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Buffered lidocaine for paracervical blocks in first-trimester abortions: a randomized controlled trial

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ABSTRACT

Objective: The objective was to evaluate if buffered lidocaine decreases injection pain as compared to plain lidocaine for paracervical blocks during first-trimester outpatient surgical abortions.
Study design: We conducted a randomized, double-blind, placebo-controlled trial among women undergoing outpatient uterine aspiration of a first-trimester pregnancy or an early pregnancy loss. Subjects received a paracervical block with either lidocaine 1% 20 mL or lidocaine 1% 18 mL plus sodium bicarbonate 8.4% 2 mL. The primary outcome was pain from injection of the paracervical block measured on a 100-mm visual analog scale (VAS). Secondary outcomes included pain after cervical dilation, uterine aspiration and overall satisfaction with pain control. Scores were compared using the Mann–Whitney *U* test. We aimed to detect a 15-mm difference in pain from injection of the paracervical block.
Results: From May 2017 to October 2018, 48 women received plain lidocaine and 50 women received buffered lidocaine. Groups were similar in demographics. We found no clinically or statistically meaningful difference in pain when evaluating median VAS scores for paracervical block injection between the buffered and plain lidocaine [30.0 (interquartile range (IQR) 15.3–64.5); 44.5 (IQR 18.3–65), respectively, p = .32]. We found no difference in secondary outcomes between buffered and plain lidocaine.
Conclusion: Buffered lidocaine for paracervical blocks in first-trimester outpatient surgical abortions does not decrease injection pain as compared to plain lidocaine.
Implications statement: Buffering the paracervical block in first-trimester outpatient surgical abortions does not decrease injection pain as compared to plain lidocaine, nor does it increase patient satisfaction. Eliminating sodium bicarbonate allows for a more cost-effective and readily available solution for paracervical blocks.

1. Introduction

First-trimester surgical abortions are one of the most common outpatient procedures worldwide. Approximately 46 million are performed annually, with over 600,000 occurring in the United States [1]. Although it is a quick procedure, 78%–97% of patients still report at least moderate pain [1]. Many different techniques have been used for pain control during this procedure. From most common to least common, providers use the paracervical block (PCB), oral anxiolytics, moderate sedation or general anesthesia, and newer research has found promise in auricular acupuncture [2,3]. Most providers use intravenous moderate sedation (38%) or the PCB with an oral medication (33%) [2].

Administration of a PCB has been shown to decrease pain during the procedure especially at earlier gestations. However, the PCB itself can be painful with a mean pain level of 54 on a 100-mm visual analog scale (VAS) as compared to 30 for sham blocks [4]. Some providers use buffered lidocaine, which includes the addition of an alkaline solution such as sodium bicarbonate [2].

Adding sodium bicarbonate to local anesthetic agents has been used in other gynecologic [5,6] and nongynecologic [7–10] procedures with conflicting results. Two studies have examined whether adding sodium bicarbonate to a PCB reduces pain at different time points of the procedure [10,11]. The first study compared buffered lidocaine 2% versus plain lidocaine 2% and found that buffered lidocaine was more effective at controlling cervical dilation pain and pain at the end of the procedure [10]. The second study compared buffered lidocaine 1% versus plain lidocaine 1% and found that buffered lidocaine was more effective at controlling aspiration pain but not postoperative pain [12]. Both studies evaluated pain using a 10-cm VAS and found differences in injection pain of approximately 1 cm between patients who received buffered lidocaine versus plain lidocaine [11,12]. Although both studies found a statistically significant difference, pain studies have found that clinically perceptible difference in pain must be at least 13–20 mm on a 100-mm VAS [13]. The authors concluded that their findings were most likely not

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clinically significant and thus not worth the extra cost of preparing the buffered solution [11].

Our standard pain management protocol is to administer 600 mg oral ibuprofen 30 min prior to the procedure and to use lidocaine 1% 20 mL for the PCB. As the only studies that have compared buffered versus plain lidocaine for PCBs during first-trimester surgical abortions may not have been powered to detect a clinically significant difference in pain, we sought to determine if buffered lidocaine decreases PCB injection pain by a clinically significant amount.

