How acidic is the lidocaine we are injecting, and how much bicarbonate should we add?

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BACKGROUND: The infiltration of local anesthetics can be painful, which is likely due, in part, to their acidity. In spite of a Cochrane study that recommended neutralizing lidocaine with bicarbonate to decrease the pain of injection, not many surgeons have adopted the practice, and there are many 'recipes' for how much bicarbonate one should add.
OBJECTIVE: To determine the acidity of lidocaine and the correct ratio of bicarbonate that should be added to neutralize lidocaine to achieve body pH.
METHODS: Fifty samples each of commonly used anesthetics (lidocaine 1% and 2%, with and without epinephrine 1:100,000) were obtained and tested for pH. Data were also analyzed according to whether the vials had been previously opened. Ten additional samples of lidocaine 1% with 1:100,000 epinephrine were titrated against sodium bicarbonate 8.4% and tested for pH and the presence of precipitate.
RESULTS: A solution of 1% lidocaine with 1:100,000 epinephrine had a mean (± SD) pH of 4.24±0.42, and 2% lidocaine with 1:100,000 epinephrine had a mean pH of 3.93±0.43. Plain 1% lidocaine had a pH of 6.09±0.16, and plain 2% lidocaine had a pH of 6.00±0.27. Epinephrine-containing solutions were more acidic when they had been previously opened. One per cent lidocaine with epinephrine required 8.4% sodium bicarbonate at a ratio of 1.1 mL:10 mL to 1.8 mL:10 mL to achieve the target tissue pH of 7.38 to 7.62.
CONCLUSION: Lidocaine with epinephrine was approximately 1000 times more acidic than subcutaneous tissue. The addition of bicarbonate to the local anesthetic solution is simple to perform and is inexpensive. The proper volume ratio of 8.4% sodium bicarbonate to 1% lidocaine with 1:100,000 epinephrine is approximately 1 mL:10 mL. Surgeons should be more aware of the simplicity and value of buffering with bicarbonate to decrease the pain of injection.

Key Words: *Anesthetics; Epinephrine; Lidocaine; Local; Pain of injection; pH*

Quelle est l'acidité de la lidocaïne en injection et combien de bicarbonate devrait-on y ajouter?

HISTORIQUE : L'infiltration d'anesthésiques locaux peut être douloureuse, ce qui est probablement causé, en partie, par leur acidité. Même si une étude antérieure a recommandé de neutraliser la lidocaïne avec du bicarbonate pour atténuer la douleur de l'injection, peu de chirurgiens ont adopté cette pratique, et il existe de nombreuses « recettes » de la quantité de bicarbonate à ajouter.
OBJECTIF : Déterminer l'acidité de la lidocaïne et le bon ratio de bicarbonate à y ajouter pour la neutraliser et parvenir au pH corporel.
MÉTHODOLOGIE : Les chercheurs ont obtenu 50 échantillons de chacun des anesthésiques couramment utilisés (lidocaïne 1% et 2%, avec et sans dilution d'adrénaline 1:100 000) et en ont vérifié le pH. Ils ont également analysé les données pour vérifier si les fioles avaient été ouvertes au préalable. Ils ont titré dix échantillons supplémentaires de lidocaïne1% contenant de l'adrénaline 1:100 000 à l'aide de bicarbonate de sodium 8,4 %, puis ont vérifié le pH et la présence de précipité.
RÉSULTATS : Une dilution 1:100 000 de lidocaïne 1 % contenant de l'adrénaline avait un pH moyen (±ÉT) de 4,24±0,42, et la lidocaïne 2 % contenant de l'adrénaline, un pH de 3,93±0,43. La lidocaïne 1 % seule avait un pH de 6,09±0,16, et la lidocaïne 2 % seule, un pH de 6,00±0,27. Les solutions contenant de l'adrénaline étaient plus acides lorsqu'elles avaient été ouvertes au préalable. De la lidocaïne 1 % contenant de l'adrénaline devait contenir 8,4 % de bicarbonate de sodium à une dilution de 1,1:10 à 1,8:10 pour parvenir au pH tissulaire ciblé de 7,38 à 7,62.
CONCLUSION : La lidocaïne contenant de l'adrénaline était environ 1 000 fois plus acide que les tissus sous-cutanés. Il est simple et peu coûteux d'ajouter du bicarbonate à une solution anesthésique locale. La bonne proportion entre le volume de bicarbonate de sodium 8,4 % et la lidocaïne 1 % accompagnée d'adrénaline 1:100 000 est d'environ 1:10. Les chirurgiens devraient connaître la simplicité et la valeur d'utiliser une solution tampon de bicarbonate pour atténuer la douleur de l'injection.

