



An Evidence-Based Assessment of Local Anesthetic Allergy Risk and Clinical Safety

ENDURA-KT is a preservative-free combination of 0.2% tetracaine, 0.4% lidocaine and 1:250,000 epinephrine. Tetracaine, an ester local anesthetic, has been used in medicine since the 1930s and lidocaine an amide, has been in use since 1948. The combination of these drugs is not new. Since 1994, “LET” gel containing 0.5% tetracaine, 4% lidocaine, and 1:1000 epinephrine has been widely utilized to anesthetize lacerations in a pediatric ER setting prior to wound closure. LET is also a cGMP compounded product. Pliaglis Cream, an FDA-approved combination containing 7% lidocaine and 7% tetracaine, is a topical preparation designed to produce cutaneous anesthesia prior to dermatologic procedures.

It remains a common misperception that ester local anesthetics are more allergenic than amide local anesthetics. This most likely originates from one prospective study authored by Aldrete and Johnson published in 1970. The study involved injecting 60 anesthetized patients with various local anesthetics (esters and amides) and observing the development of skin responses (skin wheal). They defined a “positive skin reaction” as a wheal with erythema >1cm without any evidence of itching, edema, urticaria or anaphylaxis. The authors concluded that ester anesthetics have an allergenicity rate of up to 20%. It is now recognized that Aldrete and Johnson did not report a true ester allergy, but instead, the vasoactivity of local anesthetics. Ester anesthetics except for cocaine are known to be potent vasodilators. This is one of the reasons that epinephrine containing local anesthetics are most often used by dentists and dental specialists.

Nearly 47 years transpired before a follow-up prospective study evaluating the allergenicity of local anesthetics was published by Weinscheck et al. in 2017. This was a first of its kind, prospective double-blinded, placebo-controlled study comparing type 1 IgE mediated (immediate reaction) allergenicity of ester and amide local anesthetics. No type 1 allergic reactions were observed in any agent. Procaine and mepivacaine did produced larger areas of erythema than lidocaine or saline, consistent with vasodilation rather than allergy.

Bhole et al. in 2012 published an article titled: “IgE-mediated Allergy to Local Anesthetics: Separating Fact from Perception: A UK Perspective “. They identified and analyzed 23 case series involving 2978 patients with suspected local anesthesia allergy. Of these, only 29 patients had confirmed true IgE-mediated allergy yielding a **prevalence of .97%**. Amide anesthetics were the allergens in 75% of the reported cases which is in part influenced by greater use of amide anesthetics. This outcome is consistent with other studies Verrill (1998), Giovannitti et al. (1979), Schatz et al. (1986) who report <1% occurrence of True IgE-mediated allergy to all local anesthetics.

Despite updated research over the past several decades, the perception remains that ester local anesthetics are potent allergens, when the evidence clearly does not support this interpretation. Once administered, and immediately on contact with pseudocholinesterases, particularly butyrylcholinesterase, (present in plasma and on red blood cells), Tetracaine is immediately hydrolyzed into its principal degradation product, PABA. There is no direct immunologic proof that PABA can initiate a type 1 immediate reaction. However, PABA hypersensitivity can produce a T-cell mediated type IV contact dermatitis (delayed reaction). This generally requires prior sensitization using a PABA containing product (moisturizer, lotions, brightening cream). Patients reporting a history of “PABA allergy” almost invariably report their issue as skin reddening after topical application of PABA cosmetics or older sunscreen formulations. This represents a chemical irritation, not allergy.

SUMMARY:

True IgE-mediated allergy to local anesthetics (ester and amide) accounts for <1% of reported reactions. In the literature, esters account for the minority of these events.

The traditional teaching that esters have greater allergenicity than amide anesthetics is not supported in the literature, nor by any evidence in clinical practice with Endura-KT.

The traditional teaching that esters have greater allergenicity – attributed to their PABA metabolite is based on limited and flawed older data.

Commonly experienced non-IgE mediated reactions to local anesthetics include psychomotor responses (vasovagal), adverse reactions to other agents administered concomitantly, response to procedural trauma, and delayed hypersensitivity reaction.

Ventis Pharma Chief Scientific Officer Dr. Lou Stanfield CRNA, PhD shared that over 250,000 doses of Endura-KT have been administered without a single reported adverse outcome, documented allergic reaction or LAST (local anesthesia systemic toxicity).

Contraindications to the use of ENDURA-KT are documented pseudocholinesterase deficiency, skin test proven allergy to PABA, and skin test-proven allergy to ester anesthetics. A documented pseudocholinesterase deficiency is only a relative contraindication, since the principal effect of this deficiency is to possibly extend the duration of the local anesthetic action. The concentrations of the components in Endura-KT make the possibility of LAST remote even in this circumstance.

REFERENCES:

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