2. Materials and methods

We conducted this randomized, double-blind, placebo-controlled trial at the University of Hawaii Women's Health Specialists office in Honolulu, Hawaii. We enrolled women with pregnancies less than or equal to 13 weeks and 6 days of gestation according to the American College of Obstetricians and Gynecologists' dating guidelines [14] who desired surgical termination or surgical management of an early pregnancy loss. We included women who were 14 years and older, English speaking, seeking outpatient uterine aspiration and willing to be randomized to receive buffered lidocaine or plain lidocaine. We excluded women with an inability to understand English or provide informed consent, current incarceration, age less than 14 years or medical contraindications to receiving plain or buffered lidocaine. The University of Hawaii Human Subjects Board approved this study protocol, and the study was registered on clinicaltrials.gov (NCT03107754).

Providers identified potential participants at their office visits. After identification of potential participants by the provider, research assistants trained in the research protocol then approached eligible patients, explained the study and obtained written consent after questions were answered.

After obtaining baseline demographic information, we randomized subjects 1:1. Subjects received either a PCB with lidocaine 1% 20 mL (plain) or lidocaine 1% 18 mL plus sodium bicarbonate 8.4% 2 mL (buffered). Prior to the start of the study, a statistician not involved with the conduct of the study generated study assignments in a 1:1 ratio. This statistician used a computer random number generator to generate random permuted blocks that varied in sizes of 4, 6 and 8. She then placed allocation assignment cards in sequentially numbered, sealed, opaque envelopes. We trained our medical assistants to pull envelopes individually in the sequentially numbered order and prepare the buffered lidocaine or plain lidocaine in an unlabeled syringe, which was then placed on the instrument tray and handed to the provider. These medical assistants were the only study personnel aware of study allocation and were not in the room during the procedure. Everyone else in the study, including patients, providers, research assistants and other staff, was blinded to the study allocation. A research assistant, unaware of the study allocation, was at the head of the bed to collect data from the patient.

Family Planning fellows or Obstetrics and Gynecology interns under the supervision of Family Planning faculty or faculty themselves performed the in-office procedures. The provider injected 1–2 mL of the PCB solution at the anterior lip of the cervix and placed a single-tooth tenaculum to grasp the cervix. The remainder of the PCB solution was then injected deeply at 4 o'clock and 8 o'clock at the cervicovaginal junction. The aspiration procedure was completed in standard fashion. The research assistant asked the patient to mark her level of pain on a 100-mm VAS at the following time points of the procedure: prior to the start of the procedure, after speculum placement, after PCB injection, after cervical dilation, after uterine aspiration and immediately postoperatively. Study data were collected on paper and then transferred and managed using Research Electronic Data Capture (REDCap) tools hosted at University of Hawaii [15,16]. REDCap is a secure, web-based software platform designed to support data capture for research studies.

Our primary objective was to assess if buffered lidocaine reduced injection pain associated with PCB administration for first-trimester surgical abortions more effectively than plain lidocaine. Our secondary objectives were to assess if buffered lidocaine reduced pain more than plain lidocaine at other time points of the procedure and if it improved overall satisfaction with pain control.

Previous research has shown that a clinically relevant decrease in pain is between 13 and 20 mm on a 100-mm VAS [13]. A similar study conducted on the use of PCBs in first-trimester surgical abortions found injection pain scores to have a standard deviation of 25 mm [4]. We calculated our sample size to detect a 15-mm or greater difference, with a 25-mm standard deviation, on a 100-mm VAS with 80% power and two-sided α of 0.05. We inflated this number by 10% to account for potential dropout, for a total sample size of 98 patients (49 in each group).

The focus of the primary analysis was the difference in injection pain between groups. We used IBM SPSS Statistics, version 24 (Armonk, NY, USA) to complete the statistical analysis. Due to VAS scores being nonnormally distributed, we report median scores as the primary outcome and used nonparametric testing (i.e. Mann–Whitney *U* test) to compare groups. We also used the Mann–Whitney *U* test to assess our secondary objectives by comparing the median differences in pain during other time points in the procedure and overall satisfaction with pain control.

