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- **Title: SAFETY IN IMMEDIATE RECONSTITUTION OF POLY-L-LATIC ACID FOR FACIAL BIOESTIMULATION TREATMENT**

- **Running Head: IMMEDIATE RECONSTITUTION OF POLY-L-LATIC ACID**

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Title: SAFETY IN IMMEDIATE RECONSTITUTION OF POLY-L-LATIC ACID FOR FACIAL BIOESTIMULATION TREATMENT

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ABSTRACT

Background: PLLA is presented as freeze-dried preparation of 150mg per vial and, according to consensus, the recommendation on your preparation is hydrate in sterile water for injection (SWFI) or bacteriostatic water at room temperature for ≥24 hours. (8) However, these long periods of hydration, it is time-consuming and costly for the physicians.

Goal: To demonstrate the safeness of immediate reconstitution of facial biostimulation treatment with PLLA.

Materials and Methods: A clinical prospective study with 26 latin-american female pacients, aged between 27 and 80 years, complaining of facial laxity of treated with immediate PLLA recostitution. One PLLA vial was injected per session in 12mL total dilution. All patients had their pictures taken before and after the treatment in Photo Analysis Program Vectra 3D (Canfield®). A follow up 90 days was perfomed.

Results: The total of 58 facial applications of PLLA were reported in female pacients with a mean age 52,62 (+/- 13,46) years. Pain was reported in 17 injections (29,31%) and ecchymosis in 6 (10,34%).Also, 2 patients (3,44%) developed a nodule. None of the patients presented significant bruising, edema or papules formation.

Conclusion: Despite the literature declare that a longer hydration times (up to 48 hours) have been shown to reduce the risk of nodule formation (15), our study demonstrated the safeness of injection with immediate reconstitution and a very low adverse events rate. Immediate PLLA reconstitution is a great asset for physicians, injections in account of being less laborious, less time-consuming and reducing product loss for the injector.

Keywords: Poly-L-latic acid, Collagen Remodeling, Facial Rejuvenation, Reconstitution, Collagen Bioestimulator

INTRODUCTION

The use of injectable soft-tissue fillers and neurotoxins for correcting the facial changes associated with aging is the gold standard in aesthetic medicine. (1) Poly-L-lactic acid (PLLA) is a biocompatible, biodegradable, synthetic polymer able to be tailored into various desired morphologic features. (2,3) An injectable form of PLLA (New-Fill®, Valeant US, Sinclair Pharma Paris, France) has been available in Europe since 1999 for soft tissue augmentation and the treatment of facial rhytides. In 2004, injectable PLLA received food and drug administration (FDA) approval under the trade name Sculptra® (Galderma, Lausanne, Switzerland) for the treatment of HIV-associated lipoatrophy. (4)

The mechanism through which it stimulates neocollagenesis, is by triggering a foreign body reaction to the injected material, succeeded by a cellular inflammatory response which leads to the formation of vascularized, connective tissue.(1,5,6,7)

PLLA is presented as freeze-dried preparation of 150mg per vial and, according to consensus, the recommendation on your preparation is hydrate in sterile water for injection (SWFI) or bacteriostatic water at room temperature for ≥24 hours. (8)

PLLA reconstitution is an important factor to consider when using this product; however, it is time-consuming and costly for the physicians. With these long periods of hydration, it demands a schedule of one day before the application, wasting

precious time, and dermatologists still running the risk of the patient not showing up for the appointment.

GOAL

To demonstrate the safeness of immediate reconstitution of facial biostimulation treatment with PLLA.

MATERIALS AND METHODS

A clinical prospective study with 26 latin-american female pacients, aged between 27 and 80 years, complaining of facial laxity of a single treatment center, totaling 58 sessions of PLLA. Exclusion criteria were hyaluronic acid filler treatment in the latest 6 months, permanent fillers on the face, autoimmune diseases, use of immunosuppressants, inflammation or infection active local, history of keloid or hypertrophic scars, pacients under 18, pregnancy or lactation.

Informed consent was obtained from all patients and the study protocol was complied with the laws of the country in which it was performed. All pacients had their pictures taken before and after the treatment in Photo Analysis Program Vectra 3D (Canfield®). They were also advised on the treatment and the number of sessions that were indicated according to the laxity degree, being suggested between 1 and 5 sessions.

