A 3-Tiered Approach for the Use of Calcium Hydroxylapatite Premixed With Lidocaine for Facial Applications

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The adoption of calcium hydroxylapatite (CaHA) into clinical practice has been both rapid and widespread since it was approved for facial use in 2006. As practitioners have become comfortable using CaHA as one of their therapeutic options, different applications, some of which are off label and some of which are approved by the US Food and Drug Administration, have appeared in the literature, including ones for areas of the upper face, midface, and lower face, as well as the dorsal hands. Concomitant with the growth of extended applications has been a shift in the way the product is delivered. Originally, CaHA injections were preceded by administration of anesthesia; however, in 2009, the US Food and Drug Administration cleared premixing of lidocaine with CaHA for direct injection into the dermis. In this article, I describe a 3-tiered approach to premixing different volumes of lidocaine with CaHA depending on both the depth of injection and the anatomical area(s) to be treated.

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In 2006, calcium hydroxylapatite (CaHA)(Radiesse, Merz Aesthetics, Inc) was approved for the treatment of moderate to severe facial wrinkles and folds such as nasolabial folds. As practitioners have become more familiar with CaHA, they have broadened their use of this dermal filler for treatment of marionette lines, the prejowl sulcus, oral commissures, and the posterior mandible,[1-3] as well as the temples and malar/submalar augmentation in the midface, which are off-label uses.[4-7] Applications now extend to nonfacial areas including the dorsal hands.[8-10] Calcium hydroxylapatite has become so widely used in the 6 years since its approval that dermal filler textbooks now routinely include chapters on CaHA.[11-14]

Well-developed protocols for delivery of CaHA and depth of injections have become widely available as CaHA has taken its place as a viable option for facial rejuvenation in multiple areas of the face, though some currently are off label. Although early instructions for the use of CaHA were limited to the mid dermis, practitioners have steadily expanded injection depths to the deep dermis and down to the supraperiosteal layer in some cases. This change in injection depth marks a shift in the perception of dermal fillers from a method of "chasing lines and wrinkles" to volumization or structurally lifting and contouring the face, especially in reference to CaHA and poly-L-lactic acid.[4,5,15-17] Hyaluronic acids (HAs) currently are not used as much for structural purposes as they are for remediation of fine

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lines and wrinkles (eg, rhytides around the mouth) or lip enhancement.

Perhaps the greatest change in protocol has been the delivery method for CaHA. A 2007 study by Busso and Applebaum[18] described the addition of lidocaine to CaHA through a mixing process rather than the established protocol of preanesthetization of the treatment site prior to injection. This breakthrough injection approach was quickly adopted by the aesthetic care community. Consequently, reports in the literature of the success associated with CaHA mixed with lidocaine followed in rapid succession. Although Busso and Applebaum[18] focused on treatment of the hand, other reports also have detailed the use of lidocaine mixed with CaHA in the nasolabial folds and cheeks.[4,9,10,19]

The protocol of lidocaine delivery continues to be refined. The original procedure as identified by Busso and Applebaum[18] called for 0.1 to 0.2 mL of lidocaine 2% to be homogeneously mixed with 1.3 mL of CaHA using a Luer-Lok device to connect the syringes. Since then, varying volumes and concentrations (ie, 1% vs 2%) of lidocaine to be added to the mixture have appeared in the literature. For example, Marmur et al[9] mixed 2.0 mL of lidocaine 2% with 1.3 mL of CaHA and deposited the mixture in volumes of 0.3 to 1.0 mL in 3 to 5 sites in the hand. Edelson[10] injected a bolus of 0.5 mL of lidocaine 2% in his study, and Bank[20] reported injection of a 2.0-mL bolus of lidocaine 1% without mixing, administered directly into the dorsum of the hand immediately prior to CaHA injection. A pivotal study regarding the treatment of nasolabial folds with lidocaine mixed with CaHA was part of a sheaf of documents submitted to the US Food and Drug Administration to support an application for approval of premixed lidocaine with CaHA.[21]

For many physicians, premixing lidocaine with CaHA is now a foregone conclusion; however, how much lidocaine should be mixed or injected prior to CaHA injection (as in the Bank[20] protocol) and what concentration of lidocaine should be added to a given amount of CaHA have yet to be well delineated. Practitioners have relied on their own clinical experiences to tailor their mixing processes. In this article, I present a systematic treatment protocol for the use of 3 different volumes of lidocaine premixed with CaHA, depending on the treatment areas.

