# EVALUATION OF THE EFFICACY AND TOLERABILITY OF COLLAGEN SPRAY (BIOSPRAY® EURORESEARCH) IN THE TREATMENT OF ACUTE AND CHRONIC LOW THICKNESS SKIN WOUNDS

## CONTROLLED CLINICAL TRIAL

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## CLINICAL REPORT

## INTRODUCTION

Collagen is one of the essential components of the extracellular matrix and its functions vary in relation to the interactions with other stromal molecules such as fibronectin, laminine, proteoglycans.

The synthesis of collagen magnifies during the proliferative phase of the skin tissue repair and along with neoangiogenesis it contributes to the reepithelization and contraction of wounds. The support matrix is then transformed into a collagen matrix that becomes the predominant protein of the proliferative phase. At the beginning, collagen is of type III and includes about 30% of the granulation tissue; then, during the collagen maturation, the type III is transformed into type I, that is mainly represented at dermal level.

Heterologous collagen is used in the treatment of chronic ulcers at different etiology in order to stimulate the granulation tissue and promote the tissue repair of wounds.

Recent studies have outlined the favourable efficacy of heterologous bovine collagen, used topically as a fleece, to stimulate the vessels production and the migration of keratinocytes.

In this clinical investigation, performed according to an experimental open controlled randomized model, we have evaluated the clinical efficacy, the general and local tolerability and the safety in use of the product branded BIOSPRAY®, administered to 20 patients with acute and chronic wounds.

## CHARACTERISTICS OF THE ACTIVE PRINCIPLE

BIOSPRAY® contains as active principle a type I heterologous collagen of horse origin. The active principle contributes to the stimulation of granulation tissue growth and fibroblasts induction from the bottom of the lesion, determining a marked acceleration of the tissue repair processes.

## PURPOSE OF THE STUDY

This study aimed to investigate the clinical efficacy, the general and local tolerability and the safety in use of the product under test: BIOSPRAY® *in the treatment of low thickness acute and chronic wounds*, according to an experimental open controlled randomized model between subjects.

## MATERIALS

During the investigation we used the following products:

- 1st Group (G1) - BIOSPRAY® (Euroresearch) heterologous horse collagen in spray form
- 2nd Group (G2) - KATOXYN® (Devergè) colloidal silver in spray form

Both products were supplied by the sponsor, packed in distinguishable containers that included data on the manufacturer and on the product (batch number etc..). Randomization was performed for the total of enrolled patients according to a system of closed envelopes.

## STUDY MODEL

This study was performed according to a controlled, randomized, open model between patients, product under evaluation versus competitor. Both products used have been administered at the daily dose of one topical spray application on the lesion during 4 weeks or less if healing occurred first. Periodical controls were performed before enrolment (T0), after two weeks treatment (T1) and after four weeks treatment (T2).

## METHOD OF THE STUDY

The voluntary patients have been enrolled in three different places:

1. A dispensary in a University Hospital
2. A General Medicine dispensary
3. The centre of assistance of a voluntary association

**INCLUSION CRITERIA**

a) Acute and chronic wounds at low thickness
b) Size 4x4 sq cm
c) Lesions not showing clinical signs of infection
d) Patients capable to follow the treatment
e) Patients willing to give their consent
f) Age ≥ 18 years

**EXCLUSION CRITERIA**

a) Pregnant women
b) Patients affected by diseases that might interfere with the healing process
c) Patients undergoing pharmacological treatments that might interfere with the healing process
d) Chronic lesions dated more than 6 weeks
e) Known allergy to the components of the products under test
f) Incapability of patient to follow the protocol of study

**CONSENT OF THE PATIENTS**

Before being admitted to the clinical investigation, patients had to give their content to take part to the study, after having been explained in a understandable way the nature, the scope and the possible consequences of the trial. Patient had to be informed about:

1. the fact that a clinical evaluation means research; a description of the scope of the study, of its progress and expected duration;

2. the type of treatment and the mode according to which patients will be admitted to the treatment (i.e., at random);
3. the positive effects expected from the medication being tested;
4. any eventual negative effect that might be attributable to the medication;
5. alternative therapeutical treatments;
6. his freedom to ask at any time additional information;
7. the possible extension of the confidentiality of the patients data and the possibility that competent Authorities might inspect these data.

If the patient was not able to formally agree by cause of his mental conditions, it was necessary to get the approval from his tutor, his legal representative or his closest relative, according to current laws.