RTU – Immediate PLLA reconstitution

Rubber cover was clean with an antiseptic solution (0.5% alcoholic chlorhexidine) and at room temperature, it was added 5mL SWFI to the powder, on the side of the vial and followed by immediate vigorous 1 minute agitation. This suspension was aspirated through hypodermic needle 40mm X 12mm blunt tip to a 20 ml luer lock syringe and it was added 5mL SWFI and 2mL 2% lidocaine without vasoconstrictor and it was mixed at 1-minute intervals until a uniform translucent suspension was obtained, producing a total of 12ml of PLLA. This suspension was transferred to four 3 ml syringes. (Figure 1)

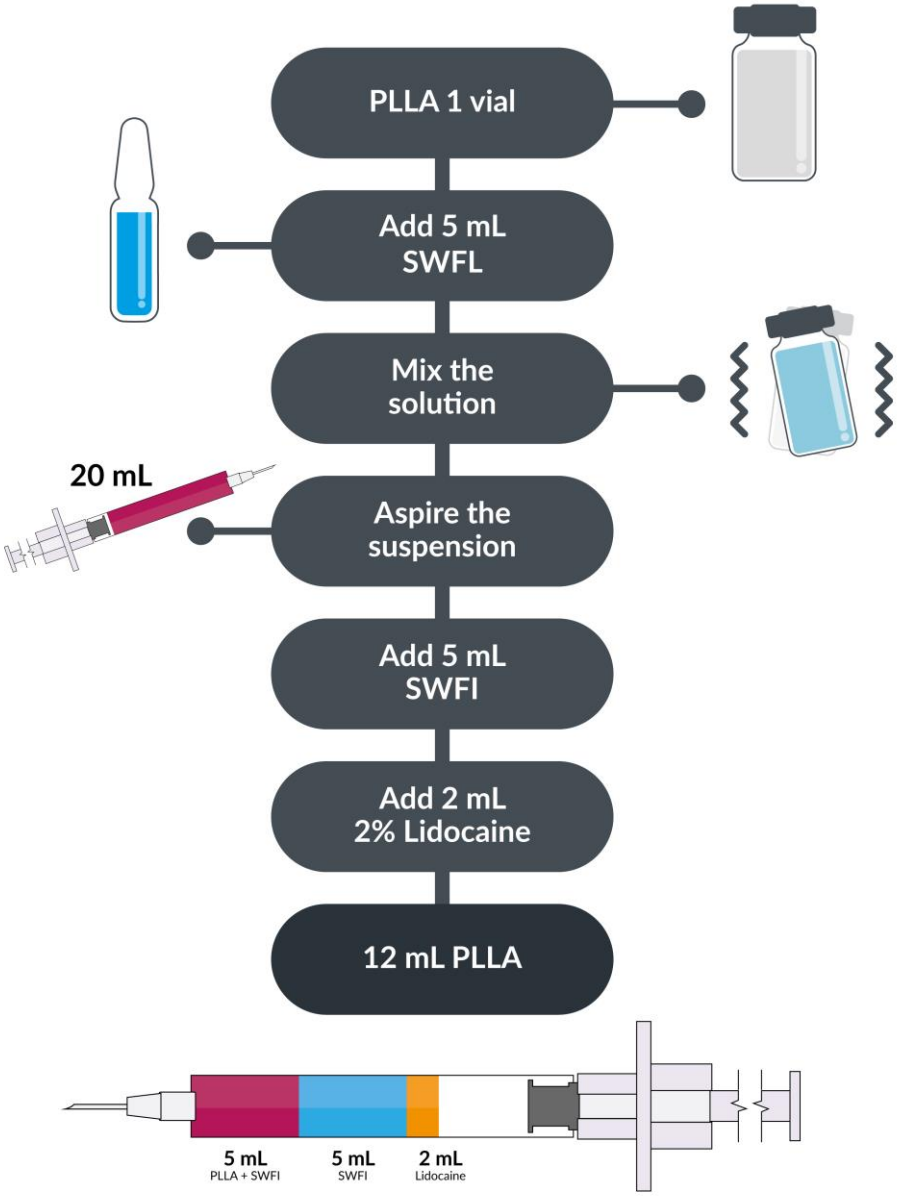

Figure 1: Step by step of immediate PLLA reconstitution.

INJECTION

Asepsis of the pacient's skin with 0.5% alcoholic chlorhexidine and topical cream anesthetic (lidocaine 10%) was applied 30 minutes before the injection. The technique consists on using a 22 gauge/5cm cannula, in a fan technique by retrograde injection, through two different insertion points in each hemiface. Approximately 24 slowly retro-injections of approximately 0.5 ml each were performed in the subcutaneous plane, in the malar, zygomatic and mandibular region. The injection was halted when 3⁄4 of the cannula becomes apparent. Areas of hyperdynamic musculature were spared (perioral and periorbicular). (Figure 2).

