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Prilocaine versus Plain or Buffered Lidocaine for Local Anesthesia in Laceration Repair: Randomized Double-blind Comparison

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Aim. To compare the effectiveness of 2% prilocaine plain solution, 1% lidocaine hydrochloride, and 1% buffered lidocaine in local anesthesia and pain reduction during injection in laceration repair.

Methods. A double-blind randomized prospective comparison study included 183 consecutive eligible adult patients with simple lacerations, admitted to the emergency department between January 2001 and June 2002. Each of the three groups of patients received different local anesthetic before laceration suturing (1% lidocaine, 2% prilocaine, or buffered 1% lidocaine). The patients were asked to assess the pain intensity on a 0-100 numerical rating scale at the site of needle entry into the skin (P1), immediately after the completion of injection (P2), and after the first puncture of the suturing needle (P3). The differences among the three patient groups were tested with one-way analysis of variance and chi-square test.

Results. The three groups of 61 patients each (one patient declined from prilocaine group) did not significantly differ in mean P1 scores (29.1±20.9 in the prilocaine, 32.2±22.9 in the lidocaine, and 33.2±21.7 in the buffered lidocaine group; $p = 0.56$). Mean P2 scores were highest in the prilocaine group (24.0±16.0), followed by lidocaine (20.9±14.9) and buffered lidocaine (16.1±11.3) groups ($p = 0.007$). Mean P3 score was significantly lower in the lidocaine group (13.4±11.3) then in the prilocaine (18.4±13.1) and buffered lidocaine (20.4±16.2) groups ($p = 0.014$). The number of patients who required additional anesthetic administration in each group was not significantly different ($p = 0.09$).

Conclusion. Injection of 1% lidocaine was associated with lower pain ratings on suturing needle puncture than with 2% prilocaine or buffered 1% lidocaine.

Key words: *anesthesia, local; anesthetics, local; prilocaine; lidocaine; lacerations; wound healing*

Lacerations account for a significant number of emergency department visits, and their treatment should involve minimum pain and discomfort. Local anesthetic agents used in infiltrative anesthesia are known to block sodium influx into neural cells, thereby inhibiting sensory transmission (1). Lidocaine hydrochloride and prilocaine are two of the most commonly used agents. They are amid-based compounds, metabolized in the liver. Lidocaine can be used in solutions ranging from 0.5 to 4%, but most studies report the use of 1% lidocaine (2-10).

Buffered lidocaine usually consists of 1 unit of 8.4% sodium bicarbonate mixed with 9 units of 1% lidocaine (3). The reported mean duration of anesthetic effect of 1% buffered lidocaine is 30 minutes vs 33 minutes of plain lidocaine (2). Prilocaine, on the other hand, is a local anesthetic that is pharmacologically similar to 1% lidocaine. It has a moderate duration (11) and in 4%-concentration (without a vasoconstrictor) maintains analgesia for almost 30 minutes (12). Currently, it is used most often for infiltration anesthesia in dentistry. The agent is used in the concentrations between 1% and 4% in various experimental and clinical pharmaceutical forms and applications (13-18). Some studies demonstrated that prilocaine was an alternative agent to 1% lidocaine and 1% buffered lidocaine, with a comparable anesthetic effect in laceration repair (8,9).

Although very commonly used, it is not exactly known which of thesee agents provides more convenient anesthesia locally while inflicting lesser pain itself. Few studies directly compared anesthetic effectiveness of local anesthetics and injection pain (10).

Slow injection, warming, and buffering are some of the effective strategies to reduce pain invoked by the local anesthetic injection (3,4,6,7,10,19,20). Local anesthetic agents are weak bases, whose shelf life is extended by formulations with pH 4-6. Buffering of lidocaine was shown to decrease the pain caused by lidocaine injection (3,4,7,8,20). This effect is thought to result from the alkalinization of the local anesthetic agent. With the utilization of this technique, the pain

of infiltration with buffered lidocaine is significantly reduced – 4.5-fold compared with plain lidocaine, with no impairment in the efficacy of the local anesthetic (10). Buffering and warming lidocaine have synergistic effects on alleviating injection pain (7,21). A disadvantage of buffering the agent is decreasing the concentration of the active agent and therefore shortening the effective shelf life down to approximately seven days (2). The shelf life of the plain 1% lidocaine is more than two weeks (3).

