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Research Article

Rigenase® and Polyhexanide combination for Wounds Treatment: The PMCF Survey

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Abstract

As the sequence of events of impaired wound healing is well characterized, the possibility to identify treatments that are already in the market and that are known to target one or, even better, many of the described molecular events can be taken into account. In this regard, several molecules with different indications have shown beneficial effects in promoting wound healing. Through these molecules, a most recent and effective one is represented by Rigenase®, a peculiar patented triticum vulgare extract which in association with polyhexanide, an antiseptic that doesn't give any resistance to bacteria, characterizes the Fitostimoline® Plus formulations. Rigenase®, consists of a mix of oligosaccharides, having consolidated activities in the wound healing process. Polyhexanide is an antiseptic that has specific activities on bacteria, fungi and some viruses. The Fitostimoline®Plus formulations are present in the form of gauzes, spray and cream and all represent a valid and safe alternative for the treatment of various type of wounds, including burns, abrasions, ulcers and lesions. In this trial, we evaluated through a survey on a large population of patients, the efficacy and tolerability of the Fitostimoline® Plus formulations considering which one is the eligible product for each specific indication, in order to help the physicians to choose among the various types of these medical devices.

Keywords: Abrasions; Burns; Fitostimoline® plus; Lesions; Wounds

Introduction

Wounds are a significant health problem worldwide. In the United Kingdom and Denmark, there are about 3 to 4 people with 1 or more wounds per 1000 population. Many of them become chronic wounds. Unfortunately, 15% of the wounds cannot recover 1 year after presentation [1]. Chronic wound formation is a challenging problem for both patients and caregivers [2]. Beyond the physical, mental, and social aspects, productivity loss in the workforce together with expensive medical interventions for wound management creates an economic burden on the health care system [3,4]. Delayed wound healing in specific populations might be prevented or improved with appropriate therapies [5-7]. Wound healing is a physiologic, very complex phenomenon that occurs when skin integrity is lost and consequently also the barrier function of the skin is impaired. This may occur quite often since the skin is much exposed to external insults and the need to avoid systemic infections drives a rapid defense mechanism [7]. Through physiologic healing, the normal status of the skin can be fully recovered although only a maximum of 70% of previous tensile strength is usually achieved7. This process progresses in different subsequent steps and usually three successive phases are recognized: an inflammatory, a proliferative, and a remodeling phase.

The standard wound-care practice for impaired wound healing includes control of the infection together with debridement, off-loading to relieve pressure, and maintenance of a moist wound bed. One of the first aims in the treatment of chronic wounds is in fact to prevent the occurrence of infection and to clean the area from non-viable tissue material. Infections can easily occur due to the loss of the innate barrier constituted by the skin layer and pathogens accumulating in the wounded area may further interfere with the healing process. Similarly, the removal of debrides and non-viable tissue, or debridement, allows exposure of healthy tissue where cells can migrate and proliferate to repair the wounded area [7]. Since the sequence of events of impaired wound healing is well characterized, the possibility to identify treatments that are already in the market and that are known to target one or, even better, many of the described molecular events can be taken into account. In this regard, several molecules with different indications have shown beneficial effects in promoting wound healing. Through these molecules, a most recent and effective one is represented by Rigenase®, a peculiar patented triticum vulgare extract which in association with polyhexanide, an antiseptic that doesn't give any resistance to bacteria, characterizes the Fitostimoline® Plus formulations. Rigenase®, consists of a mix of oligosaccharides, having consolidated activities in the wound healing process. Polyhexanide is an antiseptic that has specific activities on bacteria, fungi and some viruses.

The Fitostimoline® Plus formulations are present in the form of gauzes, spray and cream and all represent a valid and safe alternative for the treatment of various type of wounds, including burns, abrasions, ulcers and lesions. In this trial, we evaluated through a survey on a large population of patients, the efficacy and tolerability of the Fitostimoline® Plus formulations considering which one is the eligible product for each specific indication, in order to help the physicians to choose among the various types of these medical devices.

