White Paper

Rational for EnerJet intralesional injection of hyaluronic acid in treatment of keloids and hypertrophic scars

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Introduction

Current regimens for pharmaceutical management of hypertrophic scars and keloids include intralesional injection of fluorouracil (5-FU) combined with corticosteroids in several ratios and proportions. The therapy goal is to attain cell proliferation in the scar tissue with the cytotoxic antimetabolite and achieve a high concentration of the corticosteroid at the diseased site without significant systemic absorption.

Hyaluronic acid (HA) is a glycosaminoglycan that plays an important role in reorganization of extracellular matrix (ECM) during the skin wound healing process. Decreased presence of HA is a major characteristic of keloid and hypertrophic scarring.[1] EnerJet (PerfAction) utilizes a high-pressure liquid-jet technology. It provides kinetic energy-based administration of various therapeutic materials through spherical intradermal dispersion. Administration of external HA through the pressure jet injection is thought to represent a beneficial therapy for reversal of scarring (Figure 1).

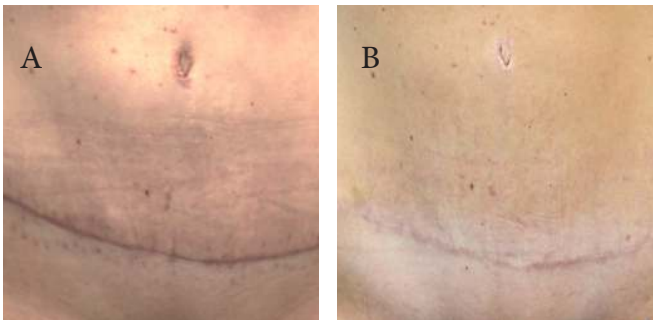

Figure 1: EnerJet treatment of hypertrophic scar post abdomenplasty surgery. A - 8 month after surgery, before EnerJet treatment. B - 8 months after 1 EnerJet treatment.

Hyaluronic acid provides hydration to the scar tissue

Hypertrophic scars and keloids are known to be detrimentally influenced by dehydration associated with absence of glycosaminoglycans. The fibrotic tissue of scars slowly invades dermal tissue and replaces its normal hydration mechanism. Sebaceous glands are typically not present in scar lesions and cannot contribute for maintaining skin moisture properties.

Lack of proper hydration causes constant irritation, dryness, and intense itching additionally contributing to patient complaints and severe disease burden. The itching forces inadvertent scratching and skin abrasion. Continuous micro-trauma caused by scratching encourages and promotes cell proliferation further causing growth of scar tissue. One of the functions of the silicone sheeting, as recommended by current guidelines, is to maintain hydration by shielding the lesion from outer dehydration.

Contrary to that, external intralesional administration of HA with EnerJet provides hydration not only to the surface but also to deeper layers of the lesion, which is much more effective than silicone sheeting. This can explain the immediate relief from itch that patients report after EnerJet treatment.

Hyaluronic acid reverses proliferation of scar tissue

Biomolecular effect of intralesional injection of HA contributes to reverse formation of fibrotic scar tissue. Increase in hyaluronan tissue level acts against the fibroblast differentiation into the scar forming myofibroblasts.[2] It also diminishes the phenotype conversion of fibroblasts to myofibroblasts in the scar tissue.[3]

The bio-modulatory mechanism of HA normalizes fibroblasts activity in comparison to the 5-FU mechanism of non-particularly suppressing cell activity in the scar. HA changes cell behavior from uncontrolled hypertrophy to healthy regeneration by regulating cellular response to growth factors and fibroblast migration. That will result in a therapeutic effect compared to the more palliative effect of steroids.[3]

Pressure injection inhibits scar perfusion

Hypertrophic scars and keloids demonstrate a high level of local micro-perfusion.[4] The EnerJet-generated jet of liquid therapeutic material forcefully penetrates the scar causing instant blanching of the injected area. This leads to immediate, and at least temporary, shut down of the excessive local microcirculation, similar to the mechanism also thought to be at the basis of the beneficial action of silicone sheeting.

However, its action is distributed differently over time and in a much milder way compared to the high-pressure injection of EnerJet.

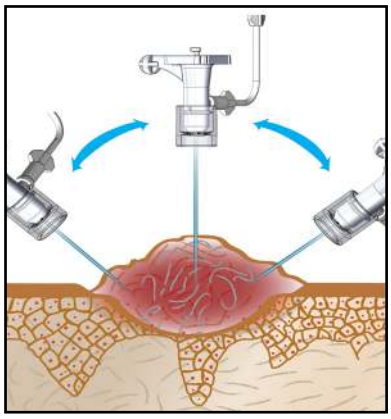

Figure 2. The raised lesions are injected with EnerJet from different directions and angles.

High-pressure injections provides efficient intralesional distribution of material

The high-pressure jet injection of EnerJet allows a more controlled and deep penetration through the full thickness of the scar – an ability which cannot be achieved neither by manual injection, nor by laser or other energy-based treatment method.

EnerJet needleless injection delivers more effective infiltration and more uniformed spread of the material than a regular needle. The jet-administered material reaches all layers and even the core of the scar lesion, for which a manual injection has limited abilities due to extreme density of the scar.

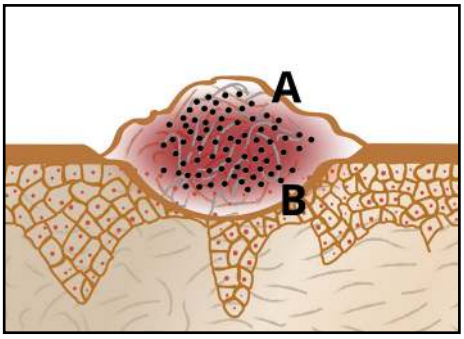

Figure 3. A schematic representation of the "sandwich" pressure injections for reaching deeper parts of thicker and bulkier lesions: (A) low injection pressure applied for superficial layer; (B) high injection pressure applied for keloid's core.

High-pressure injections offers better tolerability

The high-velocity jet injection of EnerJet delivers a short penetration momentum which contributes to a significant pain reduction compared to the manual needle injection.
The side effects of intralesional needle administration of steroids and 5-FU include injection pain, thinning and atrophy of the skin and subcutaneous tissues, capillary dilation, and development of secondary hypopigmentation. On the contrary, EnerJet-injected HA, a naturally-occurring glycosaminoglycan with the main function of skin restoration, will cause no atrophy effect.

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