The first aim of our study was to compare the magnitude of pain following the infiltration of three agents: prilocaine, plain lidocaine, and buffered lidocaine in local anesthesia for skin lacerations repair. The second objective was to compare and evaluate the effectiveness of analgesia caused by these three agents.

Participants and Methods

Participants

The randomized double-blind comparison trial included all consecutive eligible adult patients referred to our emergency department between January 2001 and June 2002. To be included in the study, the participants had to have simple, uncomplicated skin lacerations ≤5 cm in length and not deeper than 0.5 cm. All eligible patients (n = 234; Fig. 1) received detailed information on

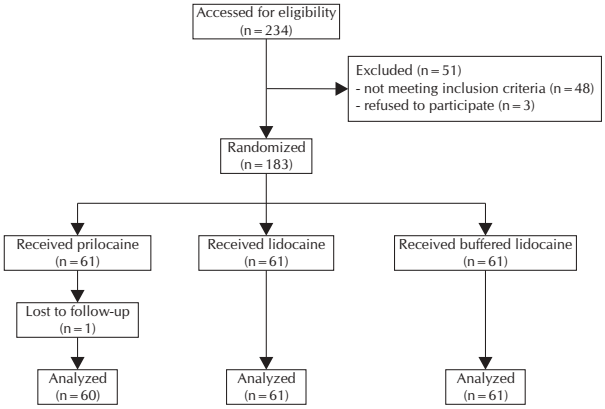

Figure 1. The flow of the patients through the study.

the study and were asked to provide a written informed consent before entering the study. Exclusion criteria were end-organ involvement, history of allergy to local anesthetic agents, altered mental status as demonstrated by Glasgow Coma Scale score less than 15, indication of procedural sedation and analgesia, suspected pregnancy, contaminated or complicated wounds requiring debridement or involving tissues perfused by end arterioles, wounds requiring use of nerve block, history of alcohol and drug abuse, and distracting painful injury. The subjects experiencing allergic reactions during the procedure were also excluded (Fig. 1). This left 183 adults to be enrolled in the study and randomized to one of three groups receiving either 2% prilocaine, or 1% lidocaine, or 1% buffered lidocaine, respectively. Each group consisted of 61 patients. The mean age of patients was 30.9±11.4 years (range, 18-73) and 121 (66.4%) patients were men.

The specific objectives of the study included comparison of the degree of pain caused by local infiltration of the anesthetic drugs and evaluation of analgesia efficacy upon completion of the first puncture. Therefore, all patients included in the study were instructed before the procedure how to use the numerical rating scale to assess the injection pain (22-24).

Residents, faculty, and attending physicians were introduced to the study protocol, scoring system by use of numerical rating scale, and potential adverse effects of the anesthetics before the commencement of the study.

Randomization and Blinding

The table of randomly generated numbers was used to allocate the participants into one of the three groups: 2% prilocaine (Citanest® 2%, Eczacibasi, Istanbul, Turkey), 1% lidocaine (Aritmal®, Haver, Istanbul, Turkey), and 1% buffered lidocaine (with sodium bicarbonate; Drogsan®, Istanbul, Turkey). All agents were inexpensive (1-2 US$ per use). The solutions were prepared on a daily basis and not more than three at a time. Five-mL prefilled syringes with 27 gauge needles were used to prepare the agent. All agents were clear solutions, kept at room temperature. The study was double-blind. The syringes were numbered by a researcher not directly involved in drug administration. Nobody but this researcher was aware of the content of any numbered syringe, which ensured allocation concealment. Buffered lidocaine 1% consisted of 1 unit of 8.4% sodium bicarbonate mixed with 9 units of 1% lidocaine.

Study Algorithm

The length and depth of the cut was determined with a sterile ruler in all patients. The eligible patients were recruited after providing written informed consent. Regular measures in the wound care and trauma resuscitation unit were not changed for study purposes. The wound was first irrigated with normal saline, and the area around the wound swabbed gently with 10% povidone iodide and rinsed with sponges.