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 wound healing. For this reason, in January 2023, we designed a questionnaire based on the national recommendations for the pharmacovigilance on medical devices. Our research group included 16 key opinion leaders belonging to different Italian Regions and a group of 100 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 ulcers, sores, lesions, first and second degree burns, abrasions, 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 lesion after the treatment with one of the formulations. 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 different type of lesions, divided in three groups basing on the type of formulation used with a 1:1:1 ratio: 1) Fitostimoline® Plus gauzes; 2) Fitostimoline® Plus cream; 3) Fitostimoline® Plus spray. Each physician should enroll the same number of patient for each medical device. The duration of treatment was of at least 14 days.

Inclusion And Exclusion Criteria

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

Inclusion Criteria

Presence of the following conditions: first or second degree burns, ulcers, sores, abrasions, lesions.

Exclusion Criteria

• Refusal to participate

• History of intolerance to triticum vulgare extract or polyhexanide

• Presence of lesions that differentiate from first and second degree burns, ulcers, sores or abrasions

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 ramework, 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

2018 patients were initially enrolled, and 1678 fulfilled the eligibility criteria and successfully completed the survey, as shown in the flow chart in Figure 1.

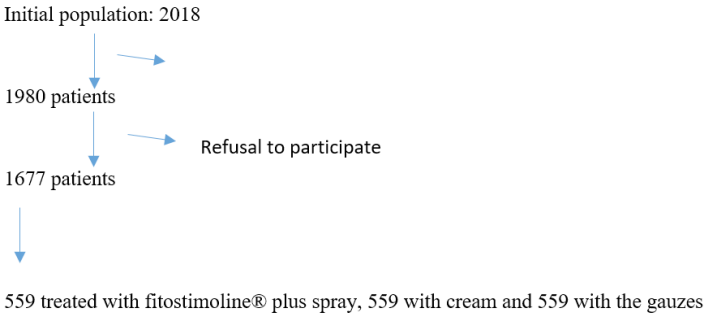

Figure 1: Flow chart of the study population enrollment.

There were no significant differences in terms of age and sex between the groups treated with either Fitostimoline® plus gauzes or cream and spray (Table 1). Following a 14-day treatment with Fitostimoline® Plus formulations, the survey revealed that patients had a significant preference for the treatment with Fitostimoline® plus spray in case of abrasions and burns. Instead, the gauzes were significantly preferred in case of ulcers or sores (Table 2 and Figure 2). All the formulations were found to be effective in their indications and only one side effect was recorded for Fitostimoline® plus gauzes and cream as an erythema, possibly related to a moderate hypesensitivity of the patient to the products (Table 3). The lesions were homogeneously distributed for all the type of treatments (Table 2 and Figure 2). The spray was found to be preferred in case of extended areas of the lesion, while the gauzes were preferred in case there was a need of keeping the medication in situ for more than one day, like for sores and ulcers. The cream instead was favored for second degree burns (Table 2 and Figure 2). Table 3 shows the very high percentage of healing obtained with each medical device. Coherently, the satisfaction score expressed by the patients was 9 or more probably on account a high percentage of healing associated with a good handling, the occurrence of pain is trivial, and very low incidence of side effects. 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 4).

Overall, the medical devices were considered by the patients effective both in their formulations and in their ability to improve the patient's quality of life (Table 5).

	Fitostimoline® Plus gauzes	Fitostimoline® Plus cream	Fitostimoline® Plus spray	P-value
N	559	559	559	-
Male Sex %	51	50	49	0.4
18-34 years %	2	3	6	-
35 – 50 years %	8	7	6	-
51-64 years %	20	70	80	-
65-80 years %	60	10	4	-
>80 years	10	10	4	-

Table 1: Main characteristics of the three populations.