The infiltration of local anesthetics can be painful, and some of this pain may be attributed to the acidity of the anesthetic solution (1). In spite of the fact that a Cochrane study recommended buffering lidocaine with bicarbonate to decrease the pain of injection (2), the use of bicarbonate with lidocaine has only been adopted by a minority of practicing surgeons.

One of the possible reasons that surgeons do not use buffered lidocaine is that most hospital pharmacies only premix bicarbonate and lidocaine without epinephrine, which is not as useful as buffered solutions containing epinephrine. In addition, there is a lack of knowledge about how exactly one is required to mix bicarbonate with the local anesthetic and what ratio of the mixture is ideal.

The present study aimed to measure the pH of commonly used lidocaine-containing anesthetic agents available at our institutions and to validate the proper concentration of bicarbonate that should be added to lidocaine with epinephrine to neutralize its pH. The present article also aims to generate awareness among surgeons about how simple and inexpensive it is to mix bicarbonate with lidocaine to eliminate the acidity-related pain of local anesthetic injection.

METHODS

Commercially available solutions of 1% and 2% lidocaine, with and without epinephrine 1:100,000 were obtained (AstraZeneca Inc, Canada; Alveda Pharma, Canada). These were collected from various settings throughout a tertiary care institution (Dalhousie University, Halifax, Nova Scotia; Saint John, New Brunswick) to capture the possible effects of prolonged storage, previously opened bottles or improper storage conditions, to simulate true clinical use conditions. A total of 200 samples were collected (50 samples of each solution) from a variety of lots and ranging in expiration dates. Note was made of whether each multiuse vial was factory sealed or had been opened previously. The pH of each sample was measured using a temperature-compensating pH meter (Model 98128, Hanna Instruments, Canada) with a resolution of 0.01 and a mean (± SD) accuracy ±0.05.

To determine the proper concentration of bicarbonate for neutralization, additional samples of 1% lidocaine with 1:100,000 epinephrine were obtained, along with samples of 8.4% sodium bicarbonate (Hospira, Canada). Ten samples of each were collected. Aliquots of sodium bicarbonate (0.5 mL) were added to 20 mL of lidocaine and

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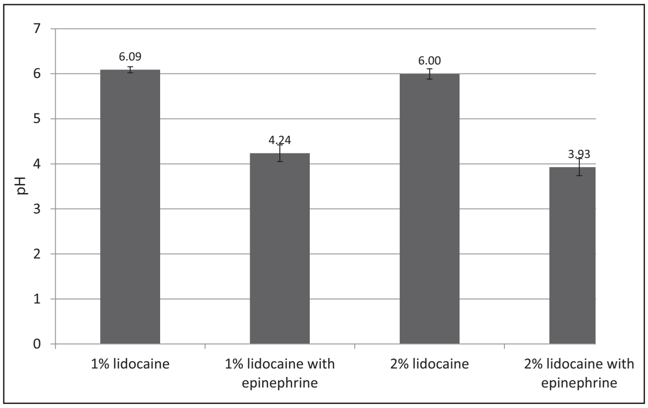

Figure 1) *pH of lidocaine 1% and 2%, with and without 1:100,000 epinephrine. Error bars represent 95% CIs*

