Reidratação injetável da pele: uma opção com resultados clínicos?

Could injectable rehydration of the skin be an option with clinical results?

Original Articles

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RESUMO

Introdução: Em dermatologia, vários medicamentos são injetados intralesionalmente com o objetivo de tratar doenças localmente. A microinjeção de ácido hialurônico não-reticulado na derme tem como objetivo restabelecer a hidratação da pele.

Objetivo: Determinar se houve melhora da hidratação da pele devida à injeção de ácido hialurônico não-reticulado puro nas rugas periorbitárias e na pele vizinha.

Métodos: Dez pacientes (entre 40 a 63 anos de idade) com rugas periorbitárias classificadas com graus entre 1 a 4 de uma escala de severidade de rugas (*Wrinkle Severity Rating Scale*) foram tratadas no ano de 2007 com microinjeções de ácido hialurônico não-reticulado nos dias 1, 15 e 30 do estudo. O médico pesquisador, o observador não-médico e os pacientes avaliaram a pele tratada no 45º dia do estudo de acordo com uma escala descritiva de resultados clínicos (ausentes, pobres, bons e muito bons). Durante 5 anos realizou-se follow-up para identificar possíveis complicações.

Resultados: Segundo a escala descritiva, os dados clínicos analisados indicaram os seguintes resultados: pacientes (pobres = 2, bons = 6, muito bons = 2); observadores não-médicos (pobres = 3 , bons = 4, muito bons = 3); pesquisador médico (pobres = 3, bons = 6, muito bons = 1). Houve ocorrência de equimoses e sangramento imediatamente após as aplicações.

Conclusão: A injeção de ácido hialurónico pode ser uma opção terapêutica para a hidratação da pele seca e danificada.

Palavras-chave: ácido Hialurônico; envelhecimento; processos fisiológicos de pele; mesoterapia

ABSTRACT

Introduction: *In dermatology, several medications are injected intralesionally to treat diseases locally and the microinjection of non-cross linked hyaluronic acid in the dermis is used for restoring skin hydration.*

Objective: *To determine whether there was improvement in skin hydration due to injection of pure non cross-linked hyaluronic acid in patients' periorbital wrinkles and surrounding skin.*

Methods: *Ten patients (between 40-63 years of age) with periorbital wrinkles rated between 1 and 4 according to the Wrinkle Severity Rating Scale were treated in the yeear of 2007 with microinjections of non cross-linked hyaluronic acid on the 1st, 15th and 30th days of the study. The medical researcher, the non-medical observer, and the patients assessed the skin at the treatment site on the 45th day of the study according to a descriptive scale of clinical outcomes (absent, poor, good, and very good). A followup evaluation was carried out during five years aimed at identifying potential complications.*

Results: *According to the descriptive scale, the analysis of the clinical outcomes data presented the following results, expressed in number of patients: patients' opinion (poor = 2, good = 6, very good = 2); non-medical observer's opinion (poor = 3, good = 4, very good = 3); medical researcher's opinion (poor = 3, good = 6, very good = 1). Echymoses and bleeding occurred immediately after the injections.*

Conclusion: *Injection of hyaluronic acid can be a therapeutic option for re-hydrating dry and damaged skin.*

Keywords: *hyaluronic acid; aging; skin phisiological processes; mesotherapy*

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INTRODUCTION

There are doubts about the validity of mesotherapy due to several factors: the fact that it combines multiple drugs, that there is lack of studies on those drugs, the interaction of mixtures of substances has an impact on the clinical outcomes, and safety issues. Specifically regarding skin rejuvenation, there is also the local response to the trauma caused by multiple perforations that characterize the Nappage technique – a fact that could explain any improvement in the aging skin. In certain countries, there is even an acceptance of mesotherapy based on the introduction of microscopic quantities of natural extracts, homeopathic agents, pharmaceuticals, and uncontrolled vitamins in the skin and/or subcutaneous tissue, as a dependable and reliable treatment modality for treating a variety of conditions. [1]

In dermatology, several drugs – such as corticosteroids for scarring, keloids, or other skin conditions – are injected intralesionally to treat diseases locally.[2] Microinjections of uncrosslinked hyaluronic acid in the dermis is theoretically intended to quickly and accurately fix the lack of hydration due to aging, directly on the area needing treatment, based on the principles of mesotherapy.

The introduction of uncrosslinked hyaluronic acid (HA) (14 mg/ml, Mesolis®, Anteis, Switzerland) for rehydrating the skin through micro-injections directly into the damaged skin has arisen as an interesting proposal. As it is intended to treat the problem locally, the techniques developed for the treatment of mesotherapy have been adapted and applied for the purpose of the present study.

