologia E Ostetricia, Centro medico CRPO Livorno, Italy

[3]Specialista in Ginecologia ed Ostetricia Poliambulatorio Golinelli Budrio (BO), Italy

[4]Pineta Grande Hospital, Castel Volturno, Italy

[5]PO "San Giuliano" - Giugliano in Campania, Italy

[6]Ambulatorio di ostetricia e ginecologia Gela, ASP Caltanissetta, Italy

[7]Ginecologia e ostetricia, ASL Taranto, Italy

[8]Dipartimento di Ostetricia e ginecologia A.O.U. San Luigi Gonzaga- Orbassano, Italy

[9]Medico Chirurgo Specialista in Ostetricia e ginecologia, Cagliari, Italy

[*]**Corresponding author:** Maria Spiga, Cagliari, Italy

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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: An analysis of a national survey performed on 525 patients across Italy. Pre-and postmenopausal women with suspicion of vulvovaginitis on account of 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, 525 (71% of fertile age and 29% in post-menopause) women were included in this study.

At the 28th follow-up examination, complete resolution of symptomatology was achieved in 499 women

(95%; $p<0.001$) within 8 +- 7 and 14 +- 8 days for those of fertile age and in post menopause, respectively ($p=0.342$). All 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 survey showed that the hydrogel based on Rigenase®(wheat extract) and polyhexanide could be a promising treatment for the relief of vulvovaginitis symptoms.

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

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 we designed a questionnaire based on the national recommendations for the pharmacovigilance on medical devices. Our research group included 9 opinion leaders belonging to different Italian Regions and a group of 58 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.

In the end of follow-up survey physicians collected data on efficacy and safety (adverse reactions) 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 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. The duration of treatment was from no longer than 14 days and the observation period was 4 weeks.

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.

Results

620 patients were initially enrolled, and 525 successfully completed the survey.

As shown in Table 1, patient age varied from 18 to 80 years. The majority of treated women was in the range 18-34 years. Following a 14-day treatment with Fitostimoline® Septagel, the survey revealed that 90% of patients had a complete symptom relief (Table 2). Coherently, the high satisfaction score expressed by each patient was most probably due to the large percentage of complete symptom relief, the occurrence of pain was trivial, and the incidence of side effects very low.

	Fitostimoline® septagel	p-value
N	525	-
18-34 years %	210	-
35-50 years %	163	-
51-64 years %	100	-
65-80 years %	52	-

Table 1: Main characteristics of the examined population.

Efficacy	Fitostimoline® septagel
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
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
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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Appendix 1: list of physicians who participated in PMCF survey

Mara	Musconi
Mariangela	Massaro
Filippo	Ninni
Nunziata	Pace
Angela	Passaretta
Barbara	Del Bravo
Giovanni	Cavalli
Carmine	Romano
Carolina	Axiana
Katia	Palombino
Carmela	Mancuso
Antonella	Guernieri
Roberto	Passaro
Lara	Yaylayan
Angela	Giordano
Federica	Pirozzi
Liviana	Gammi
Maria	Magliarditi
Maria Pia	Marino
Gabriele	Saccone
Alice	Bologna
Giuseppe	Iorio
Vincenza	Franconeri
Paola Anna	Filardo
Antonella	Pellegrinotti
Rossana	Favia
Massimo	Pileri
Ivana	Matassa
Raffaele	Nigro
Marco	Monti
Mario	Leonardi
Carolina	Tammaro
Isabella	Gazzani
Antonios	Kenanidis
Elena	Arnoletti
Gianpaolo	Garone
Marco	Battistello
Roverto Luca	Merz
Liliana	Luraschi
Giulia	Chiarello
Liselotte	Wittenberg
Franca	Novelli
Carmela	Lo Re
Michelina	Vitagliano
Said	Asha
Laura	Carlini
Francesco	Moscuzza
Rossana	Parducci
Alessandra	Rosi
Annamaria	Spiga
Annunziata	Carlea
Lucia	Ricci Maccarini
Roberta Daniela	Mombelli
Concetta	Palena
Maria Clarice	Vieira
Loredana	Zingaro
Fiorella	Tosoni
Francesco Paolo	Improda