

How I do?

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Atrophic scars treatment with subcutaneous insulin

Tratamento das cicatrizes atróficas com insulina subcutânea

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ABSTRACT

Atrophic acne scars are persistent and undesirable sequelae that have a negative cosmetic and psychosocial impact on patients. This issue becomes more delicate when such scars are located in the presternal region due to the risk of hypertrophic scars appearing when performing these procedures in the area. The literature has long recognized the role of insulin in promoting protein and fat synthesis. Insulin properties as a growth factor to treat these sequelae seems logical and has proved cosmetically satisfying, with quality of life improvement.

Keywords: Acne Vulgaris; Atrophy; Scar; Wound healing; Injections, subcutaneous; Insulin; Ambulatory surgical procedures; Quality of life; Tissue therapy

RESUMO

As cicatrizes atróficas de acne, sequelas persistentes, são indesejáveis e causam impacto negativo cosmético e psicossocial nos pacientes. A questão torna-se mais delicada quando tais cicatrizes localizam-se na região pré-esternal, pelo risco do surgimento de cicatrizes hipertróficas com a realização de procedimentos na região. O papel da insulina na promoção da síntese de proteínas e gorduras é, há muito tempo, reconhecido. A utilização de suas propriedades como fator de crescimento para tratar estas sequelas parece lógica e provou ser gratificante cosmeticamente, com melhora na qualidade de vida.

Palavras-chave: Acne vulgar; Atrofia; Cicatriz; Cicatrização; Injeções Subcutâneas; Insulinas; Procedimentos Cirúrgicos Ambulatoriais; Qualidade de Vida, Terapêutica

INTRODUCTION

Acne scars have a negative impact on the quality of life and lead to feelings of shame and low self-esteem.^{1,2} Destruction of the extracellular matrix (ECM) components at the beginning of acne lesions is a foundation for the resulting atrophic scars.³ Jacob *et al.* classified this pattern of scars into the three basic types: icepick (<2 mm, narrow scars that taper as they extend to the deep dermis), rolling (4–5 mm, the depressed scars with sloping and shallow edges), and boxcar (1.5–4 mm, round to oval depressions with markedly demarcated vertical limits).^{1,4} There are several treatments to mitigate these scars.^{1,3} However, the pre-sternal region presents a tendency to hypertrophic scarring,⁵ discouraging the aggressive approach. Few observations of subcutaneous insulin administration suggest a good response in atrophic scars.^{6–8}

CASE REPORT / METHODS

A 20-year-old man (ACC) with no morbidities presented rolling and boxcar atrophic acne scars. The scars were distensible and hypochromic in the pre-sternal region.

We divided the sternal region into two parts (upper and lower) and applied 5 units of NPH insulin, according to the protocol described in Figures 1 and 2. We observed petechiae, erythema, and edema after microneedling.

One week later, the treated area presented hyperemia and hyperchromia, in addition to partial improvement of some scars. Given the clinical improvement, we applied NPH insulin over the entire length of the lesion.

On each session, up to 15 units of NPH insulin were infused due to the extent of the lesions. Eleven sessions were held, with a weekly interval. There were no adverse events such as hypoglycemia or lipothymia.

The patient presented a satisfactory result, with improvement in atrophy, as showed in the follow-up photographs after seven months (Figures 3 and 4).

DISCUSSION

Insulin is a peptide hormone and growth factor with numerous physiological roles. In addition to the regulation of serum glucose levels, it plays a promoting role in wound healing.⁹ We know that its deficiency slows tissue repair. Burned patients submitted to its systemic administration evolve with lesion improvement, in part, by improving the local protein balance.¹⁰ However, systemic administration generates metabolic changes and imbalances (hypoglycemia and hypokalemia) that limits its use.¹⁰

Insulin topical administration has been described in animal models and clinical trials.¹¹⁻¹³ The local insulin application prevents systemic repercussions while maintaining its beneficial action on local healing. Liu *et al.* observed that insulin acts through its receptors, helping in the migration of keratinocytes in wounds without interaction with epidermal growth factor receptors.¹⁴ It is believed that the direct action on fibroblasts and keratinocytes, cells in which the presence of the insulin receptor has been identified, mediates its effect.⁹

Evidence from the literature suggests the role of insulin in regulating energy metabolism, protein synthesis, cell differentiation, and growth. Thus, its local injection promotes the granulation tissue's growth and development, with consequent healing.¹⁵⁻¹⁸

Insulin stimulates the incorporation of (3H) thymidine in the skin's fibroblasts, resulting in collagen synthesis.¹⁹ Topically, it accelerates wound healing in diabetes by improving the Protein Kinase B (AKT) and Extracellularly Regulated Kinase (ERK) pathways. It is assumed that insulin uses these two routes to increase repair.¹⁶ Upon connecting to the receptor, the intracellular tyrosines located in its b-subunits are phosphorylated and allow the Src 2 homology and collagen-A protein, found in the cytosol, to bind through the Src-2¹⁴ homology domains. The signal is transduced through a series of messenger molecules to activate Ras (a member of a large family of small molecular weight GTP binding proteins)¹⁶ and transmitted via Raf, MEK (members of the GTP binding protein family), and ERK.²⁰ It moves to the nucleus, where the cell receives the command to replicate DNA and multiply, with consequent tissue repair and wound healing.⁹ In the other pathway, the insulin receptor substrate 1 and 2 binds to it and transduces the signal via PI (3) kinase, PDK, and AKT. Such a reaction induces nitric oxide (NO) production, increased blood flow, cell survival, morphogenesis, and angiogenesis. The increase in phosphorylation of GSK-3 β (Glycogen Synthase Kinase-3 β) by AKT decreases its activity, which may be another mechanism to increase collagen production, reduce apoptosis, and accelerate wound closure.²¹

