The 3Dose syringe like a new injective technology in aesthetic facial Biostimulation: a clinical study of 63 patients.

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Introduction

Biostimulation (BS) is an anti-aging treatment which consists in injecting into the skin of the face some substances, called "primers" (including hyaluronic acid and aminoacids) to restore the elasticity and tone of the skin. BS acts on fibroblasts, favoring the natural process of synthesis of collagen and elastin with the aim of restoring the correct trophism of the dermo-epidermal complex. The skin is an extremely vital tissue and is subjected to continuous cycles of renewal, which in young people are fast, while with advancing age they tend to slow down due to the loss of ability by fibroblasts to produce collagen; moreover, the skin, being in contact with atmospheric external agents (like solar radiation and pollutants) and with addictions, such as cigarette smoke, tends to age faster and be subject to degenerative processes. BS is in great demand in Aesthetic Medicine because it helps to replenish the substances that our body can no longer produce, such as many aminoacids; in addition, the decrease of hyaluronic acid is one of the triggers of tissue aging, for its moisturizing properties. The best method to nourish the dermis and restore its essential substances, is the injective one that can overcome the thick epidermal barrier thereby micro-injections, for this motive the BS is performed. The most widely used products are non-animal linear hyaluronic acid based cocktails, which unlike those used as fillers are capable of moisturizing, stimulating the formation of new collagen, counteracting free radicals and revitalizing the skin. All body areas are susceptible to biostimulant treatment, although the most treated areas are the face, neck, décolleté and dorsal region of the hands. As mentioned, the method is performed through micro-injections on the area to be treated, which cause a slight discomfort with skin redness for a few hours.

The injective mode

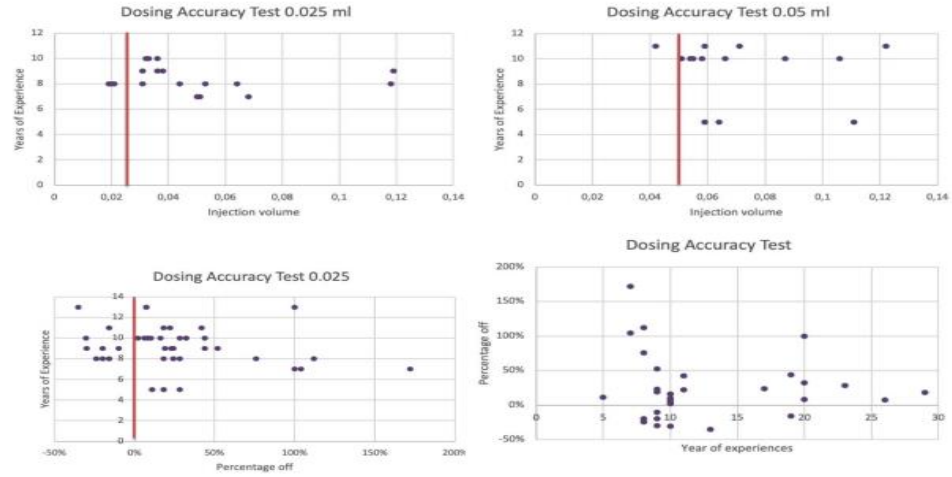
The technique used in BS is superficial intradermal mesotherapy with the formation of the classic dermal “wheal". This method is described as early as 1793, but its spread in the medical scientific world is thanks to Michel Pistor MD since 1952. Mesotherapy is an injection technique described by its creator: "a method to bring therapy closer to the place of pathology". Simple in its conception, it requires adequate training to be performed effectively. The advantage of this technique is to be able to use reduced doses of active substance, doses that spread in the tissues underlying the inoculation and persist for longer than the route of

intramuscular administration, with advantages such as the prolonged effect over time, reduced involvement of other organs and reduced risk of adverse events or side effects. Aesthetic mesotherapy applied to the skin areas of the face and hand poses two kinds of problems: it can be slightly painful, in relation to the speed of infusion and the pressure exerted on the syringe plunger; it is not possible to quantify exactly the amount of product injected in each individual injection. For definition, in fact, the dermal wheal is manifested by volume increases in the dermis between 0.03 and 0.06 ml of injected product, having as variable also the exact depth of deposition. The lack of standardization and reproducibility of the quantity of injected volume in each single infiltration in the treated areas can affect the final result, since there is a variable of the injected quantity that can be estimated, on average, up to double, with considerable repercussions on the effectiveness of the treatment and with the frequent occurrence of not being able to fully distribute the product in the predetermined area.

