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Utilizzo di OZOILE® nel trattamento di lesioni ad eziologia mista

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The skin lesions mainly those of the lower limbs have various etiopathogenesis, appearing in different locations with characteristics sometimes very different from each other.

In more complex cases, they present a chronic condition (> 4 weeks) and they can interest cutaneous, subcutaneous and bone tissues, in relation to importance and gravity, altering the healing mechanisms that come into action when tissue damage occurs; moreover, pharmacological multitherapy is frequently associated.

Worldwide, about 80 million people are affected by chronic skin ulcers, and in Italy skin ulcers affect more than 2 million people, representing 0.4% hospitalizations. They are responsible for about 1% of all hospitalization days, with an increasing incidence on the elderly population and repercussions on the treatment costs; it is estimated that in the future about 1-2% of the whole budget for healthcare spending will be absorbed by the treatment of skin ulcers.

Currently in Italy, the healthcare spending is around 850 million euros, three times higher than in other European countries (221 million in France, 225 million in Germany, 435 million in UK), equal to the United States expenditure (around 1 billion), where the population is however five times larger than the Italian one.

The current trend, also related to the reduction of pharmaceutical spending, is aimed at an ever greater reduction in hospitalization, without there being a worsening of local or general conditions during home therapy.

Therefore an optimal treatment presupposes the possibility of doing home therapy, with a consequent reduction of healthcare spending and at the same time a faster healing with improved life quality sensed by patient.

About that, the aim of our study is to clinically verify the anti-inflammatory, antimicrobial, regenerating and tissue repairing action of Rigenoma® spray and cream with Ozoile® in acute and chronic skin lesions of different etiology, evaluating the lesion's improvement after 30 days of treatment or the healing time.

Rigenoma® spray and cream are advanced dressing with Ozoile® (Stable ozonides with Vitamin E acetate), is a pool of innovative molecules obtained from a Patented process, in which Ozone binds to the Oleic Acid producing Stable Ozonides. In literature there are

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molecular biology studies that enhance the anti-inflammatory and tissue regenerating action of Ozoile® also vs Steroids. [1] [2] [3]

Ozoile® regulates the main metabolic pathways, stimulates the endogenous defense system and induces the regulation of gene transcription, enhancing the tissue regeneration and the repairing of lesions.

Ozoile® a powerful anti-inflammatory inhibits COX-2, decreases the levels of pro-inflammatory cytokines (TNF-α, IL 1β, IFN-Y) and increases the levels of anti-inflammatory cytokines (IL-13) counteracting pain, redness, burning, swelling, degenerative processes and radiation damages. [4]

Ozoile® is an effective tissue repairer as it decreases the transcription of proteins and enzymes related to structural and morphological tissue alterations, such as TG2 and NOS, in case of hypoxia increases the expression of the transcriptional factor HIF-1α, responsible for cellular resistance to oxygen deficiency, promotes angiogenesis increasing the transcriptional levels of VEGF and induces the correct re-epithelialization of tissues as it increases the transcriptional levels of E-Cadherins, responsible for the correct adhesion between new cells [1][3][5].

Ozoile® is a broad spectrum microbicide because of the high affinity for lipoproteic components of the bacterial and fungal wall and the oxidizing action of Bioperoxides [6][7] as shown in the table below, where in vitro tests about the ability of Ozoile® of inhibit bacterial and fungal growth have been conducted.

Reduction of bacterial and fungal growth (%) – University of Pavia				
Time (h)	4h	12h	24h	48h
Sample	**OZOILE®**	**OZOILE®**	**OZOILE®**	**OZOILE®**
E. coli	99,40	99,99	98,20	98,20
P. aeruginosa	99,99	99,99	98,99	98,99
S. aureus	99,07	99,99	99,70	99,70
C. albicans	99,99	99,99	99,99	99,99
C. glabrata	99,99	99,99	99,99	99,99
A. niger	-	-	-	-
G. vaginalis	87,50	99,99	99,99	99,99
P. mirabilis	96,47	99,99	99,99	99,99
P. acnes	99,99	99,99	99,99	99,99
E. faecalis	82,77	99,99	99,99	99,99
S. epidermidis	99,99	99,99	99,99	99,99
T. mentacrophy	99,99	99,99	99,99	99,99
S. agalactiae	48,75	99,99	99,99	99,99
E. cloacae	68.60	99,99	99,99	99,99
B. cepacia	90,00	99,99	99,99	99,99
k. oxytoca	99,99	99,99	99,99	99,99
A. baumannii	99,99	99,99	99,99	99,99
C.pseudodiphtericum	99,99	99,99	99,99	99,99