The insulin-like growth factor-1 (IGF-1) stimulates the production of an extracellular matrix component²² and induces the transformation factor-beta (TGF- β) in dermal fibroblasts, corroborating wound healing.^{23,24}

Collens first described the reversing diabetic lipotrophy technique by injecting the purest forms of insulin.²⁵ Insulin is an anabolic hormone in the metabolism of fats and proteins. Adipose tissue is exquisitely sensitive to insulin; minimal amounts can inhibit lipolysis⁶ and promote the synthesis of proteins and fats.⁷

Amroliwalla administered subcutaneous insulin injections and achieved complete post-vaccine atrophic scars regression.⁶ Likewise, Kalil-Gaspar *et al.* achieved complete lesions remission in lipotrophy inducing insulin and corticosteroids, respectively.⁷ Hallam *et al.* conducted a randomized controlled study to assess the potential of insulin as an anti-scar therapy, analyzing patients undergoing bilateral cosmetic breast operations. They observed that subcutaneous injections into scars reduced their appearance compared to placebo and suggested that the properties of insulin in lowering scars were more effective in individuals who were at risk of excessive or pathological scarring.⁸

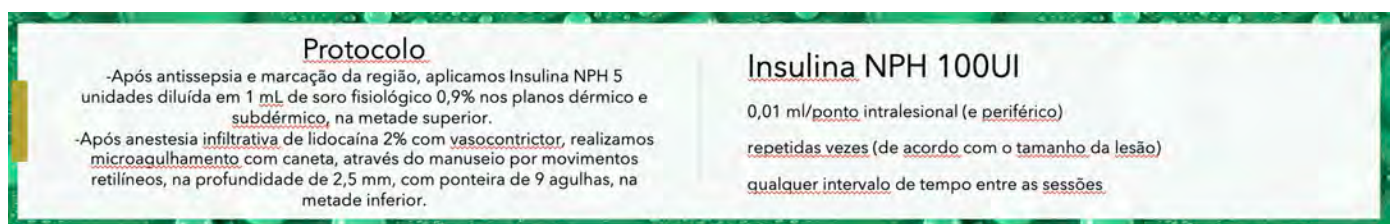


FIGURE 1: Protocol used in the first session, when the patient underwent insulin intralesional infiltration in the upper part of the pre-sternal region and microneedling in the lower part; detail of the use of insulin in atrophic scars



FIGURE 2: Initial marking in two parts: upper (I) and lower (R) (they would be treated differently)

Faced with a very distressed patient presenting extensive boxcar and rolling scars in the pre-sternal region, insulin infiltration, a technique overlooked by many dermatologists, could benefit tissue recovery. The most significant advantage of the method would be the ease of finding the drug and its cost. Moreover, its major disadvantage would be the need to repeat the scheme for a long period. Our patient was treated with weekly intralesional infiltration sessions for three months. The studies of Amroliwalla⁶ and Kalil-Gaspar⁷, which maintained therapy with daily frequency and an average time of 90 days, indicated continuity for a longer period. However, the patient was a university student and would be hindered from attending the clinic in the coming months for academic reasons. After seven months (free of treatment), although there is great difficulty in photographic documentation (two-dimensional) of normochromic atrophic scars, the patient and the attending physicians observed genuine lesions improvement. Today's use of purer insulin forms can explain the maintenance of results without the long-term lipoatrophy produced by insulin in the past.

CONCLUSION

Insulin increases protein synthesis in the skin and stimulates the growth and development of different cell types. It also affects the proliferation, migration, and secretion of keratinocytes, endothelial cells, and fibroblasts.^{26,27} Therefore, it can correct keratinocyte proliferation blockade and replace excessively destroyed collagen, which would help recover some of the



FIGURE 3: Enlarged boxcar and rolling scars in the pre-sternal region, before and seven months after treatment, with partial improvement of atrophic scars




FIGURE 4: Scars in the pre-sternal region, closer image, before and after treatment

defects responsible for atrophic acne scars.³ It is interesting for wound care and scarring treatment, mainly because of its low cost compared to other growth factors and its universal availability. Further studies are needed to better understand insulin's role in wound healing and more precisely outline which individuals can benefit from anti-scar insulin therapy. ●

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Approval of the final version of the manuscript; study design and planning; preparation and writing of the manuscript; active participation in research orientation; intellectual participation in propaedeutic and/or therapeutic conduct of studied cases; critical literature review; critical revision of the manuscript.

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