

The importance of the early use of hyaluronidase in the treatment of arterial occlusion resulting from hyaluronic acid based cutaneous filling

A importância do uso precoce de hialuronidase no tratamento de oclusão arterial por preenchimento de ácido hialurônico

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ABSTRACT

Cutaneous ischemia, caused by arterial embolism, is one of the vascular adverse events resulting from the application of hyaluronic acid. Early application of hyaluronidase will lead to the successful degradation and reversal of the condition – which might be severe and cause harm to the patient. The authors report cases with suspected arterial occlusion in which degradation was performed with hyaluronidase at different timepoints. This analysis has evidenced that the degradation time and the procedure's effectiveness are correlated to the intervention timepoint.

Keywords: Dermatology; Ischemia; Reperfusion

RESUMO

A isquemia cutânea é um dos eventos adversos vasculares decorrentes da aplicação de ácido hialurônico, causada por embolia arterial. A aplicação precoce de hialuronidase representará o sucesso da degradação e reversão do quadro que pode ser grave e causar danos ao paciente. Relatam-se casos com suspeita de oclusão arterial no qual foi realizada degradação com hialuronidase em diferentes períodos. Tal análise permitiu observar que o tempo de degradação e a eficácia do procedimento relacionam-se com tempo de intervenção.

Palavras-chave: Dermatologia; Isquemia; Reperusão

INTRODUCTION

Cutaneous ischemia is one of the most serious and undesirable complications following application of hyaluronic acid in aesthetic rejuvenation and facial volumization procedures. It is triggered by arterial embolism caused by hyaluronic acid or occlusion caused by compression, often with immediate manifestations. Its diagnosis is clinical. Changes range from livedo reticularis, erythema to pallor and, more rarely, necrosis. The use of hyaluronidase in the right concentration and early application to treat occlusion will most certainly lead to the successful degradation and reestablishment of local blood flow.¹

This adverse effect constitutes a potential aesthetic discomfort and risk of irreversible damage to the patient if early diagnosis and early degradation are not carried out. The authors of the present paper report two cases of ischemia after use of hyaluronic acid in aesthetic procedures, reversed with hyaluronidase at different time points, for the reversion of the picture, demonstrating that early degradation led to a considerably faster resolution of the picture.

Indications and contraindications for the use of hyaluronidase

The indications listed by the US Food and Drugs Administration (FDA) for the use of hyaluronidase are classified into three situa-

Case Reports

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tions:²⁻⁴ 1) facilitation of absorption and dispersion of other injectable drugs; 2) aid in the infusion of subcutaneous fluids; and 3) use in subcutaneous urography. In dermatology, this drug has been indicated for hair transplant and for tumescent liposuction. More recently, it has also been used in cutaneous filling procedures followed by ischemia, aiming at reducing the time of tissue revascularization and aiding in the healing process, leading to a favorable prognosis. Side effects of hyaluronidase use have a low incidence – among them is pruritus due to local application, described by Sopakar et al. in only two patients within a sample of 100 individuals.²⁻⁴ Another side effect is related to home-made bovine origin hyaluronidase, associated with the occurrence of spongiform encephalopathy.⁵⁻⁷

CASE REPORT

CASE 1

MBF, a 27-year-old female patient, sought medical attention due to dissatisfaction with the aesthetics of her nasal region, even though she had previously undergone rhinoplasty. After evaluation, 0.8 ml of hyaluronic acid (Emervel Deep®, Galderma, Otten, Switzerland) was applied in the columella and nasal tip region with a needle, aspirating before the injection, with no alteration being observed at the moment of the procedure. The patient returned to the practice 36 hours after, with intense local pain, pallor interspersed with *livedo reticularis* areas, compatible with arterial occlusion. Hyaluronidase Biometil® (Laboratório Biometil, São Bento do Sul, SC, Brazil) was used for reverting the picture in a single 1,600 IU application, associated with the following oral drugs: 100mg/day Aspirin® (Bayer, Barmen, Germany), 100mg 12/12 hours cilostazol (Eurofarma, São Paulo, Brazil), 40 mg/day prednisone (Eurofarma, São Paulo, Brazil), 20 mg/day rivaroxaban (Bayer, Barmen, Germany), 500mg 12/12 hours ciprofloxacin (Eurofarma, São Paulo, Brazil), and 300mg 12/12 hours clindamycin (Teuto-Brasileiro S/A, Anápolis, GO, Brazil), for 15 days. Doppler ultrasonography of the site was performed, showing normal arterial and venous blood flow. Three hyperbaric chamber sessions were carried out in the first three days, and warm compresses were applied several times a day for 7 days. The patient evolved with progressive improvement and complete resolution of the condition after 3 weeks.

CASE 2

MSM, a 31-year-old female patient, sought medical attention aimed at undergoing facial harmonization treatment. Hyaluronic acid was applied to several sites of the face, among them in the deep proximal nasogenian sulcus (piriform fossa) – 0.1ml Emervel Deep® (Galderma, Otten, Switzerland), with a needle positioned at 90° and aspiration prior to the injection. An erythematous-purplish area emerged instantly, extending from the left lateral region of the nasal wing to the medial region of the ipsilateral nasogenian sulcus. In face of the persistence of the picture and hypothesis of arterial occlusion for 12 hours, the authors decided for the early degradation using 400 IU of hyaluronidase (Biometil®) and 100 mg/day sildenafil, 40 mg/day Clexane (Sanofi-Aventis Farmacêutica Ltda, Suzano, São Paulo,



FIGURE 1: Therapeutic progression after the application of hyaluronidase in the nasal tip, respectively on the 1st and 7th post-procedure days, and 3 months after the application



FIGURE 2: Therapeutic progression after the application of hyaluronidase in the nasolabial sulcus, respectively on the 1st, 4th and 21st post-procedure days

Brazil), 40 mg/day prednisone (Eurofarma, São Paulo, Brazil), 500mg 12/12 hours ciprofloxacin (Eurofarma, São Paulo, Brazil), and 500mg 12/12 hours clarithromycin (Eurofarma, São Paulo, Brazil) for 15 days. Doppler ultrasonography of the site was also performed, showing normal blood flow. Improvement

in the coloration was observed 2 days after the degradation, with complete resolution after 4 days.

DISCUSSION

With the increased numbers of hyaluronic acid based esthetic procedures, knowledge of the possible adverse reactions and respective handling is necessary. The pathophysiology of the embolic process caused by these procedures has not yet been elucidated, nevertheless the decrease in blood flow may be linked to the volume injected and the site of injection of high viscosity fillers.⁸ In both cases reported, alterations in the blood flow resulting from application of hyaluronic acid were observed, with typical manifestations at different time points. The chronology of the dermatological manifestations of embolic processes usually follows the sequence *bleaching*, emergence of *vesicles*, *bedsores* and

necrosis, meaning it is crucial for the practitioner to recognize them early.¹ The use of hyaluronidase is recommended for the degradation of the material, which leads to the normalization of the blood flow and prevents sequelae. The supportive therapy is based on increased perfusion, decreased inflammatory process and prophylaxis of associated infections, and may rely on vasodilators, corticosteroids, antimicrobials and antiaggregants.²

Comparing the cases reported and observing their development in Figures 1 and 2, it is possible to observe that the time for degrading hyaluronic acid had a significant impact on the prognosis and normalization of the local blood flow. In addition, it was possible to see that hyaluronidase only degrades injectable hyaluronic acid and does not interfere with what exists in the body, given that a large amount was used in Case 1 with absence of alterations whatsoever in the patient's previous physiognomy. ●

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