OBJECTIVE

Patients were selected with the specific proposal of rehydrating periorbital wrinkles and the surrounding skin, with the injection of a pure, uncrosslinked HA. The goal of the authors was to determine whether there was clinical improvement of the skin after the treatment.

METHODS

A descriptive study of a group of 10 patients was carried out. A term of free and informed consent was signed by each participant, and the technique and indication for treatment were approved by the Clinical Research Committee of the institution. All patients were female, aged between 40 and 63 years, bearing periorbital wrinkles ("crow's feet") classified with grades 1 to 4 according to the Wrinkle Severity Rating Scale (WSRS). The "crow's feet" were treated (in 2007) with microinjections of 14mg/ml uncrosslinked HA on days 1, 15, and 30 of the study (Table 1).

The injections were administered on the surface (superficial/middle dermis) with a 30G needle throughout the length of the wrinkles, with punctures as close as possible to each other. The injected micro droplets had sufficient volume to fill the wrinkles. The applications were performed with slow and precise movements, with the needle bevel facing down. The volume of the papules ranged from 1 to 2 mm. The surrounding area of the periocular region was also injected through papules in an ordered layout, with spaces of 3 to 4mm between them. The mesotherapy technique of Nappage was used, consisting of multiple microinjections performed with very rapid upward movements of the needle, with the syringe moving gradually,

Table 1: Distribution of study patients by age, WRSR, injection volume, and evaluation of outcomes according to patients, a non-medical evaluator, and a researcher physician. Follow-up conducted from 2007 to 2012.

Patient	Age	WSRS	Volume mL (day 1)	Volume mL (day 15)	Volume mL (day 30)	Total volume	Self-evaluation by patients	Evaluation by non-medical evaluator	Evaluation by researcher physician	Follow-up
1	44	2	0.5	0.5	0.45	1.45	Poor	Poor	Poor	2007-2008
2	45	3	0.6	0.6	0.5	1.7	Good	Poor	Poor	Loss of follow up
3	63	4	0.8	0.8	0.8	2.4	Good	Good	Good	Underwent different treatment for "crow's feet" after 2007
4	40	1	0.5	0.45	0.45	1.4	Poor	Poor	Poor	2007-2011
5	63	4	0.8	0.8	0.8	2.4	Good	Good	Good	2007-2012
6	60	4	0.7	0.7	0.6	2	Good	Good	Good	2007-2012
7	63	4	0.8	0.8	0.8	2.4	Very good	Very good	Very good	2007-2011
8	48	3	0.6	0.6	0.5	1.7	Very good	Very good	Good	2007-2012
9	50	3	0.6	0.6	0.5	1.7	Good	Good	Good	2007-2012
10	49	3	0.6	0.6	0.5	1.7	Good	Muito bom	Good	2007-2011
Average	52,5	3,1	0.65	0.645	0.59	1.525				

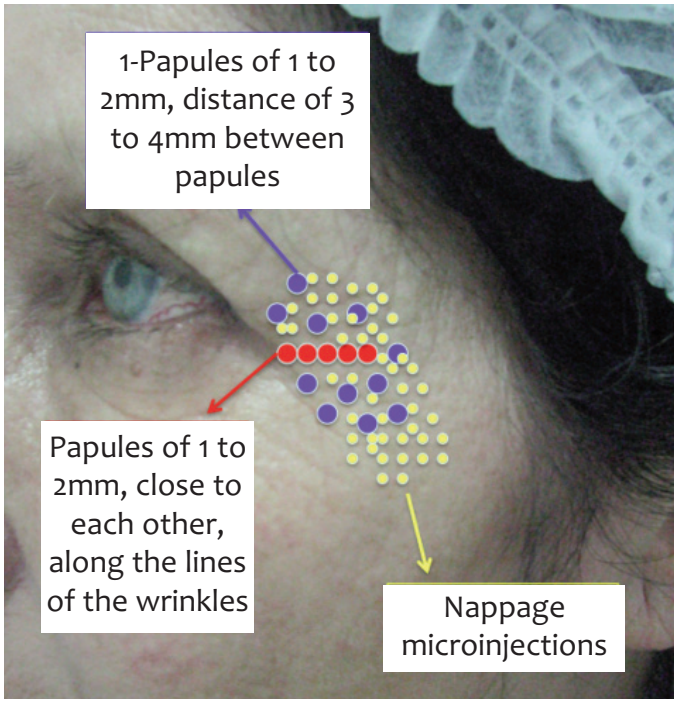

Figure 1: Patient 4, pre- and post-treatment (Table 1). The clinical outcome was deemed poor by the physician