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Materials and Methods

During the 01/01/2018 – 31/01/2019 period, n°50 patients with acute and chronic skin lesions of different etiology related to the *Vulnology Clinic for the treatment of complex wounds and diabetic foot* (belonging to the Simple Structure of Vulnology of the Department of Surgery of Ospedali Riuniti della Valdichiana Senese - Montepulciano – Siena) were enrolled.

The aim of our study was to clinically verify the effectiveness of Rigenoma® spray and cream with Ozoile® in the treatment of acute and chronic skin lesions of different etiology, evaluating the reduction of inflammation, the antiseptic and control action of the microbial flora, as well as the activation of tissue repair processes.

About that, we decided to enroll different kinds of lesions of multiple etiology (pressure, vascular, diabetic foot ulcers, post traumatic injuries and from radiotherapy and CHT, etc) by **size**, **time to onset** (acute and chronic), **infected or not infected**, and in this last case we decided to make a comparison between the results of in vitro tests regarding the inhibition of the bacterial and fungal growth mediated by Ozoile® and the microbicide action of dressing containing Ozoile® in vivo.

In particular we checked:

1) The action on the inflammation with the reduction of skin redness, itching, burning and local edema
2) The percentage of complete healing of skin lesions
3) The percentage of improvement of skin lesions with reduction of healing times
4) The microbicide action

all through:

1) The pain assessment through the Visual Analogic Scale (VAS)
2) The reduction in size of lesion through photographic documentation
3) The complete healing of the lesion
4) The assessment of the local infection (using culture swab + antibiogram), treated with targeted antibiotic therapy

To verify the effectiveness of Rigenoma® spray and cream, a group of patients was recruited adopting the following ***inclusion criteria:***

1) Skin lesion presents from 2 weeks to 18 months
2) Lesion diameter less than or equal to 30 cm^2
3) Lesion with granulating bottom not exceeding the dermal layer, poorly/moderately exuding, with poor/absence of fibrin/slough (type II EPUAP)

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4) Excellent patient compliance
5) Adequate informed consent

The ***exclusion criteria***, however, were the following:

1) Skin lesion presents for less than 2 weeks and more than 18 months
2) Lesion diameter greater than 30 cm^2
3) Hyperexudative lesion
4) Frankly infected lesion and/or serious systemic infection
5) Lesion with skin necrosis not subjected to preventive surgical debridement
6) Neoplastic lesions
7) Presence of Autoimmune diseases in chronic treatment with Steroids and/or immunosuppressive drugs
8) Patiens with cardio-circulatory failure not under drug therapy
9) Severe liver diseases of different etiology
10) I.R.C not adequately treated
11) COPD under therapy with corticosteroids and/or bronchodilators
12) Patiens with poor/absent compliance and/or absence of reliable caregivers
13) Allergy for one or more components in question
14) Pregnancy
15) Age under 16 years

In the group there are:

- 50 patients (32F, 18M)
- Average age 65,5 (range 42-90)
- 13 acute lesions (occurred for more than 2 weeks)
- 37 chronic lesions (occurred for more than 4 weeks)
- Lesion diameter less than 30 cm^2, average diameter 9,5 cm^2 (range 3,6 – 30cm^2)
- 23 infected lesions (4 acute, 19 chronic)
- 14 lesions present polymicrobial infection (11 lesions ->2 germs, 3 lesions ->3 germs)
- 9 lesions present infection of a single germ
- 10 types of germs found (Staphilococcus aureus 16, Pseudomonas Aeuriginosa 8, Enterococccus Faecalis 4, Escherichia Coli 4, Klebsiella Oxytocica 2, Proteus mirabilis 2, Acinetobacter Baumannii 1, Staphilococcus Epidermidis 1, Enterococcus cloacae 1, Candida albicans 1)
- Average VAS index 7,1 (range 4-9) at T0
- Average VAS index 3,6 (range 0-4) at T15
- Average VAS index 0,3 (range 0-2) at T30