After the application of anesthetic with 27 gauge needles, 5 minutes were allowed for the injections to become effective before suturing. The injection technique was standardized according to the modified criteria by Colaric et al (4): 1) the needle was inserted to the level of the superficial dermis in a single continuous motion; 2) adequate time was allowed for the pain from the needle puncture to subside before injecting the anesthetic agent; 3) the agent was injected at a constant rate over 10 seconds (0.1 mL/s); 4) all injections were given by educated and blinded operators (emergency physicians); and 5) the operators were not allowed to give more than 40 injections without a rest, to prevent variation in the technique caused by fatigue.

Five minutes after injection, the sensory status was checked with a needle point. Another half dose of the same agent was injected if required. Standard 1% lidocaine injection was used for further anesthesia in case of inadequate antinociception at 10 minutes. Suturing started as soon as the lacerated area became painless. The first suture was placed at the middle of the laceration.

The outcome measures in the current study were the degree of pain inflicted by the injection of the anesthetic agents, and the magnitude of pain following the agents in response to puncture of the suturing needle. The operator asked the patient to determine the degree of pain invoked by the injection or infiltration using the numerated rating scale. The patients ranked the pain at three points: immediately after the first puncture of the needle (P1), immediately after completion of infiltration (P2), and after the completion of the first puncture of suturing needle (P3). Mean P2 values represented the pain caused by the injection of a given agent, whereas mean P3 values represented the efficacy of local anesthesia associated with the agent.

Pain scores between 0 (no pain or the least pain felt) and 100 (the worst pain ever experienced) were noted on a numerated rating scale.

Statistical Analysis

To calculate the sample size needed in each group with 90% power, we estimated the standard deviation to be 25, the mean numerated rating scale for 1% lidocaine to be 50, and alpha value 0.05. Fifteen percent difference in the pain resulting from both suturing and local anesthetic infiltration was considered to be clinically significant, ie, lower than that reported elsewhere (25,26). This required the sample size of at least 58 subjects in each group.

Baseline values of age, cut length, drug volume, mean pain scores (P1, P2, and P3) at 100-point numerated rating scale for each group, and requests for extra anesthetic were statistically an-

alyzed by use of the SPSS statistical package for Windows, version 11.0 (SPSS Inc, Chicago, IL, USA). One-way analysis of variance (ANOVA) was performed to compare baseline values. Significant differences among the three patient groups in the mean level of injection pain were assessed by ANOVA, with post-hoc Tukey test; significance level was set at 0.05. Categorical variables such as receiving additional anesthetic were analyzed with chi-squared test. Alpha value was set at 0.05 with 95% confidence intervals.

Results

Only a single patient from the prilocaine group left the study before the completion of pain ratings and was excluded from the data analysis. There were no statistically significant differences between the three groups with respect to sex (women-to-men ratio was 0.46 in prilocaine group, 0.48 in lidocaine group, and 0.56 in buffered lidocaine group; Pearson's chi-square, p = 0.78), age, and duration of the procedure (mean ± SD, 17.0 ± 5.3 min; Table 1). None of the subjects had taken analgesic medications within 12 h before the procedure.

Table 1. Relevant characteristics of the study participants receiving different local anesthetics before the laceration repair

	Characteristics (mean ± SD)		
Anesthetic group	age (years)	cut length (cm)	anesthetic volume (mL)
Prilocaine (n = 60)	32.6 ± 10.2	3.6 ± 1.3	3.5 ± 1.6
Lidocaine (n = 61)	29.3 ± 12.3	3.9 ± 1.4	3.6 ± 1.7
Buffered lidocaine (n = 61)	30.7 ± 12.8	3.8 ± 1.4	3.4 ± 1.5
p*	0.31	0.16	0.62

*ANOVA.