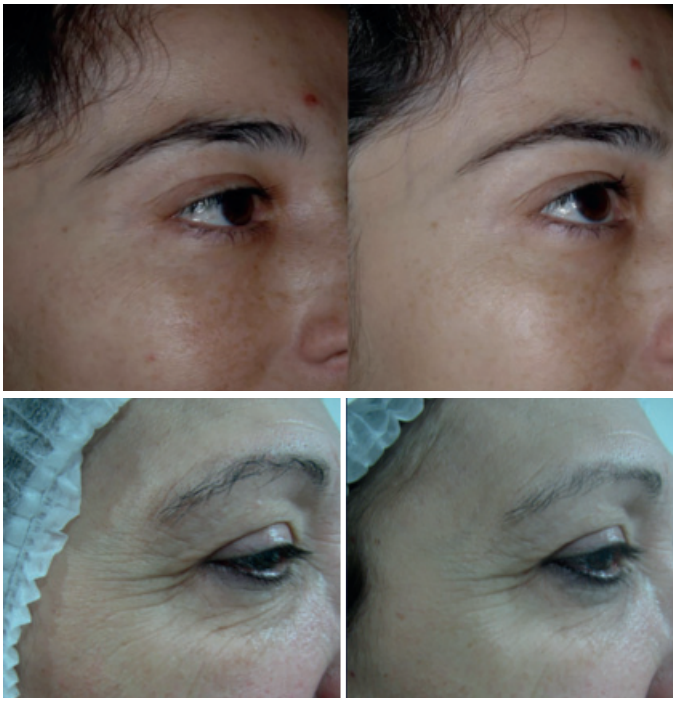

Figure 2: Patient 9, pre and post-treatment (Table 1). The clinical outcome was deemed good by the physician

covering the treated zone with very superficial injections in the epidermis and the superficial dermis. (Figure 1)

The amount of HA injected into each patient per session, as well as the total volume, were recorded. The result of the pretreatment was analyzed through pre- and post-application digital images recorded through the Canfield system, by a researcher physician, a non-medical evaluator, and the patients, on the 45th day of the study, according to the following scale: absence of improvement (no change), poor (improvement of around 25%), good (improvement of about 50%), and very good (improvement of about 75% or more). Follow-up with the patients was also carried out through annual interviews up until 2012, with an aim of verifying the occurrence of any complications or side effects.

RESULTS

The evaluation of the patients (mean age = 53 years) resulted in an average score of 3.1 according to the WSRS. The average volume for the first treatment was 0.650ml; for the second, 0.645ml; for the third 0.590ml. The total volume was 1.525ml. On the patients' self-assessment scale, the clinical results showed the following number of opinions per rate: poor = 2, good = 6, very good = 2. In the evaluation of the non-medical evaluator, the perception was as follows: poor = 3, good = 4, very good = 3. In the opinion of the researcher physician, the results were: poor = 3 (Figure 1), good = 6 (Figure 2), and very good = 1 (Figures 3 and 4). (Table 1)

There were immediate complications, such as ecchymosis (3 patients) and bleeding (4 patients), (Figure 5) while the injections were slightly painful on 3 patients. The patients devel-

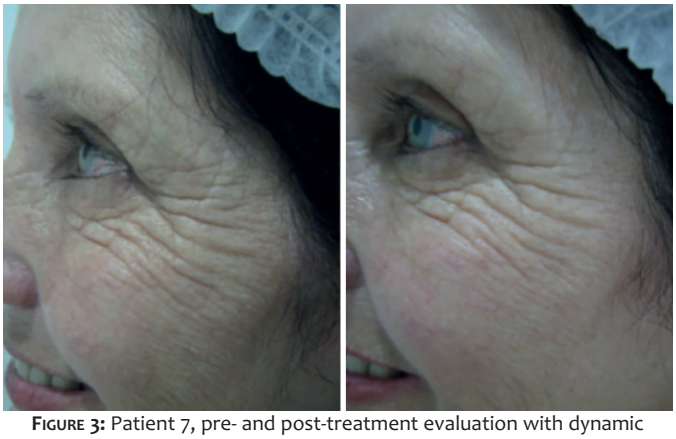

Figure 3: Patient 7, pre- and post-treatment evaluation with dynamic contraction of "crow's feet" (Table 1).

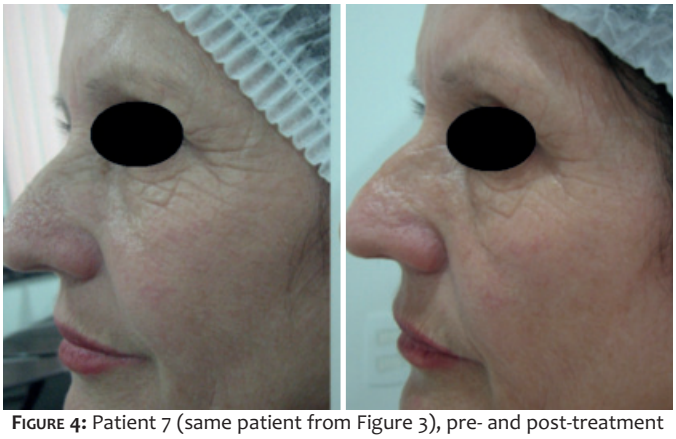

Figure 4: Patient 7 (same patient from Figure 3), pre- and post-treatment without contraction of "crow's feet". The clinical outcome was deemed very good by the physician.