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- Associated pathologies: type II Diabetes, ischemic heart disease, high blood pressure, hyperuricemia, F. A.)
- 7 smokers (4M, 3F)

Each patient in charge has been subjected to:

- Compilation of anamnesis
- Arterial and venous Eco Color Doppler examination (in relevant cases)
- Pain assessment with Visual Analogic Scale (VAS)
- Culture swab + antibiogram (if applicable)
- Etiopathogenetic classification of the lesion
- Dressing: cleansing with 0.05% sodium hypochlorite solution, surgical debridement if necessary, application every one, two or three days of Rigenoma® Spray (one spray every 4 cm^2) on the bottom of the lesion and Rigenoma® cream on the perilesional skin and the surrounding region, covering the lesion with advanced or non-adhesive dressing and/or elastic stocking.

  During the re-epithelialization phase and subsequently as maintenance and prevention, the application of Rigenoma® cream on the area to be re-epithelized and on the surrounding region to improve trophism and possible lipodermatosclerosis.

Each patient was also checked at 7, 15, 30 and 60 days after taking charge, during these intervals:

- Photograph of the lesion, with measurements of the area and its diameters
- Pain measurement with Visual Analogic Scale (VAS)
- Culture swab and antibiogram, in relevant cases (T 7 and T 30)

Results

From the analysis of the treated patients at 30 and 60 days after taking charge we have obtained the following results:

- Evident macroscopic improvement of the lesion with diameter reduction in all patients.
- 90% complete healing in patients
- Pain reduction with Visual Analogic Score (VAS) index measurement at 15 (VAS 3.4) and 30 (VAS 0.3) days
- Reduction of inflammation parameters (redness, itching, burning and local oedema) in all patients already at 7 days (T7)
- Microbicidal action (with culture buffer evaluation)
- No infection in negative cases of admission to the study
- Good trophism of regenerated skin with good elasticity, no signs of drying and/or retraction at 60 days (T 60)

Discussion

From the evaluation of the results we can conclude that the use of Rigenoma® spray and cream with Ozoile® has led to the following improvements:

1. Decrease in healing time
2. Decrease of inflammation
3. Decrease in the use of antibiotics
4. Decrease in the use of corticosteroids
5. Pain reduction (assessed by the SEA method)
6. Decrease in outpatient access (limited to 3/30 days)
7. Improvement of tissue repair even at a distance
8. Improvement of the perceived quality of life and compliance for the patient and family members also due to the reduction of lost work days and/or loss of income for the community
9. Decrease in health care expenditure due to reduced commitment of medical and nursing staff, less medication material, less use of medical means of transport

Conclusions

The treatment of skin lesions plays a very important role improving the healthcare quality provided by the National Health Systems and reducing healthcare costs, as well as in guaranteeing and protecting the quality of life of each individual.

In parallel with a multi-professional and multidisciplinary approach that remains fundamental in establishing the best and specific care programme for each patient, prevention is a fundamental step in this struggle.

It is also clear that the use of dressings Rigenoma® spray and cream with Ozoile®, can be useful in the treatment and prevention of acute and chronic skin lesions of different etiology, with considerable aid in the home management of the patient having demonstrated a reduction in the diameter of ulcers, treatment time, less use of antibiotic and corticosteroid therapy, better results of tissue regeneration, reduced outpatient access and the use of advanced dressings with a reduction in healthcare spending and an improvement in the relationship cost/benefit.