**TREATMENT GROUPS**

Patients were randomized in alternate way in two groups. First group (G1) was treated with heterologous type I horse collagen BIOSPRAY® reformulated in order to achieve a better practicality of use. Collagen was supplied in 75 ml aluminium cans and its was applied on the lesion through a peculiar erogator. Once applied, the product layered under form of fine white powder lining. Second group (G2) was treated with colloidal silver in spray form, a product that has been selected being representative of the most common OTC medication in use for the treatment of minor wounds.

**MODE OF TREATMENT**

Immediately after enrolment, patients were instructed in details on the use of the two products under trial.

After detersion of the lesion using a chlorexidine solution at first application, patients treated themselves their lesion, under strict control of the clinical monitor.

The lesion was then covered with a non adherent medication. Patients were instructed not to get into water during the study time, but they were allowed to wash themselves daily. Patients were also instructed how to renew the medication daily or – if necessary – more frequently, and how to record each change on the clinical daybook.

**EVALUATION PARAMETERS**

The lesions have been evaluated during the study time according to the following parameters:

- Simplicity in use of the medication
- Easiness to remove the medication
- Pain in removal of the medication
- Duration of the medication
- Healing rate
- Side effects

**BASIC EVALUATION**

The enrolment data included: the kind of the lesion, its location, the rising cause. Prior to application of the product, the pain intensity was controlled (absent, slight, moderate, severe) and haemostasis was checked (present or absent).

**PATIENTS AND CHARACTERISTICS OF THE LESIONS**

40 patients (26 male – 14 female) aged between 19 and 76 took part to the investigation. They were suffering from acute (28) and chronic (12) wounds at low thickness, sized no more than 4x4 sq cm.

Patients were splitted in the two treatment groups following an alternate random system:

G1 – 20 patients, BIOSPRAY®

G2 – 20 patients, KATOXYN®

Typology of acute lesions:

- Low thickness burns 14
- Grazes 9
- Cut wounds 5

Typology of chronic lesions:

- Decubitus II degree 4
- Diabetic foot ulcers 3
- Vascular ulcers 5

Average size of the lesions:

- Average length 2.8 cm
- Average width 1.3 cm

**STATISTICAL EVALUATION**

The statistical significance of the comparison between the two groups has been performed according to the Student test for independent samples or by ANOVA test for the variations in time and for the differences between the clinical parameters of the two groups.

**RESULTS**

All the 40 enrolled patients fulfilled the study following the fixed protocol. The two treatment groups were similar in the main clinical aspects, including age, sex, typology and size of the wounds.

At the end of the study no statistically significant differences were noted between the completely healed patients of the two groups (Table 1).

Table 1 – Healing rate at 4 weeks

| Groups | G1 | G2 | P |
|---|---|---|---|
| Complete healing | 100% (20) | 90% (18) | 0.492 |

First group (G1) showed a healing speed remarkably faster than the second group (G2) (Table 2).

Table 2 – Healing time

| Groups | G1 | G2 | P |
|---|---|---|---|
| Days | 8.2 | 17.4 | 0.002 |

When asked to quantify the pain during treatment according to the fixed scheme, patients replied as follows:

| Pain | Absent | Slight | Moderate | Severe |
|---|---|---|---|---|
| G1 | 25% | 66% | 9% | -- |
| G2 | 22% | 34% | 44% | -- |

No significative differences were recorded between the two groups concerning the mode of application and removal of the products under trial, that showed both to be easy and safe to be used.

## ADVERSE CASUALTIES

No significant adverse casualties were recorded during the study. However, two patients (G2) developed vesicular erythematous lesions in perilesional area that were reconducted by the clinical monitor to irritative reactions to the secondary medication used to cover the active principle.

## CONCLUSIONS

In this open controlled randomized study we have evaluated a new formulation in spray form of Type I heterologous horse collagen, versus an OTC product based on colloidal silver.

The product under test proved to be excellent in promoting the tissue repair of acute and chronic wounds at low thickness. Its simplicity of use and the size of the can make BIOSPRAY® extremely handy for all first aid and emergency needs in small traumatology. The spray collagen proved to be more advantageous against the control product currently in use in medical practice, especially for the reduced healing time and a better pain control.

The absence of side effects confirms the safety of heterologous horse collagen.

The peculiar formulation of collagen in spray powder forms a this layer on the lesion, that determines a fast bleeding control and allows to control the exudates of the lesion.

The clinical judgement of the clinical monitors involved in the trial proved to be much highly positive compared to the control medication in terms of protection to the lesion and stimulation of the granulation tissue until reepithelization.

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