Figure 5: Ecchymosis, edema, erythema, and bleeding immediately after the injections.

oped mild erythema and edema immediately after the injections, however with the duration of only a few minutes to 2 hours. The papules resulting from the injections remained visible for 24 to 48 hours, disappearing more rapidly with the application of massage.

Four patients questioned the effect of the product regarding the filling effect that was obtained, receiving the explanation that the treatment was conducted only for the purpose of hydrating the skin and that the procedure was not aimed at providing the effects of cutaneous filling. Even though the HA had the effect of softening the wrinkles, it was necessary that the patients understood why the substance had not filled them. There were no complications or side effects when evaluated in the long run.

DISCUSSION

Visible aging comprises changes in the skin's appearance over time as a result of the degradation of its components, variations in texture, and color alterations. It is also known that there is an intrinsic physiological aging, which depends on genetics and time lapse, as well as a process of extrinsic aging caused by exposure to the sun, an unhealthy lifestyle, the effects of gravity, environmental pollutants, and chronic inflammation. In addition to analyzing the complexity of aging, the present study examines one of the effects occurring during this process: the drying and dehydration of the skin. [3-6]

When dryness and dehydration are discussed, it is understood that the reduction of natural moisturizing factors leads to an increased transepidermal water loss and to a delay in the desquamation, lending the corneum layer a compact, intensively scaly, and rough appearance, with the deceleration of the production of glycosaminoglycans (GAG). Due to extrinsic factors, an overproduction of hyaluronidase also takes place, reducing the HA levels and its interaction with collagen and elastin. As a result, there is a reduction of the bonds with water, contributing to the changes observed in the aging skin, including wrinkles, changes in the elasticity, reduction of turgor and a diminished capacity to provide support to the microvasculature. This picture can worsen due to the use of aggressive topical substances, cleaning products, and materials not suitable for hydration. [3-6]

HA is a glycosaminoglycan disaccharide consisting of repeatedly alternating units of D-glucuronic acid and N-acetyl-D-glucosamine. It has physiological pH, mainly exists as a sodium salt and is part of the extracellular matrix found in many human tissues, including the skin, the vitreous fluid of the eye, and the existing structure within the synovial fluid and joints. The largest amount of HA resides in the cutaneous tissue (7 to 8g per average adult human), corresponding to approximately 50% of the total HA existing in the body (~ 2.0 to 4.0 mg/ml in the epidermis and ~ 0.5 mg/ml in the dermis). As a polyanionic polymer with physiological pH, HA binds to water extensively. [6-8] Also a major component of GAGs, HA can bind to volumes of water corresponding to 1,000 times its weight, and may help the skin to retain and maintain water, and is therefore considered a natural free radicals scavenger. It is found in all connective tissues and is produced in the skin, mainly by fibroblasts and keratinocytes. HA is not only located in the dermis, but also in the intercellular spaces of the epidermis, especially in the middle stratum spinosum, however it is not found in the stratum corneum and stratum granulosum. [3,9-11]

Aging skin is characterized by reduced levels of HA, which decreases over the years and reaches about one third or less at 75 years of age, compared to the level that exists at 19 years of age. The function of HA in skin hydration is not clear, and this substance does not penetrate the skin via topical application. [12,13] In its natural state, HA has limited biomechanical properties as a cutaneous filler, nevertheless it has an excellent biocompatibility and affinity for water molecules, [13,14] which is the reason for using an uncrosslinked HA injected directly into the dermis with the aim of increasing the water content of the skin and compensating for the lack of endogenous HA. HA is also a soluble polymer that is quickly eliminated when injected into normal skin.

CONCLUSION

The patient series in the present study offered a sample of the effects of uncrosslinked HA when injected directly into the skin. Although HA in this form is eliminated in a few hours, it seems to be effective as a hydrating substance due to its affinity for water and the residual local hydration, which remains for a longer time than that provided by the skin's own HA. A greater mastery of the knowledge of pure uncrosslinked HA and its isolated, controlled, and safe injection, aimed at re-hydrating and restoring the brightness, vitality, and elasticity of dry and damaged skin, can constitute an additional tool in the usual armamentarium of treatment options for facial rejuvenation. ●

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