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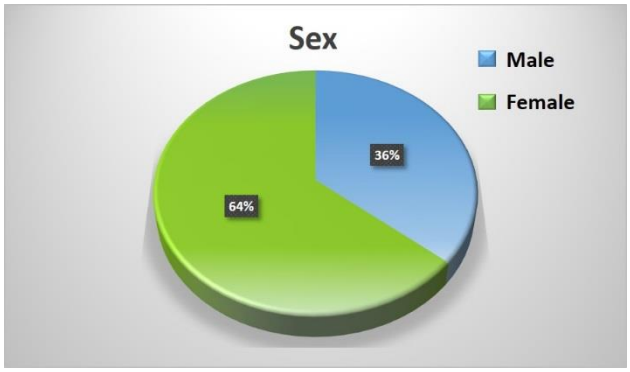
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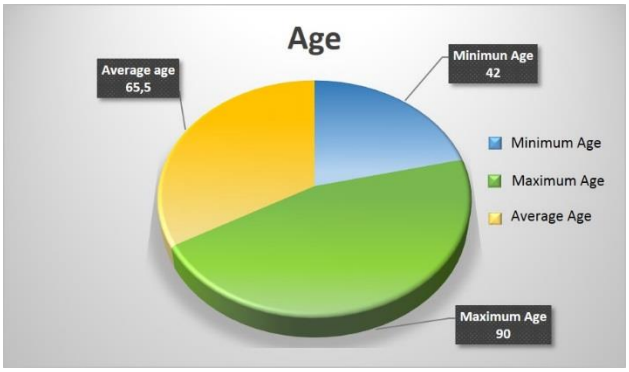
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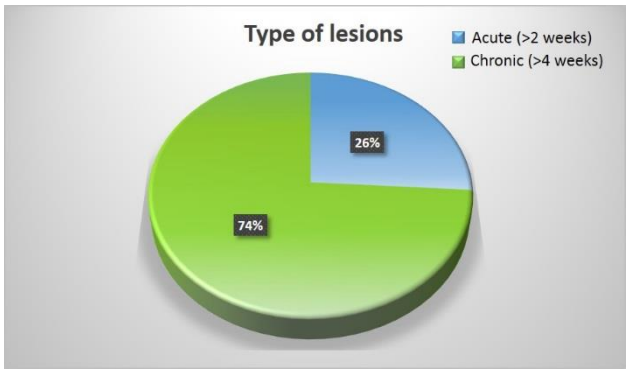
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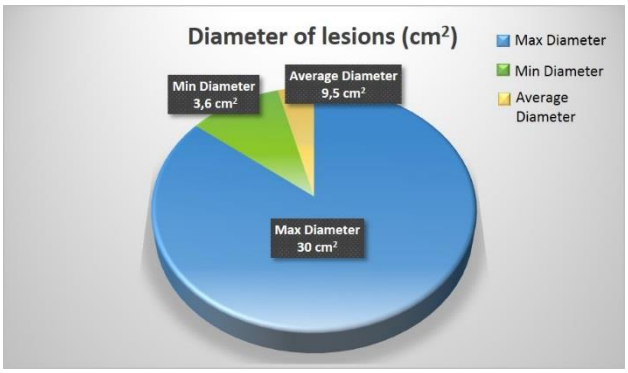
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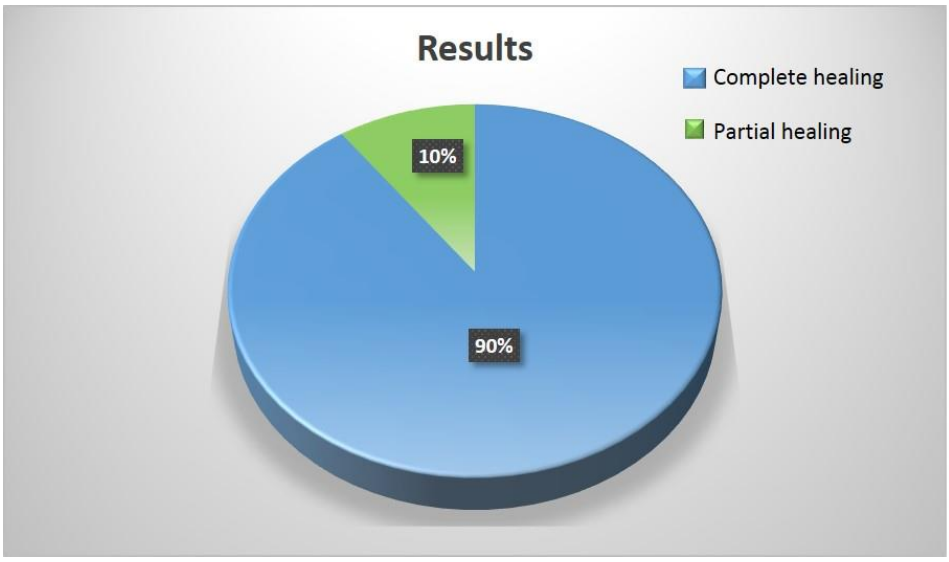
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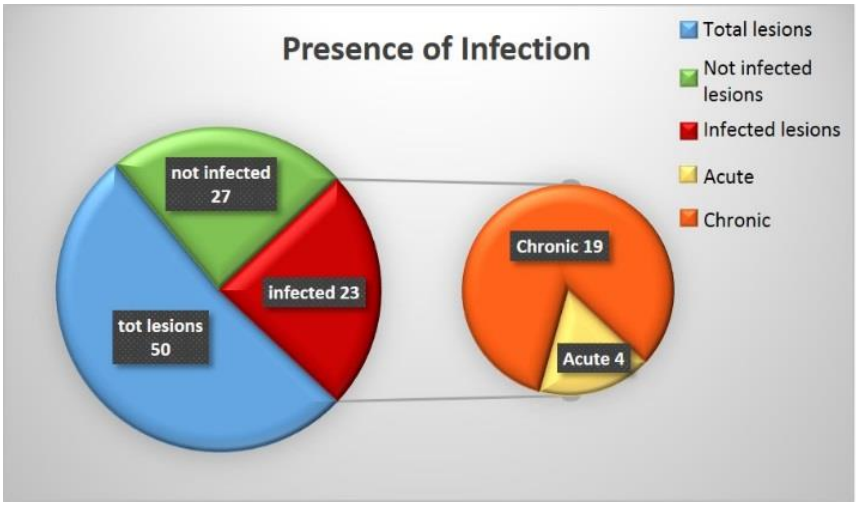