The distribution of skin lacerations in the sample was as follows: 37 (20.3%) on the face and the neck; 21 (11.6%) on the scalp; 54 (29.6%) on the upper extremities, and 46 (25.3%) on the lower extremities. The remaining 24 (13.2%) lacerations were in other body regions. The mean length of the lacerations was 3.7 ± 1.5 cm (range, 1.2-5.0). There were no significant differences between the three treatment groups in the length of lacerations (p = 0.74; Table 1). Mean volume of the agents administered to each patient was 3.5 ± 0.9 mL. The difference between the drug volumes administered to the patients was not significant (p = 0.82).

There were 7 (11.6%), 2 (3.2%), and 8 (13.1%) patients receiving additional local anesthetic in prilocaine, lidocaine, and buffered lidocaine groups, respectively (chi-square test, p = 0.09).

None of the participants experienced any adverse events, e.g., allergic reactions, seizures, or numbness.

For the self-rated numerical rating scale, the mean pain scores and 95% confidence intervals (CI) were calculated (Table 2). Total mean scores elicited at three points were 31.5±21.8 for P1, 20.3±14.5 for P2, and 17.4±13.9 for P3. The differences between the means were statistically significant (mean P1 vs mean P2, p < 0.001; mean P1 vs mean P3, p < 0.001; and mean P2 vs mean P3, p = 0.044).

The differences among groups in the means obtained at three predetermined points were compared with ANOVA (Table 2). Mean P1 did not significantly differ among the groups (ANOVA, p = 0.56). On the other hand, mean P2 was the highest for prilocaine, followed by lidocaine and buffered lidocaine (Table 2). In other words, patients receiving prilocaine rated their pain on the injection site of the anesthetic agent higher than the patients who had received buffered lidocaine or plain lidocaine.

Table 2. Degree of pain elicited by anesthetic injection as assessed by numerical rating scale scores*

	Degree of pain at each point (mean ± SD)		
Anesthetic group	P1	P2	P3
prilocaine (n = 60)	29.1 ± 20.9	24.0 ± 16.0†	18.4 ± 13.1
1% lidocaine (n = 61)	32.2 ± 22.9	20.9 ± 14.9	13.4 ± 11.3†
buffered 1% lidocaine (n = 61)	33.2 ± 21.7	16.1 ± 11.3	20.4 ± 16.2
Total	31.5 ± 21.8	20.3 ± 14.5	17.4 ± 13.9

*On rating scale, 0 denoted no pain and 100 denoted the worst pain ever experienced; P1 – degree of pain immediately after the first puncture of the needle; P2 – degree of pain immediately after completion of infiltration; P3 – degree of paint after the completion of the first puncture of suturing needle.
†Significantly different from other groups: p = 0.007 for prilocaine in P2, and p = 0.014 for lidocaine in P3 (one-way ANOVA, with post-hoc comparison Tukey's).

The mean P3 in 1% lidocaine group was significantly lower than in the other groups (p = 0.014, ANOVA with post hoc Tukey test), ie, patients receiving 1% lidocaine reported lower degrees of pain on the first puncture of suturing needle than the other patients.

Discussion

We compared three common local anesthetics for both the pain associated with the injection of the agent itself and anesthetic effectiveness. The anesthetic effectiveness of 1% lidocaine was greater than that of 2% prilocaine or 1% buffered lidocaine. Pain ratings elicited just after the completion of local anesthetic injection were significantly higher in prilocaine group. Prilocaine caused significantly more pain than lidocaine, either plain or buffered.

As our study protocol employed strict blinding measures, we could not link the difference in the results to the failure of blinding or randomization.

Several studies compared 1% plain lidocaine with 1% buffered lidocaine. Fatovich and Jacobs (6) found that patient scores on visual analog scale after administration of plain 1% lidocaine were not significantly different from those after 1% buffered lidocaine. Brogan et al (21) established that buffered lidocaine 1% was as efficacious as plain lidocaine 1% in a prospective study. Our results were similar. Newton et al (5) compared the effectiveness of anesthesia by plain and buffered 1% lidocaine in an unblinded study in neonatal circumcision, and found no significant difference by adding a buffering agent to plain 1% lidocaine. Bartfeld et al (8) reported that plain and buffered lidocaine were equally efficacious during suturing. Our study, on the other hand, showed that lidocaine was superior to both buffered lidocaine and prilocaine in the efficacy of anesthesia. This discrepancy of findings could have resulted from use of numerical rating scale in our study, as well as from sociodemographic differences in the study participants.