DILUTION OF LIDOCAINE MIXED WITH CaHA BY TREATMENT AREA

Clinical observation has led to the discovery that a uniform volume of lidocaine-to-CaHA in panfacial applications is less useful than a tiered approach. With the tiered approach, the volume of lidocaine is titrated according to the area being treated; the volume of CaHA is not altered, except when less CaHA is needed in some areas of the face than in others, depending on the degree of severity of the aesthetic loss. Instead, the volume of mixed lidocaine is changed, though the initial concentration remains 1%. Although varying the amount of lidocaine that is mixed with CaHA currently is not an approved delivery method, results in clinical practice have been productive using a 3-tiered lidocaine dilution regimen. The Table shows the tiers, volumes, and areas to be injected.

Tier A: Supraperiosteal Applications

Certain treatment areas, such as the malar and submalar regions of the face, temples, and piriform aperture, lend themselves to deeper depth of injection than others. Calcium hydroxylapatite injections are beneficial in these anatomical applications because of the particularly high G′ (lifting ability) associated with CaHA.[15]

Three-tiered Dilution of Lidocaine 1% for Use With CaHA

Tier	Injected Volumes	Areas Treated	Injection Depth
A	0.3 mL of lidocaine 1%; 1.5 mL of CaHA	Malar and submalar regions, temples, piriform aperture	Supraperiosteal
B	0.5 mL of lidocaine 1%; 1.5 mL of CaHA	Oral commissures, prejowl sulcus	Postsubcutaneous-presupraperiosteal
C	1.0 mL of lidocaine 1%; 1.5 mL of CaHA	Cheeks, hands	Juncture of the dermis and the subcutaneous layer

Abbreviation: CaHA, calcium hydroxylapatite.

For areas requiring deeper depth of injection, 0.3 mL of lidocaine 1% is mixed with 1.5 mL of CaHA via a Luer-Lok device. Deposition may be achieved either through threading, fanning, or depot technique, usually using a 28-gauge, 0.75-in needle or a 27-gauge, 1-in blunt cannula. Standard pretreatment protocols of site cleansing and marking are observed as well as post-treatment protocols of massage by the clinician in the clinical setting but not by the patient post-discharge, coupled with ice application and other interventions to limit edema and ecchymosis. Typical results using the tier A dilution are shown in Figure 1. The patient in these photographs was treated with 3 syringes of 0.3 mL of lidocaine 1% mixed with 1.5 mL of CaHA.

Tier B: Postsubcutaneous-Presupraperiosteal Applications

Areas that call for greater depth of injection than the dermal/subcutaneous juncture but not deep enough for supraperiosteal placement, such as the oral commissures and prejowl sulcus, require a mixture of 0.5 mL of lidocaine 1% and 1.5 mL of CaHA. This volume of lidocaine also increases the spreadability of the CaHA but does not appear to compromise the product's ability to remain in place without migrating. Using a 27-gauge, 1-in blunt cannula is beneficial. Standard pretreatment and post-treatment protocols are observed. Typical results using the tier B dilution are shown in Figures 2 and 3. In these photographs, the patients were treated with 0.5 mL of lidocaine 1% mixed with 1.5 mL of CaHA.

Tier C: Subcutaneous Applications

Other treatment areas are better suited for injection at the juncture of the dermis and the subcutaneous level, such as the cheeks and hands. For treatment at this depth, 1.0 mL of lidocaine 1% mixed with 1.5 mL of CaHA works nicely when deposited either in a bolus (for example, in the hand) or in aliquots, delivered using threading, fanning, and cross-hatching techniques. The added volume of lidocaine reduces the extrusion force and allows more spreadability of the product where dissemination is advantageous. The most atraumatic method of delivering CaHA with 1.0 mL of lidocaine in these anatomical areas is with the use of a 25-gauge, 2-in blunt cannula. Standard pretreatment and post-treatment protocols are observed.

DILUTION OF LIDOCAINE WITH HA

Lidocaine dilution is not limited to CaHA only. In my practice, HA remains the treatment of choice for certain areas of the face, such as rhytides around the mouth and the tear trough. I currently achieve effective results when I combine HA (Restylane, Medicis Aesthetics, Inc) with lidocaine 1% in a 1:1 ratio for treatment of rhytides and the tear trough. Although the Tyndall effect

Figure 1. A 59-year-old patient before (A) and 3 weeks following supraperiosteal application of 0.3 mL of lidocaine 1% mixed with 1.5 mL of calcium hydroxylapatite (3 syringes)(B). Photographs courtesy of Z. Paul Lorenc, MD, and Miles Graivier, MD.

Figure 2. A 48-year-old patient before (A) and 3 weeks following postsubcutaneous-presupraperiosteal application of 0.5 mL of lidocaine 1% mixed with 1.5 mL of calcium hydroxylapatite (B). Photographs courtesy of Z. Paul Lorenc, MD.