The accurate dosage

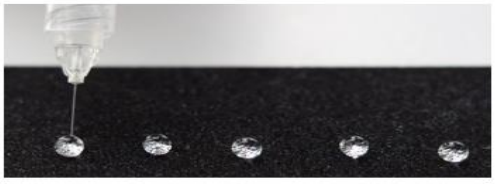
The possibility of using a tool able to guarantee the accuracy of the dosage of injected volume comes from the experience gained in recent years in the method of treatment with botulinum toxin (BoNT). The technique of applying the BoNT has evolved from an approach suitable for everyone towards the adoption of a customized treatment protocol, ensuring the individual patient an aesthetically pleasing, natural and relaxed. Numerous clinical studies have shown that changed from fixed doses delivered at fixed time intervals into fixed anatomical sites, all of which were required for regulatory approvals, to patient-centric treatments of variable doses delivered into variable anatomical points at time intervals individually tailored to each patient. This complete change in approach has also helped to exchange the “frozen look” for the “natural look” for the majority of patients.

An accurate dose of injection has become essential to ensure patients to have excellent aesthetic results reproducibly in the current treatment paradigm: Small volumes with high doses distributed over a greater number of injection sites are more effective and greater than a large injection volume with low dose. To perform this unique dosing strategy with small volumes, doses must be accurate, predictable and reproducible. Numerous studies have shown that the accuracy of the injection with the freehand method differs significantly from the expected amount. The mean deviation is 24% more than the expected injection volume. Other studies have recently reported that the average accuracy error associated with the free-hand injection of 40 single consecutive units (0.025 ml / unit) from a 1.0 ml disposable syringe was



Source: Dr. Dalvi Humzah, 2017

about 10%. Moreover is reported that product waste at the injection site due to needle dripping was almost three times worse with freehand injection compared to injections performed with the VLow Medical device. So a new level of experience was needed to constantly provide small volumes of doses at different depths of tissue and have the ability to precisely adapt to areas that require specific dosages of bont units based on characteristics patient specifications. The specific answer to this problem is the 3Dose syringe designed and built in the Netherlands by VLow Medical. It is a technologically advanced product designed for treatments with botulinum toxin (BoNT) that revolutionizes and simplifies procedures. The patented mechanism offers a precise "click" system to always ensure the same dosage, introducing the concept of unit/ click than the classic unit/ ml. The tactile and sonic feedback of the syringe allows injections of extreme accuracy and, consequently, calculation errors in units are virtually eliminated. It is proposed in two versions with different graduated scale, in relation to the different dosage of units of BoNT on the market: orange and green color.



Source: Vlow Medical – Equal doses, 2017

Materials and methods

Any clinical trial is scheduled with a goal and outcome. The question we asked was: does the current protocol encoded for the BS of the face need a tool with greater effectiveness than the

common 1 ml syringe? A tool that guarantees accurate dosing (without waste of product) with perfect homogeneity of the final result and without any pain for the patient? The objective of this clinical study was to demonstrate the effectiveness and superiority of the injection applied with the new 3Dose syringe compared to that carried out with the common 1 ml syringes in use for facial Biostimulation. For this study the 3Dose green syringe was used, because the protocol adopted provided for the administration of 2 ml of product on 20 injection sites per side; therefore, every single injection had to be exactly 0.05 ml (3Dose green > blue scale: 1 click = 0.05 ml). The result was the specific clinical aspect capable of providing the answer, in detail we considered it indicative to evaluate an objective data (like the difference in the amount of the volume of product used in two individual treatment moments) and two subjective parameters (like the reduction of the pain symptom and the patient's liking). The profile of the study was randomly controlled clinical: the persons who participated in the study were randomly assigned to the group receiving the treatment or to the group receiving a standard (control) treatment. Randomization minimizes the selection effect and comparison groups allow the determination of the possible effects of the treatment to be tested compared to the group without treatment (control), while the other variables are kept constant. For the analysis of subjective outcomes the two attached scales were used: the visual analog scale (VAS) modified with smileys and patient satisfaction index, proposed with a Likert scale modified in five degrees.