Number of cases over 1677 patients	Indication	Fitostimoline® Plus cream	Fitostimoline® Plus gauzes	Fitostimoline® Plus spray	P
281	Abrasions %	8	7	85	<0.001
280	Ulcers %	18	75	7	<0.001
278	Sores %	40	55	5	<0.001
280	First degree burns %	40	10	50	<0.001
280	Second degree burns %	55	40	5	<0.001
278	Lesions%	35	30	35	-

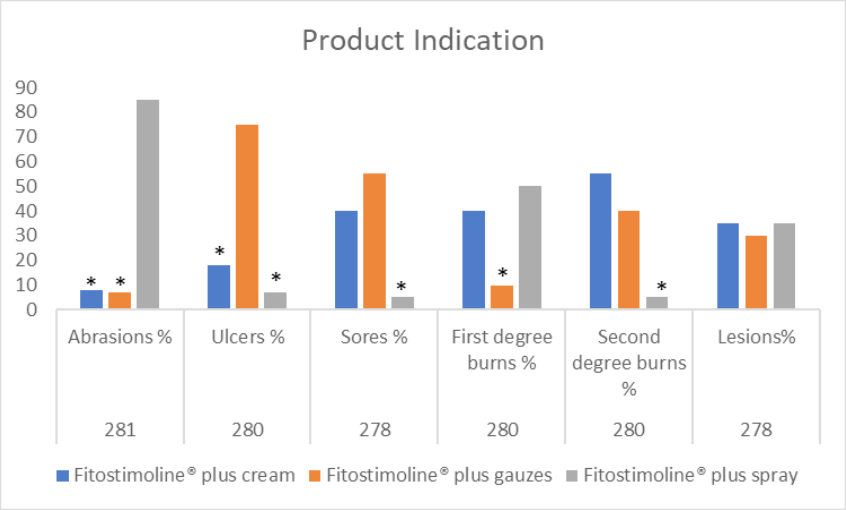

Table 2 and Figure 2: PMCF results indications

Efficacy	Fitostimoline® Plus cream	Fitostimoline® Plus gauzes	Fitostimoline® Plus spray	P
Healing %	86	87	90	-
Pain%	0	1	1	-
Satisfaction score	9.5	9	9.6	-
Side effects No	0	1	1	-

Table 3: PMCF Efficacy results.

	Fitostimoline® Plus cream	Fitostimoline® Plus gauzes	Fitostimoline® Plus spray	P
Leaflet Indications clarity %	90	95	90	-
Safety %	98	98	90	-

Table 4: PMCF safety results.

	Fitostimoline® plus cream	Fitostimoline® plus gauzes	Fitostimoline® plus spray	p
Product texture	good	Very good	good	-

Product grade	good	good	Excellent	-
Product improvement of the quality of life (QoL) %	95%	94%	95%	-

Table 5: Customer satisfaction.

Discussion and Conclusions

The size and location of the wound must be considered in the choice of any product, but particularly in the choice of advanced therapies. Their effectiveness could be compromised if, for example, a tissue equivalent is used on a plantar DFU and the patient is non-adherent to offloading. Wound healing located over a pressure point in most cases cannot be achieved without appropriate offloading. Many products are incompatible with, and should not be used in, an infected wound. Effective, yet costly, treatment options should be avoided in situations where patient non-adherence may prejudice the effects of the therapy. Careful discussion with the patient and a clear understanding of their social situation and personal goals are required to assure that an appropriate product is used. In order to solve all these questions it is required that physician are well aware of the characteristics of the devices and of the judgments and complains expressed by patients that have used that type of device for the same pathologic condition.

Thus, the present study was aimed to obtain such information for the three formulations containing Rigenase® and Polyhexanide. All the formulations were considered efficacious in their indications. Particularly, Fitostimoline® Plus spray was favored in its indication for first degree burns and abrasions while Fitostimoline® Plus gauzes were favored for ulcers and sores. The cream instead was preferred for the treatment of the lesions. These results are in accordance with the type of administration of the medical devices which favors the indication of the spray for higher surfaces like abrasions or burns of first degree and the other formulations for sores and lesions. In fact, the patients were overall satisfied by the treatments both because they were efficacious and also for the way through which the products are formulated and studied. Finally, the medical devices were considered also to be safe for the indicated treatments.

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 three different medical devices 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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