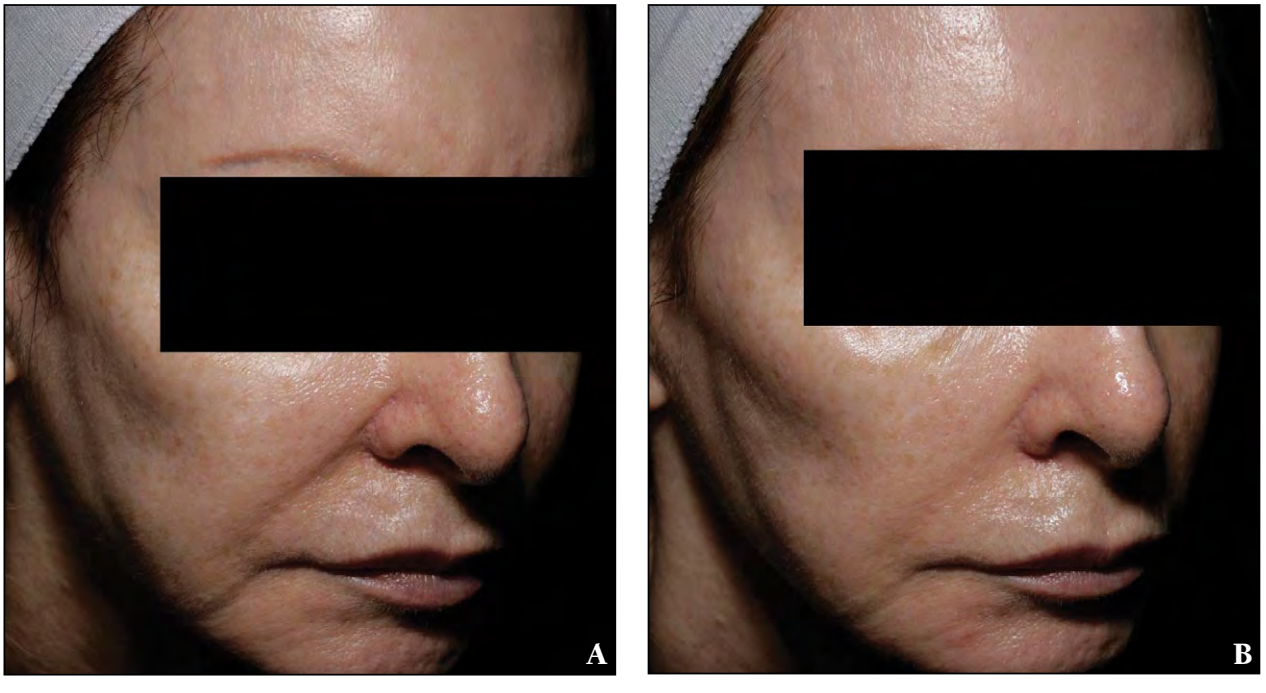

Figure 3. A 71-year-old patient before (A) and 8 weeks following application of 0.5 mL of lidocaine 1% mixed with 1.5 mL of calcium hydroxylapatite (B). Photographs courtesy of Z. Paul Lorenc, MD.

(bluish appearance following HA injection) sometimes is observed after treatment, I have yet to see it occur after injection with premixed lidocaine with Restylane, which may be because the insoluble HA particles within Restylane become more dispersed throughout the dermal or subdermal treatment area when mixed with lidocaine, which likely lowers the viscosity and the concentration of the product. In comparison, Belotero Balance (Merz Aesthetics, Inc), a new HA filler that was approved by the US Food and Drug Administration in November 2011 for moderate to severe facial wrinkles and folds, has produced no reported visible Tyndall

effect in clinical practice or during clinical trials, with or without the addition of lidocaine (Kuhne U, Imhof M, Grotelüschen M, et al; unpublished data; 2012).[22,23]

COMMENT

Any consideration of diluting lidocaine for use with dermal fillers elicits queries about the effect the altered dilution may or may not have on efficacy. In an in vitro study that mixed lidocaine 2% in varying volumes with CaHA, researchers found decreases in viscosity and extrusion force but not in other alterations in the physical properties of the CaHA.[24] A commentary by one of the original authors of the in vitro study suggested varying volumes according to treatment area and need,[25] which is similar to the protocol I have discussed here. In another study, longevity up to 6 months (the length of the study) was not affected by the addition of lidocaine to CaHA.[19] Further studies will continue to elucidate what effects, if any, premixed lidocaine has on CaHA as well as HA.

CONCLUSION

It has become clear that the addition of premixed lidocaine to CaHA has dramatically reduced the pretreatment protocol of administering local anesthesia without sacrificing patient comfort. The 3-tiered, zonal approach described in this article offers practitioners an opportunity to increase the versatility of CaHA, but perhaps HAs as well, depending on anatomical areas to be treated and the physicochemical properties of dermal fillers.

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