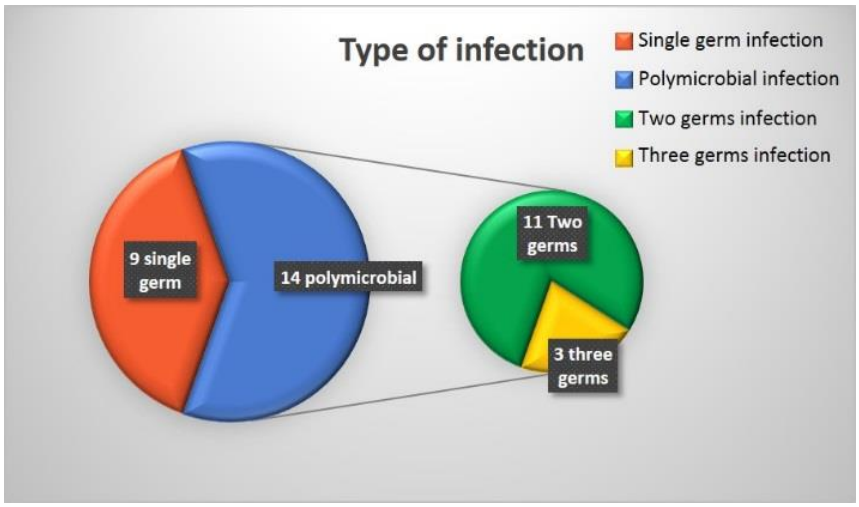


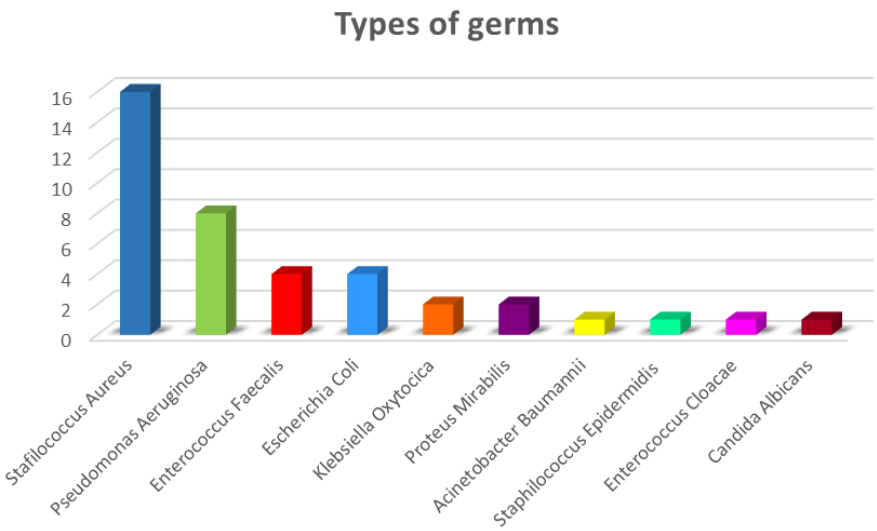




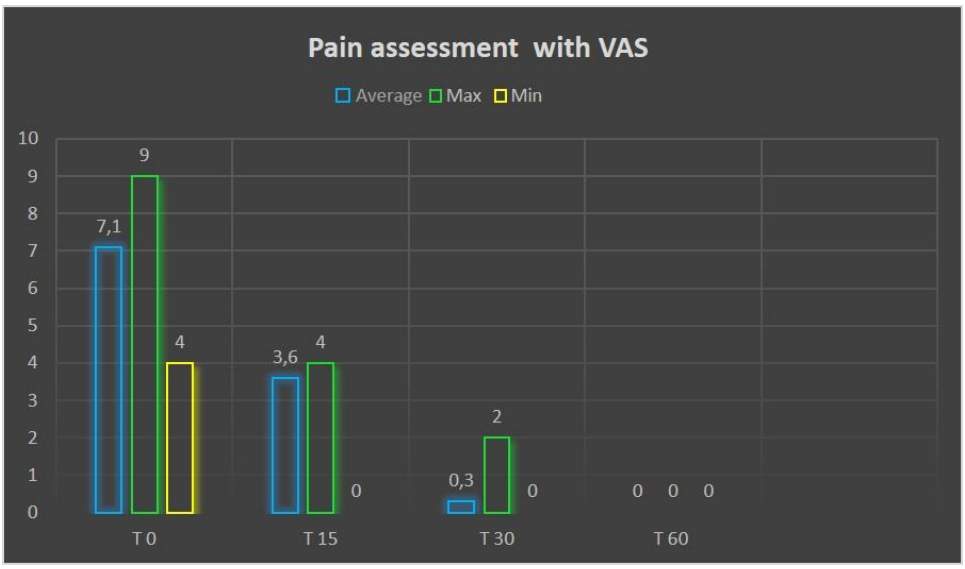
