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INDUSTRY EDUCATION

Understanding Topical Anesthetics

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Topical anesthetics are widely used in cosmetic dermatology, with one recent survey conducted in 2021 and 2022 reporting that 97.5% of dermatology practices utilize topical anesthetics for a variety of procedures including laser and light-based procedures, ablative skin resurfacing, injectable fillers, and tissue tightening among others. While commercially available anesthetic combinations, such as EMLA (combination lidocaine 2.5%/prilocaine 2.5%) are used frequently, over half of the survey respondents reported using compounded anesthetics, with Benzocaine 20%, Lidocaine 6%, Tetracaine 4% being the most commonly used of the compounded options.[1] In this blog post we will address common questions and concerns regarding the use of topical anesthetics with regards to both safety and efficacy.

How are topical anesthetics used?

Topical anesthetic preparations prepared as creams or ointments are often applied 30-90 minutes prior to procedure. It is important to note that while surface layer numbing (about 1mm in depth) can occur in relatively shorter periods of time, it may take 60 minutes or so to achieve the deeper penetration (about 3mm) needed prior to certain procedures with a maximum depth of 5mm being achieved after approximately 120 minutes of application.[1,2,3] In fact, the commercially available lidocaine 2.5%/prilocaine 2.5% package insert recommends at least 1 hour of exposure for minor dermal procedures, and up to 2 hours of exposure for major dermal procedures.[4] Commercially available lidocaine 7%/tetracaine 7% cream recommends application for 20-30minutes prior to superficial dermatological procedures such as non-ablative laser facial resurfacing, but recommends application 60 minutes prior to procedure with for procedures such as laser assisted tattoo removal.[5] After this exposure time, remaining cream or ointment is typically wiped off with dry gauze before the

skin is cleaned with wet gauze prior to procedure. Some products have been applied under occlusion to help achieve a quicker onset of action, however, caution must be considered with this approach as there have been at least two instances of death reported to the FDA regarding the application of numbing creams for laser hair removal to the legs under occlusion.[3]

How much to apply?

By their very nature, compounded drugs are not FDA approved products and so they do not undergo the same real world patient testing with regards to safety and efficacy. Determining a correct amount to apply per a given surface area to get appropriate numbing effect, but avoid potential serious local adverse reactions or systemic adverse effects is a challenge. For some anesthetics, referencing the commercially available products can help when trying to determine reasonable maximum application amounts. For example, commercially available lidocaine 7%/tetracaine 7% cream recommends approximately 1mm thick of cream spread across the skin surface, and then offers a table on how much cream to apply that ranges from 1g for a 2 square inch area up to a maximum of 53g (equivalent to 3,710mg lidocaine, and 3710mg tetracaine) for a 62 square inch area. An approximately thickness of 1mm is recommended for covering a given area to be numbed. If you were applying a higher concentration lidocaine preparation, say, a 30% product, as seen in some studies for numbing prior to intense pulsed light treatment, that 3,710mg lidocaine equivalent would be found in approximately just 12g of your preparation.[5,6] Though direct comparison between compounded products and FDA approved products is difficult, using the commercially available products as a reference can help to guide decisions regarding maximum appropriate dose of a given product per surface area. It is important to note that these parameters are for single doses prior to procedure, and not for repeated topical dosing of anesthetics, for which a much lower maximum would be expected. It is also important to note that commercially available product recommended maximums for the above products are based on intact skin, much higher levels of anesthetic may be absorbed through inflamed, damaged, or otherwise compromised skin.[3]

Adverse Effects

Topical anesthetics may be associated with both local and systemic adverse effects. One survey of practices found 17.9% of respondents reported a history of adverse events including lidocaine toxicity, contact dermatitis, allergic reactions, and corneal abrasion.[1] Commercially available lidocaine 7%, tetracaine 7% cream notes common adverse effects to be more localized effects including erythema (47%), skin discoloration including blanching, ecchymosis, and purpura (16%), and edema (14%). Systemic adverse effects were noted in approximately 1% of patients and were mainly headache, vomiting, dizziness, and fever. Less commonly patients experienced syncope, hypotension, hyperventilation, and sweating among other serious adverse effects.[5] After topical application of anesthetic, an initial blanching may occur within 90 minutes or so of application, and may be followed by a rebound vasodilation that causes skin erythema or redness, it is important to counsel patients regarding the likelihood of cutaneous reactions as they are fairly common with topical anesthetic application.[3]

Anesthetics and Vasoconstrictors

Anesthetics are sometimes combined with vasoconstrictors. Vasoconstrictors such as epinephrine or phenylephrine slow mobilization of the anesthetic thereby prolonging the effect and reducing peak blood levels and systemic absorption.[7] Vasoconstrictors are more commonly added to anesthetics meant for application to mucous membranes (such as those used in dental procedures), or injected anesthetics for local use. Vasoconstrictors may enhance the risk of skin blanching combined with anesthetics, and studies on common combinations such as lidocaine/epinephrine/tetracaine gel or solution applied prior to minor procedure have noted skin blanching as a relatively common effect of treatment as have injectable combination products utilizing epinephrine.[8,9]

HCl Salts vs Base Forms

Anesthetics are often available in hydrochloride salt forms and in non-salt or “base” forms. The salt form chosen can impact how the API behaves and which types of vehicles it is compatible with. For example, while HCl salts are more soluble, the base forms, when mixed together, have a eutectic effect meaning that the melting point of both drugs is lowered when they are combined.[10] This can result in smooth incorporation into anhydrous systems without the need for a wetting agent, but can also impact the integrity of some cream bases, resulting in a thin or separated preparation. Though information specifically comparing formulations applied to intact skin using HCl vs base forms is not widely available, the lower melting point of eutectic mixtures may facilitate penetration through the skin.[10] Alternatively, the HCl salts have superior aqueous solubility as compared to the base forms of these anesthetics and for application to areas where penetration enhancer is generally not needed (such as mucous membranes in the case of anesthetics for dental use or nasally prior to an ENT procedure) the HCl salts offer the advantage of high solubility in aqueous vehicles often used for these routes of administration.

Formulation Notes

Anesthetics can be tough on thickening systems, below are some quick notes on our Fagron, Humco, and Letco branded bases and their compatibility with anesthetics:

Vehicle	Compatibility with HCl Salts	Compatibility with Base Forms	Notes
SaltStable LS Advanced	Yes	Yes*	If using base forms additional precautions must be taken to prevent separation and consistency issues such as the addition of SET gel or Sepineo P600
Salt Durable	Yes*	Yes	If using HCl salts, a thickener such as Sepineo P600 or SET gel is recommended to avoid separation overtime
Versatile	Yes	Yes*	*If using high concentrations of base forms (greater than BLT 20/6/4), additional thickener such as SET gel may be needed
Lipolayer	Yes*	Yes*	*Lipolayer may be used with base or HCl forms, however, SET gel or Sepineo P600 should be added
Occluvan	No	Yes	Occluvan works well with base forms of anesthetics, combined via eutectic technique and mixed directly into the base
Jelene	No	Yes	Jelene works well with base forms of anesthetics, combined via eutectic technique and mixed directly into the base
Plasticized Ointment Base	No	Yes	Plasticized Ointment Base works well with base forms of anesthetics, combined via eutectic technique and mixed directly into the base
SaltStable Lo	Yes	Yes	Concentrations higher than BLT 20/6/4 may need additional SET gel or Sepineo P600
Cream Concentrate	Yes*	No	Concentrations higher than BLT 20/6/4 with the HCl salts may need additional SET gel or Sepineo P600

Sources:

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