

# Growth factors and healing: experience in a Dermatology service

Fatores de crescimento e cicatrização: experiência em um serviço de Dermatologia

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## ABSTRACT

**Introduction:** Healing is a phenomenon that occurs after tissue injury and involves complex cellular and molecular mechanisms. Growth factors seem to be an effective and safe complement for the treatment of wounds.

**Objective:** To evaluate wound healing after electrocoagulation, comparing the vehicle in isolation and its association with epidermal growth factor.

**Methods:** Double-blind clinical trial in a Dermatology service between 2016 and 2018. Patients of both genders, older than 18 years of age, submitted to electrocoagulation of two lesions and subsequent application of the vehicle (*cold cream*) on one and epidermal growth factor in *cold cream* on the other were included. Evaluations after 7, 14 and 28 days, analysed erythema, edema, crusting, discharge and healing. Analyzed: edema, edema, crusting, discharge and healing. The binomial test was used for two ratios and Fisher's exact test was used for dichotomic data.

**Results:** Variable results were found regarding erythema, edema, crusting and discharge, sometimes favoring the vehicle, sometimes the growth factor, however with no statistical significance. Regarding healing, epithelialization was quicker with epidermal growth factor ( $p < 0.05$ ).

**Conclusions:** This study evaluated the impact of epidermal growth factor in the healing process, and its results reinforce scarce data of the current literature and are a foundation for future studies.

**Keywords:** Epidermal growth factor; Evaluation; Wound healing

## RESUMO

**Introdução:** A cicatrização é um fenômeno que ocorre após lesão tecidual e envolve mecanismos celulares e moleculares complexos. Os fatores de crescimento parecem ser um complemento eficaz e seguro no tratamento das feridas.

**Objetivo:** Avaliar a cicatrização de feridas após eletrocoagulação, comparando-se o veículo isolado à sua associação com o fator de crescimento epidérmico.

**Métodos:** Ensaio clínico duplo-cego em Serviço de Dermatologia entre 2016 e 2018. Incluídos pacientes de ambos os sexos, acima de 18 anos, submetidos à eletrocoagulação de duas lesões e posterior aplicação de veículo (*cold cream*) em uma e fator de crescimento epidérmico em *cold cream* na outra. Avaliações com sete, 14 e 28 dias, analisaram: eritema, edema, crosta, secreção e cicatrização. Utilizou-se o teste binomial para duas proporções e o teste exato de Fisher para dados dicotômicos.

**Resultados:** Em relação a eritema, edema, crosta e secreção foram encontrados resultados variáveis, ora favorecendo o veículo, ora o fator de crescimento, porém sem significância estatística. Quanto à cicatrização, a epiteliização mostrou-se mais rápida com fator de crescimento epidérmico ( $p < 0,05$ ).

**Conclusões:** Os resultados deste estudo, que avaliou o impacto do fator de crescimento epidérmico no processo de cicatrização, corroboram os dados da escassa literatura atual e servem de base para estudos futuros.

**Palavras-Chave:** Avaliação de medicamentos; Cicatrização; Fator de crescimento epidérmico

## Original Articles

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## INTRODUCTION

Healing is a phenomenon that occurs after tissue injury of any nature and involves complex cellular and molecular mechanisms. Inflammation, proliferation, angiogenesis, reepithelization, tissue regeneration and remodeling are part of this biological process.<sup>1</sup> Thermal burns (accidental or intentional) generate areas of necrosis that extend beyond the wound, even causing obstruction of blood and lymphatic vessels.<sup>2</sup>

The process of tissue repair is modulated by growth factors, that are produced by epidermal and epithelial cells, such as macrophages, fibroblasts and keratinocytes. Growth factors are biologically active molecules and act directly from within the cell, regulating the cell cycle.<sup>3</sup> However, the availability of these growth factors can be insufficient in the bed of the wound resulting from burns due to their excessive degradation or reduced production. Therefore, treatment with growth factors seems to be an effective and safe complement to the treatment of wounds.<sup>4,5</sup> The objective of this study was to evaluate wound healing after electrocoagulation comparing the vehicle alone (cold cream) to its association with epidermal growth factor.

## METHODS

This is a comparative, double-blind clinical trial, conducted at a Service of Dermatology between June 2016 and July 2018. Patients from both genders and older than 18 years of age were included, with two lesions similar in nature and size, on the same body area. Both lesions were submitted to electrocoagulation, with subsequent daily application of the vehicle (cold cream) on one and 5% epidermal growth factor in cold cream (Epifactor®) on the other, for 28 days. Evaluations were performed after 7, 14 and 28 days, and the wounds photographed according to the standardization. These photos were then evaluated by an independent researcher (dermatologist). The variables analyzed were: erythema, edema the use of the vehicle alone. However, on the 28<sup>th</sup> day, both groups had a coinciding end result for this variable. (presence or absence and intensity), crust, discharge (presence or absence) and healing (crust, ulceration and epithelization). Tables were made. For the comparison between two independent samples, the binomial test was used for two of significance adopted was  $\alpha = 5\%$ , and the statistical program used was *BioEstat* 5.0. The study was approved by the Committee ratios and Fisher's exact test for dichotomic data. The level of Ethics in Research of the institution under the number 1.861.616.

## RESULTS

Thirteen patients were included (seven men and six women), with minimum and maximum ages of 36 and 86 years, respectively.