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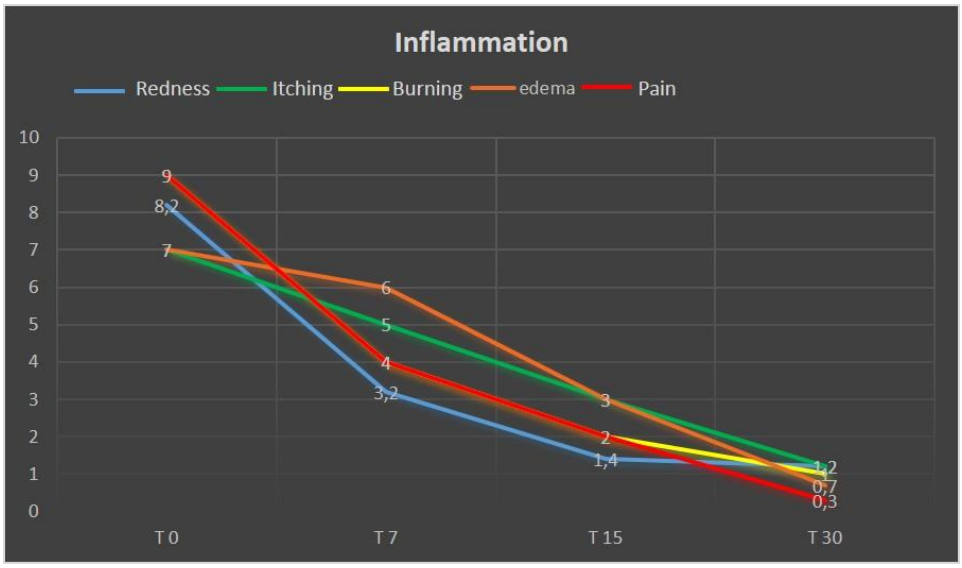






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