Our results that buffered 1% lidocaine inflicted less pain than 1% lidocaine is in accordance with findings by Colaric et al (4), who also reported that buffered 1% lidocaine was significantly less painful than plain 1% lidocaine, although warming the buffered solution was more effective in pain reduction than buffering alone. On the other hand, Fatovich and Jacobs (6) compared the pain after lidocaine and buffered lidocaine administration and found that buffered lidocaine did not cause less pain than plain 1% lidocaine either in adults or in children. In our study, 2% prilocaine inflicted more pain than the other two agents, which has not been previously reported.

Our study had several limitations. Instead of visual analog scale used in most similar studies to record pain ratings (27), we used numerical rating scale. The reason for preferring numerical rating scale to score pain was to eliminate the use of pen-and-paper while being sutured and to eliminate the effect of social and economical inequalities. Despite this strength, more data are needed to reach firm conclusions about the efficacy and validity of numerical rating scale compared with visual analog scale in a given population. Nonetheless, literature data assure that use of numerical rating scale to assess pain is valid (28). No patient experienced any difficulty in using the tool during the study. The rapid decline in mean pain scores elicited shortly after the administration of the local anesthetic agents supported the proper use of the tool in this study.

The study did not employ a placebo to compare the effects of the anesthetics. It was not considered to represent a weakness of the study because it would be an ethical problem to suture the patients without proper anesthesia.

The dosages of the agents employed fall within the range of accepted dosages used in other studies, but a true equivalence study between 1% lidocaine and prilocaine could not be identified in an extensive literature search. While this point can be viewed as a weakness of the area, the results of the present study can be considered as a preliminary attempt to find out the equivalent doses.

This study covered only a short time period after the administration of the agents and completion of the procedure. Further follow-up of the patients throughout and after the repair of the lacerations would have given more complete information on the effects if anesthetic agents. Future research should try to determine late-onset adverse effects or the cosmetic results of the wound repair after administration of local anesthetic agents.

Norris et al (3) suggested that it was necessary to allow 5-10 minutes before the effect of local anesthetic agents in the wounded tissue becomes evident. In our study, we allowed 5 minutes to elapse before the start of the procedure. It is an acceptable practice provided that P3 scores are well within the range of "mild pain" as determined by Collins et al (29), who found that the visual analog scale scores of most patients who rated their pain as "mild" or "none" were below 30/100. The scores on the numerical rating scale in our study were between these limit values. Furthermore, in emergency situations the responsible physician has to commence suturing as soon as the pain rated by the patients is clinically acceptable.

In conclusion, our study showed that in the given doses, 1% lidocaine was more acceptable than 2% prilocaine and buffered 1% lidocaine for wound repair in acute situations.

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References

1 Liebelt E, Levick N. Acute pain management, analgesia and anxiolysis in the adult patient. In: Tintinalli JE, Kelen GD, Stapczynski JS, editors. Emergency medicine: a comprehensive study guide. 5th ed. New York: McGraw-Hill Professional; 1999. p. 251-68.

2 Bartfield JM, Homer PJ, Ford DT, Sternklar P. Buffered lidocaine as a local anesthetic: an investigation of shelf life. Ann Emerg Med 1992;21:16-9.

3 Norris RL Jr. Local anesthetics. Emerg Med Clin North Am 1992;10:707-18.

4 Colaric KB, Overton DT, Moore K. Pain reduction in lidocaine administration through buffering and warming. Am J Emerg Med 1998;16:353-6.

5 Newton CW, Mulnix N, Baer L, Bovee T. Plain and buffered lidocaine for neonatal circumcision. Obstet Gynecol 1999;93:350-2.

6 Fatovich DM, Jacobs IG. A randomized controlled trial of buffered lidocaine for local anesthetic infiltration in children and adults with simple lacerations. J Emerg Med 1999;17:223-8.

7 Mader TJ, Playe SJ, Garb JL. Reducing the pain of local anesthetic infiltration: warming and buffering have a synergistic effect. Ann Emerg Med 1994;23:550-4.