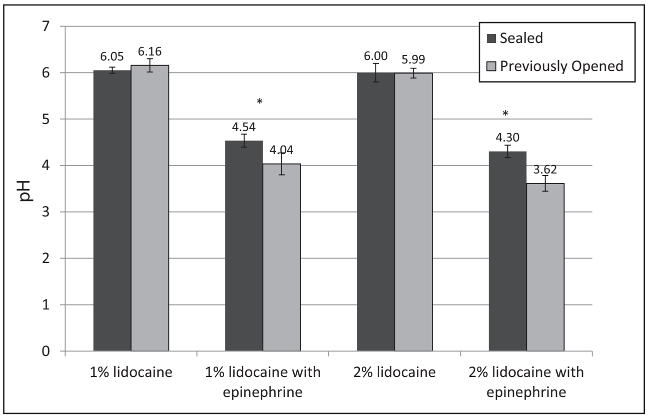

Figure 2) *pH of factory sealed versus previously opened multiuse vials of lidocaine. Error bars represent 95% CIs*

pH was recorded after mixing. After each addition, samples were analyzed against light and dark backgrounds to check for the presence of precipitate.

Statistical analysis was performed using Microsoft Excel (Microsoft Corporation, USA). Student's *t* tests were used to compare means. Statistical significance was set at $P<0.05$. Results are presented as mean ± SD.

RESULTS

A solution of 1% lidocaine with 1:100,000 epinephrine had a mean pH of 4.24±0.42, and 2% lidocaine with 1:100,000 epinephrine had a mean pH of 3.93±0.43. Plain 1% lidocaine had a mean pH of 6.09±0.16, and plain 2% lidocaine had a mean pH of 6.00±0.27 (Figure 1). The epinephrine-containing solutions were more acidic than their plain counterparts by an absolute magnitude of 1.85 for 1% lidocaine and 2.07 for 2% lidocaine ($P<0.05$). There was no significant difference in the pH between the 1% and 2% solutions.

Comparison of factory-sealed multidose vials with those that had been previously opened revealed no difference in pH in plain 1% solutions (6.05±0.12 versus 6.16±0.19, respectively) nor plain 2% solutions (6.00±0.34 versus 5.99±0.16) ($P>0.05$) (Figure 2). Previously opened epinephrine-containing 1% lidocaine solutions were more acidic than those that were factory sealed (pH 4.04±0.42 versus pH 4.54±0.20, respectively [difference = 0.50]) as were epinephrine-containing 2% solutions (pH 3.62±0.29 versus pH 4.30±0.21 [difference = 0.69]) ($P<0.05$).

Figure 3 represents a titration curve of 1% lidocaine with 1:100,000 epinephrine versus 8.4% sodium bicarbonate. A ratio of 1.1 mL:10 mL achieved a mean pH of 7.38±0.12. A dilution of 1.8 mL:10 mL achieved a mean pH of 7.62±0.12. No precipitate was identified in any samples in concentrations up to 2 mL:10 mL, which produced a mean pH of 7.66. SDs were low across the titration curve once sodium bicarbonate was introduced (<0.13 at all data points).

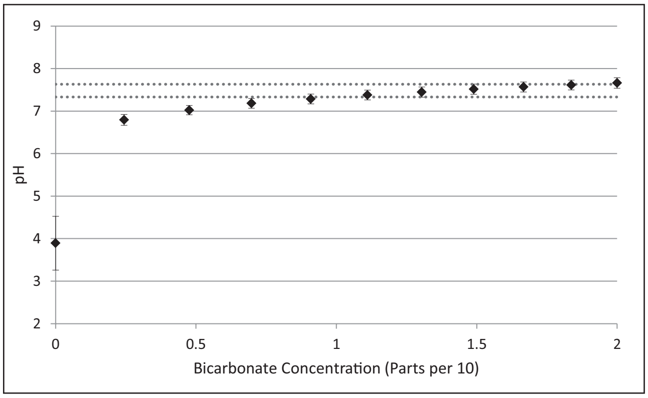

Figure 3) *Titration curve of 8.4% sodium bicarbonate against 1% lidocaine with 1:100,000 epinephrine. Dotted lines represent tissue pH (7.38 to 7.62) (3). Error bars represent 95% CIs*

DISCUSSION

One per cent lidocaine with 1:100,000 epinephrine at our institution was found to be a factor of 1000 more acidic than subcutaneous tissue, the latter having a pH of approximately 7.3 to 7.6 (3). Epinephrine-containing solutions (approximate pH 4) were markedly more acidic than lidocaine without epinephrine (approximate pH 6). We also verified that the proper volume ratio of 8.4% bicarbonate to 1% lidocaine with 1:100,000 epinephrine is approximately 1 mL:10 mL to neutralize the pH to 7.4, as was previously suggested by Momsen et al (4).

