



Buffered lidocaine 1%/epinephrine 1:100,000 with sodium bicarbonate (sodium hydrogen carbonate) in a 3:1 ratio is less painful than a 9:1 ratio: A double-blind, randomized, placebo-controlled, crossover trial

Alexandra Vent, MD,^a Christian Surber, Dr phil nat,^a Nicole Tracy Graf Johansen, Dr phil nat,^b Verena Figueiredo, MSc,^c Georg Schönbächler, Dr sc nat,^d Laurence Imhof, MD,^a Caroline Buset, MD,^a and Jürg Hafner, MD^a
Zurich, Winterthur, and Schlieren, Switzerland

Background: Neutralizing (buffering) lidocaine 1%/epinephrine 1:100,000 solution (Lido/Epi) with sodium hydrogen carbonate (NaHCO_3) (also called sodium bicarbonate) is widely used to reduce burning sensations during infiltration of Lido/Epi. Optimal mixing ratios have not been systematically investigated.

Objectives: To determine whether a Lido/Epi: NaHCO_3 mixing ratio of 3:1 (investigational medicinal product 1) causes less pain during infiltration than a mixing ratio of 9:1 (IMP2) or unbuffered Lido/Epi (IMP3).

Methods: Double-blind, randomized, placebo-controlled, crossover trial ($n = 2 \times 24$) with 4 investigational medicinal products (IMP1-4).

Results: The 3:1 mixing ratio was significantly less painful than the 9:1 ratio ($P = .044$). Unbuffered Lido/Epi was more painful than the buffered Lido/Epi ($P = .001$ vs IMP1; $P = .033$ vs IMP2). IMP4 (NaCl 0.9% [placebo]) was more painful than any of the anesthetic solutions ($P = .001$ vs IMP1; $P = .001$ vs IMP2; $P = .016$ vs IMP3). In all cases, the anesthesia was effective for at least 3 hours.

Limitations: Results of this trial cannot be generalized to other local anesthetics such as prilocaine, bupivacaine, or ropivacaine, which precipitate with NaHCO_3 admixtures.

Conclusions: Lido/Epi- NaHCO_3 mixtures effectively reduce burning pain during infiltration. The 3:1 mixing ratio is significantly less painful than the 9:1 ratio. Reported findings are of high practical relevance, given the extensive use of local anesthesia today. (J Am Acad Dermatol 2020;83:159-65.)

Key words: 3:1; admixture; bicarbonate; burning sensation; controlled; double-blind; epinephrine; lidocaine; local anesthesia; placebo; randomized; ratio; sodium hydrogen carbonate; trial; unbuffered.

Lidocaine, an anesthetic of the amide class, is one of the most commonly used local anesthetics. It is available in a variety of concentrations (0.5%-2.5%). A concentration of 1%,

with or without epinephrine, is the most commonly used. Epinephrine is added at a concentration of 1:100,000; it causes vasoconstriction, resulting in less bleeding, longer action, and less systemic toxicity.¹

From the Department of Dermatology, University Hospital of Zurich^a; Graf Biostatistics, Winterthur^b; Hospital Pharmacy of the University Hospital Zurich, Schlieren^c; and Institute of Psychology, University of Zurich.^d

Funding sources: Supported by the JH Rahn Foundation and Bruno Bloch Foundation.

Conflicts of interest: None disclosed.

IRB approval status: This study has been approved by the local ethical committee (KEK-ZH, Nr2015-0531) and by Swissmedic.

Accepted for publication September 12, 2019.

Correspondence to: Jürg Hafner, MD, Department of Dermatology, Gloriastrasse 31, CH-8091 University Hospital of Zurich, Switzerland. E-mail: juerg.hafner@usz.ch.

Published online January 17, 2020.

0190-9622/\$36.00

© 2020 by the American Academy of Dermatology, Inc.

<https://doi.org/10.1016/j.jaad.2019.09.088>