8 Bartfield JM, Gennis P, Barbera J, Breuer B, Gallagher EJ. Buffered versus plain lidocaine as a local anesthetic for simple laceration repair. Ann Emerg Med 1990;19: 1387-9.

9 Bartfield JM, Crisafulli KM, Raccio-Robak N, Salluzzo RF. The effects of warming and buffering on pain of infiltration of lidocaine. Acad Emerg Med 1995;2:254-8.

10 Christoph RA, Buchanan L, Begalla K, Schwartz S. Pain reduction in local anesthetic administration through pH buffering. Ann Emerg Med 1988;17:117-20.

11 McQuay HJ, Carroll D, Moore RA. Post-operative orthopaedic pain – the effect of opiate premedication and local anaesthetic blocks. Pain 1988;33:291-5.

12 Nik SN, Drake D, Rood JP. The effects of pre-operative blockade with 4% prilocaine on the post-operative pain experienced by patients undergoing removal of impacted mandibular third molars. Ambul Surg 1998;6: 35-7.

13 Product information. EMLA, lidocaine/prilocaine. Westborough (MA): Astra Pharmaceutical Products; 1993.

14 Thompson DF. Computer software. EMLA cream-use for topical anesthesia. Denver (CO): Micromedex Inc.; 1995.

15 Moehrle M, Breuninger H. Dermatosurgery using subcutaneous infusion anesthesia with prilocaine and ropivacaine in children. Pediatr Dermatol 2001;18: 469-72.

16 Gunaydin B, Demiryurek AT. Effects of prilocaine and articaine on human leucocytes and reactive oxygen species in vitro. Acta Anaesthesiol cand 2001;45:741-5.

17 Janzen PR, Vipond AJ, Bush DJ, Hopkins PM. A comparison of 1% prilocaine with 0.5% ropivacaine for outpatient-based surgery under axillary brachial plexus block. Anesth Analg 2001;93:187-91.

18 Uckan S, Guler N, Sumer M, Ungor M. Local anesthetic efficacy for oral surgery: Comparison of diphenhydramine and prilocaine. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1998;86:26-30.

19 Achar S, Kundu S. Principles of office anesthesia: part I. Infiltrative anesthesia. Am Fam Physician 2002;66: 91-4.

20 Masters JE. Randomised control trial of pH buffered lignocaine with adrenaline in outpatient operations. Br J Plast Surg 1998;51:385-7.

21 Brogan GX Jr, Giarrusso E, Hollander JE, Cassara G, Maranga MC, Thode HC. Comparison of plain, warmed, and buffered lidocaine for anesthesia of traumatic wounds. Ann Emerg Med 1995;26:121-5.

22 Gencosmanoglu R, Sad O, Koc D, Inceoglu R. Hemorrhoidectomy: open or closed technique? A prospective, randomized clinical trial. Dis Colon Rectum 2002;45: 70-5.

23 Svensson P, Cairns BE, Wang K, Arendt-Nielsen L Injection of nerve growth factor into human masseter muscle evokes long-lasting mechanical allodynia and hyperalgesia. Pain 2003;104:241-7.

24 Grauers A, Liljeroth E, Ĺkeson J. Propofol infusion rate does not affect local pain on injection. Acta Anaesthesiol Scand 2002;46:361-3.

25 Todd KH, Funk JP. The minimum clinically important difference in physician-assigned visual analog pain scores. Acad Emerg Med 1996;3:142-6.

26 Todd KH. Clinical versus statistical significance in the assessment of pain relief. Ann Emerg Med 1996;27: 439-41.

27 Marquié L, Raufaste E, Lauque D, Mariné C, Ecoiffier M, Sorum P. Pain rating by patients and physicians: evidence of systematic pain miscalibration. Pain 2003; 102:289-96.

28 Price DD, Bush FM, Long S, Harkins SW. A comparison of pain measurement characteristics of mechanical visual analogue and simple numerical rating scales. Pain 1994;56:217-26.

29 Collins SL, Moore RA, McQuay HJ. The visual analogue pain intensity scale: what is moderate pain in millimetres? Pain 1997;72:95-7.

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