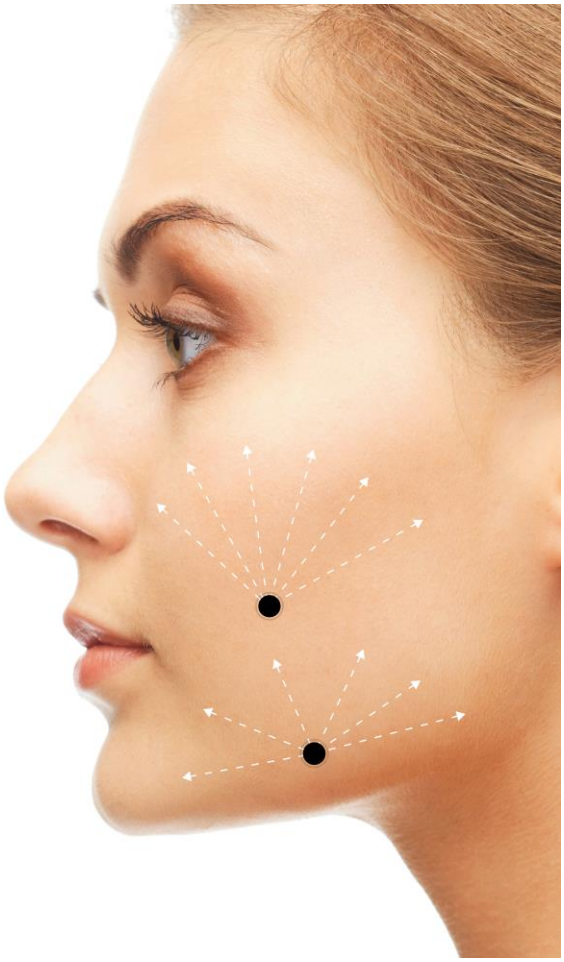

Figure 2: Injection technique.

POST-TREATMENT

It has been instructed post-treatment massage according to the 5-5-5 rule (5 times per day for 5 minutes for 5 days). All patients were seeing within 30 days, in order to look for adverse events.

RESULTS

The total of 58 facial applications of PLLA were reported in female pacients aged between 27 and 80 years, with a mean age 52,62 (+/- 13,46) years. One PLLA vial was injected per session in 12mL total dilution.

Two patients (3,44%) developed a nodule within the first month and had complete regression after intervention with dilution with 1,0 mL of 0.9% saline solution injected into the nodule twice with an interval of 1 week and local massage. Also, pain was

reported in 17 injections (29,31%) and ecchymosis in 6 (10,34%) . None of the patients presented significant bruising, edema or papules formation.

There were performed between 1 and 5 session, mean of sessions is 2.23, with a minimum interval of 28 days and a maximum of 121 days between sessions, mean 46.71 (+/- 23,3) days and median 40 days. A follow-up 90 days was performed. (table 1).

Age	Day Intervals	Total Sessions	Adverse Effects
57	-	1	pain
46	62	2	pain
43	56	3	-
32	30	2	pain
60	-	1	pain
51	63	2	pain
43	40	3	pain
42	53	2	ecchymosis
67	94	3	-
39	40	2	pain + nodule
45	36	2	pain
53	-	1	pain
49	-	1	pain
71	43	2	pain + ecchymosis
69	50	3	pain
42	-	1	pain
65	49	2	-
80	32	3	ecchymosis
41	62	3	pain
28	121	2	-
62	30	2	pain + ecchymosis
55	31	5	pain + ecchymosis
44	43	2	-
71	28	2	nodule
58	28	3	ecchymosis
68	33	3	pain

Table 1: Age, interval between sessions, number of sessions and complications

DISCUSSION

PLLA (Sculptra®) is presented as freeze-dried preparation of 150 mg per vial and, according to consensus, the recommendation on your preparation is the addition of 7–8 mL sterile water for injection or bacteriostatic water slowly to the powder and hydrate at room temperature for ≥24 hours.

Before the facial injections, a final dilution of 9 mL is recommended, and may be achieved by the addition of 1–2 mL lidocaine. This dilution leads to easier injection, with reduced risk of complications for example needle blockage and incidence of papules and nodules. Warming PLLA to body temperature before injection could facilitate injection (8).

Common side effects, that usually resolve within 1 to 7 days, include localized swelling, tenderness, redness, itching, and bruising. Nodules and papules that occur several months after injection have also been reported (1,9,10,11). These undesired subcutaneous papules may result from inadequate reconstitution, variations in filling volumes, uneven product distribution in the suspension, imprecise or superficial injection technique, allergic or inflammatory host response or lack of post-treatment massage (12, 13, 14).

Appropriate product reconstitution, hydration, handling, and placement are central to avoiding adverse events. Despite the literature declare that a longer hydration times (up to 48 hours) have been shown to reduce the risk of nodule formation (15), our study demonstrated the safeness of injection with immediate reconstitution and a very low adverse events rate. In a total of 58 sessions, only 2 nodules were found. Important to quote that the nodules were diluted with saline injection. Pain and eccchymosis were also reported, however are not influenced by time reconstitution.

As a strength of this study, we can state that the dilution and injection techniques were standardized in all investigated patients to guarantee the consistency of the information. Also, 58 vials were applied by a single injector physician, decreasing the chances of technical variations. To track the adverse events consistently, a follow-up of 90 days past the last application was executed.

We can emphasize that our results are similar to the hydration period of 24 hours, with this PLLA dilution and application through a 22 gauge cannula, no clogging occurred.

Further well-designed human trials to validate its efficacy and to complement this technique treatment would be required.

Conclusion

Immediate PLLA reconstitution is a great asset for physicians, injections in account of being less laborious, less time-consuming and reducing product loss for the injector.

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