In spite of the fact that a Cochrane study recommended buffering lidocaine with bicarbonate to decrease the pain of injection and that buffering has been found to be useful in carpal tunnel surgery, the use of bicarbonate-buffered lidocaine with epinephrine has only been adopted by a minority of practicing surgeons (1,5).

We found that the ratio of lidocaine and bicarbonate required to achieve a tissue pH of 7.3 to 7.6 was between 1.1 mL:10 mL and 1.8 mL:10 mL, although a ratio of 1 mL:10 mL produced nearly the same pH (3). Our data indicate that there is no risk of precipitate forming at these concentrations. For practical purposes, we recommend mixing 10 mL of 1% lidocaine with 1:100,000 epinephrine with 1 mL of 8.4% sodium bicarbonate solution. Clarifying the proper mixture ratio is important because there have been many mixtures of different concentrations of lidocaine and bicarbonate advocated in the literature. For instance, the recent Cochrane review included studies that reported ratios of sodium bicarbonate ranging from 1 mL:2 mL to 1 mL:33 mL (1,6,7).

There are two ways by which surgeons can obtain buffered lidocaine. The first, and most useful, is that surgeons buffer their own lidocaine with a solution such as 8.4% sodium bicarbonate (Figure 4), which is readily available and costs less than CAD$5 per bottle. It is easily mixed just before injection and can be mixed in a syringe or in the bottle of lidocaine. It is a fortunate coincidence that a 10 mL syringe holds 11 mL of liquid, and that a 20 mL syringe holds 22 mL of liquid. In practice, we usually draw 1 mL of bicarbonate and then 10 mL of 1% lidocaine with 1:100,000 epinephrine into a 10 mL syringe so the two solutions are mixed to a total of 11 mL of volume in the 10 mL syringe, resulting in a ratio of 1 mL:10 mL (Figure 5).

The second way to obtain buffered lidocaine is to have the hospital pharmacy buffer it. However, in our hospitals, the pharmacy only prepares buffered 1% lidocaine solution without epinephrine. No prebuffered epinephrine-containing solutions are available. From our data, it is clear that the potential benefits of neutralizing a plain solution would be less than the benefits of neutralizing an epinephrine-containing solution based on the approximately 70-fold increased acidity of the latter (pH 4.24 versus pH 6.09 for 1% solutions).

Figure 4) *Bicarbonate 8.4% is readily available and costs less than CAD$5 per bottle. It has no preservative, and is therefore usually discarded at the end of the day*

Furthermore, buffered lidocaine without epinephrine is not very useful in our practice. Since the death of the epinephrine myth and the validation of the phentolamine antidote to epinephrine vasoconstriction, we seldom use lidocaine without epinephrine in finger and hand surgery, or in any other part of the body (8-11). The epinephrine increases the duration of lidocaine's anesthetic effect and decreases surgical bleeding (12).

Figure 5) *Syringes with 1 mL 8.4% bicarbonate (top) and with 1 mL sodium bicarbonate and 10 additional mL 1% lidocaine with 1:100,000 epinephrine for a total of 11 mL of solution (bottom)*

It is interesting to note that much of the existing literature regarding the buffering of lidocaine to reduce pain involves lidocaine solutions without epinephrine (13-19). The addition of epinephrine and the necessary preservatives decreases the pH of the solution and, therefore, increases the potential beneficial effect of buffering (13,14, 20,21). The literature should be viewed with this in mind, and clinical application and future research tailored accordingly.

SUMMARY

Lidocaine with epinephrine is very acidic compared with subcutaneous tissue. The addition of 8.4% bicarbonate at a volume ratio of 1 mL:10 mL neutralizes the acidity of 1% lidocaine with 1:100,000 epinephrine. Neutralizing the pH of lidocaine has been previously shown to decrease the pain of injection. It is simple, inexpensive and can easily be performed by surgeons shortly before local anesthetic injection.

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