Table 1 demonstrates the progression of erythema along the 28 days. After 14 days, there were similar percentages between the two groups for this variable, predominating mild erythema. In table 2, we can evaluate data regarding edema. There was an apparent lower initial edema (7<sup>th</sup> and 14<sup>th</sup> day) with regarding the variable 'crust formation', data can be seen on table

3. Most wounds (in both groups) showed crust after seven days. The elimination of the crust was faster with the use of the vehicle alone (69.23% of the lesions had no crust on the 14<sup>th</sup> day).

Table 4 illustrates the variable 'discharge'. In it, we can observe a faster resolution of the discharge in the wounds where Epifactor® was used (100% on the 14<sup>th</sup> day).

Regarding healing, only 7.69% of the wounds (from both groups) had ulceration on the 7<sup>th</sup> day (Table 5). The epithelization occurred faster in the wounds where Epifactor® was used (46.15% versus 0% - 14<sup>th</sup> day),  $p < 0.05$ .

Figure 1 illustrates epithelization of the wound treated with Epifactor® and with vehicle on the 14<sup>th</sup> day.

## DISCUSSION

This original study, evaluating the impact of epidermal growth factor in the healing process, supports the literature

TABLE 1: Erythema regarding its intensity and the time of evaluation in percentage

Evaluation Erythema	7 days		14 days		28 days	
	EP	CC	EP	CC	EP	CC
	%	%	%	%	%	%
Mild	38.46	46.15	76.92	69.23	69.23	69.23
Moderate	46.15	46.15	23.08	30.77	23.08	23.08
Intense	15.38	7.69	0	0	0	0
Absent	0	0	0	0	7.69	7.69

EP: Epifactor®; CC: Cold cream

TABLE 2: Edema regarding its intensity and time of evaluation in percentage

Evaluation Edema	7 days		14 days		28 days	
	EP	CC	EP	CC	EP	CC
	%	%	%	%	%	%
Mild	15.38	23.08	15.38	69.23	69.23	69.23
Moderate	53.85	38.46	38.46	30.77	23.08	23.08
Intense	15.38	15.38	0	0	0	0
Absent	15.38	23.08	0	0	7.69	7.69

EP: Epifactor®; CC: Cold cream

TABLE 3: Crust regarding the presence or absence and time of evaluation in percentage

Evaluation Crust	7 days		14 days		28 days	
	EP	CC	EP	CC	EP	CC
	%	%	%	%	%	%
Absent	15.38	30.77	46.15	69.23	84.62	92.31
Present	84.62	69.23	53.85	30.77	15.38	7.69

EP: Epifactor®; CC: Cold cream

**TABLE 4: Discharge regarding presence or absence and time of evaluation in percentage**

Evaluation Discharge	7 days		14 days		28 days	
	EP	CC	EP	CC	EP	CC
	%	%	%	%	%	%
Absent	61.54	61.54	100	84.62	100	100
Present	38.46	38.46	0	15.38	0	0

EP: Epifactor®; CC: Cold cream

**TABLE 5: Healing – Crust, ulceration, epithelization – at the time of evaluation in percentage**

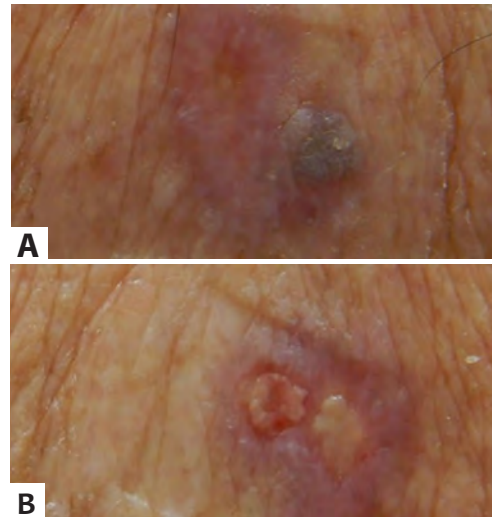
Evaluation Healing	7 days		14 days		28 days	
	EP	CC	EP	CC	EP	CC
	%	%	%	%	%	%
Crust	84.62	69.23	53.85	30.77	15.38	15.38
Ulcerated	7.69	7.69	0	69.23	0	0
Epithelialized	7.69	23.08	46.15	0	84.62	84.62

EP: Epifactor®; CC: Cold cream

where studies on this subject are still scarce, what made difficult the discussion of the results found. Regarding the variables erythema, edema, crust and discharge, there was a mild predominance of a better result sometimes for one group, other times for the other, however, with no statistical significance. Healing (epithelization) was faster in the group using epidermal growth factor, supporting the findings by Zhang *et al*, who demonstrated that the topical use of growth factors significantly reduced healing time for partial thickness burn wounds.<sup>4</sup> Limitation: Factors not taken into account in this study, such as gender, age, site, comorbidities, could have interfered with our findings.

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**FIGURE 1:** Epithelization.  
**A** – Wound treated with Epifactor®;  
**B** – Wound treated with cold cream (still ulcerated/ fibrine) – 14<sup>th</sup> day

## CONCLUSION

This study allowed for the evaluation of the healing of wounds after electrocoagulation, comparing the vehicle alone to its association with epidermal growth factor and concluded that the topical use of epidermal growth factor accelerated wound epithelialization, significantly reducing healing time. ●

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**DECLARATION OF PARTICIPATION:**

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Statistical analysis, approval of the final version of the manuscript, design and planning of the study, preparation and writing of the manuscript, data collection, analysis and interpretation, active participation in mentoring the research, intellectual participation in propaedeutics and/or therapeutics of the cases studied, critical review of the literature, critical review of the manuscript.

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