The study

The rationale of this study was to research a method to increase patient comfort by eliminating the painful sensation, and standardize and make reproducible, in every single drug infiltration, the exact amount of product to make the final result as homogeneous as possible and, consequently, increase patient satisfaction for the achieved result. From September to November 2022 we enrolled all patients who came to our observation with clinical diagnosis of chrono-aging who needed the protocol of face BS. At the end of the study the group consisted of 63 patients, of whom 51 were female and 12 male (F / M = 4.25) with average age = 52.4 (range 41 - 68); all patients were in phototypes III and IV of the Fitzpatrick classification. Everyone was asked for the necessary authorisation for the study and had

informed consent signed, as is standard practice. We divided the patients, by chronological access, into two groups (3Dose and control) that were homogenous by gender, but not by age. The product administered to all patients selected in the study was a 2 ml solution containing: vasoactive peptides, hyaluronic acid, organic silicon and DMAE(di-methyl-amino-ethanol). We provided for the preliminary design of the areas to be treated (as shown in the attached photos) with grates that divided the entire area into 20 microareas per half. At the center of each microarea, after skin disinfection, it was practiced the infiltration of biostimulant product (0.05 ml) maintaining the syringe angle between 45 - 60° and introducing the needle to a depth of about 2 mm (surface dermis) with the formation of characteristic dermal wheal.

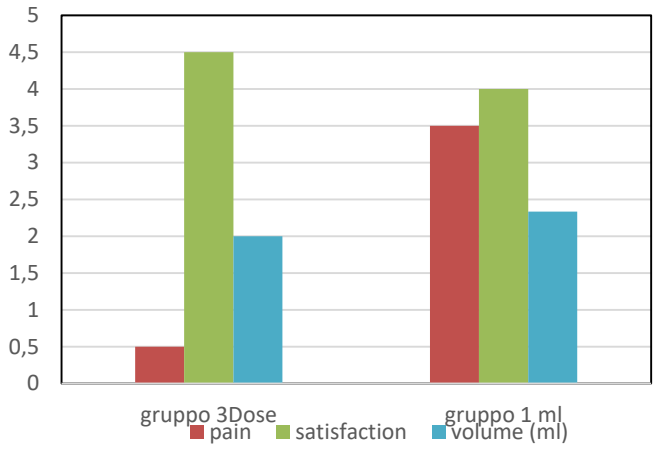
In both groups a high compliance needle for the patient was used: 32 G of calibre x 8 mm in length. In the first group (32 patients, F = 26 / M = 6, white grate) the 3Dose syringe was used for mesodermal injection; instead, in the second group (31 patients, F = 25 / M = 6, black grate) we used for treatment the common 1 ml syringe for insulin therapy. A total of 2520 injection sites were treated.

Results

Data analysis for the VAS pain scale showed: for the 3Dose group the mean value = 0,5 / 10 and for the control group the value = 3,5 / 10.

The data expressed for the satisfaction index were: 4.5 / 5 for patients who practiced BS with the 3Dose, 4 / 5 for those who were treated with 1 ml syringe (control).

The difference in the amount of volume, for each individual patient, was measured at two points in the treatment: at the end of the first half (twentieth point) and at the end of the treatment (fortieth point). For the 3Dose group the results were identical: a deviation of +/- 0% in both intermediate and final measurement. For the control group there was a particular fact: at the first measurement we recorded an average deviation in excess of the volume of residual product (+ 0.184 ml); at the final measurement, however, there was a deficit in volume with the impossibility of finishing the treatment, on average, on 3 injection sites (about 0.15 ml missing) with the need to use another vial to complete the treatment. Thus the mean error of the amount of volume of product administered in the control group was: 0.184 + 0.15 = 0.167 ml, that is +/- 16.7%. Having assumed the hypothesis of obtaining a determined result, from the observed data we can conclude that the analysis of the aggregated values for this clinical observational study has demonstrated the statistically significant superiority ($p < 0.05$) the use of the 3Dose syringe compared to the conventional 1 ml syringe in the face Biostimulation.



Conclusion

The BS of the face requires the perfect and homogeneous distribution of the product over the entire predetermined surface for an optimal result. From this study emerges and the mental mechanism that unconsciously guides the hand of the operator during this type of treatment is made manifest. In a first phase (during the initial treatment of the first half of the face) there is

a tendency to under-dose the amount of volume injected, fearing not to be able to treat all 20 programmed points and the residual product in the syringe. Starting the treatment of the second half of the face tends to overdose the injected volume (> 0.05 ml), often reaching the point of failure to treat the last drawn points (on average = 3). The variable and uneven pressure applied to the syringe piston at the injection can cause slight discomfort and pain. Moreover, being forced to constantly look at the graduated piston of the syringe distracts attention from the field of work with possible errors of the injective technique and increased risk of pricking a capillary (hematoma). This study showed that the error rate, in the free-hand injection, was equal to 16.7%, therefore it seems justified and recommended the adoption of the 3Dose syringe to solve this problem. Finally, the use of the 3Dose syringe frees the BS of the face from subjectivity, restoring to this method the dignity of an objectively reproducible protocol, in complete absence of pain for the patient and in the absence of waste, with economic savings.

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