3. Results

We assessed 287 women for eligibility between May 2017 and October 2018 and excluded 189 women mostly due to lack of interest in the study or enrollment in another ongoing study. Nineteen of these women were ineligible for enrollment due to logistics, usually because a research assistant was unavailable. Thus, we randomized 98 participants: 48 in the plain lidocaine group and 50 in the buffered lidocaine group (Fig. 1). We did not have any postrandomization exclusions or loss to follow-up. Table 1 describes the demographic characteristics of participants. The ethnic and racial breakdown of our participants reflects the diversity of Hawaii's population. Three procedures were performed for early pregnancy loss, and none of these patients presented with bleeding. A minority of our patients were taking pain or antipsychotic medications regularly, and few had pre-existing anxiety or depression. Five patients experienced adverse events: three in the plain lidocaine

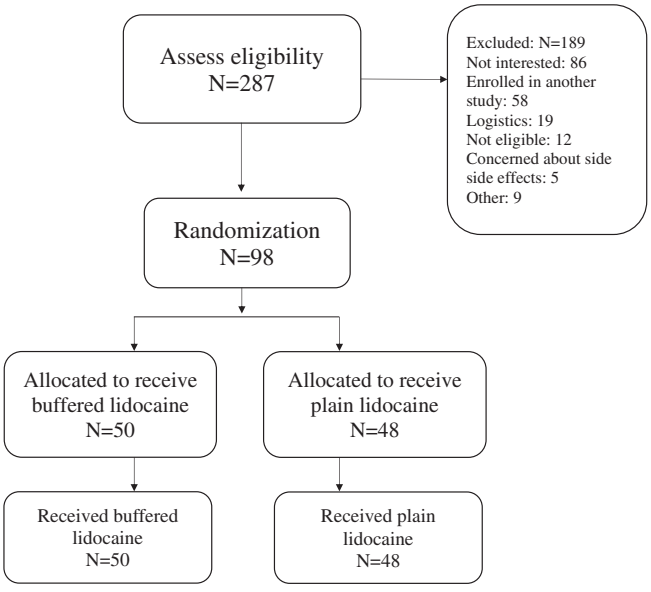

Fig. 1. Study flow of participants seeking uterine aspiration for pregnancies up to 13 weeks and 6 days of gestation.

Table 1
Demographics of participants in a randomized, double-blind, placebo-controlled trial with unwanted or failed pregnancies up to 13 weeks and 6 days of gestation in plain versus buffered lidocaine group

Demographic	Plain lidocaine $n = 48$	Buffered lidocaine $n = 50$
Age (years)	30.2 ± 6.8	28.5 ± 7.0
Median gestational age (completed weeks)	8	8
BMI (kg/m^2)	28.3 ± 7.4	25.9 ± 6.4
Race[a]		
White/Caucasian	18 (37.5)	17 (34)
Black/African American	3 (6.3)	2 (4)
Asian	26 (54.2)	31 (62)
Native Hawaiian/Pacific Islander	23 (47.9)	22 (44)
American Indian/Alaska Native	3 (6.3)	2 (4)
Hispanic/Latino	5 (10.4)	4 (8)
Other	0 (0)	1 (2)
Marital status		
Single, no partner	11 (22.9)	10 (20)
Single, with a partner	26 (54.2)	24 (48)
Married	11 (22.9)	16 (32)
Level of menstrual symptoms		
Easy or mild cramping	42 (87.5)	45 (90)
Requiring medical treatment/unable to work	6 (12.5)	5 (10)
Prior procedures		
Surgical abortions	23 (57.5)	14 (37.8)
Vaginal deliveries	30 (75)	29 (78.4)
Cesarean sections	10 (25)	11 (29.7)
Any previous cervical procedures	11 (22.9)	9 (18)
Home medications		
Pain medications	8 (30.8)	5 (21.7)
Antipsychotic medications	4 (23.5)	5 (29.4)
Pre-existing conditions		
Anxiety	3 (6.3)	2 (4)
Depression	0 (0)	1 (2)
Level of provider		
Intern	10 (25)	15 (31.9)
Fellow	14 (35)	10 (21.3)
Attending	16 (40)	22 (46.8)

Data are mean ± SD or *n* (%) unless otherwise stated.
[a] Percentages total > 100 because participants were allowed to select more than one race.

group and two in the buffered lidocaine group. One of the patients who received plain lidocaine experienced leg numbness, which resolved without intervention. In another patient, the provider noticed a lack of gestational sac upon examination of uterine contents, and an in-office ultrasound demonstrated an ongoing pregnancy. The patient was offered reaspiration or medication abortion. The patient opted for medication abortion and received mifepristone that day; however, she returned 2 days later requesting reaspiration, which was performed without complication. In another patient, the provider was unable to dilate past 9 mm due to patient discomfort and thus completed the procedure in the operating room under general anesthesia without complication. Among patients who received buffered lidocaine, one required 400 mcg of vaginal misoprostol after her procedure for increased bleeding which did not require further treatment, and another required reaspiration after examination of uterine contents showed incomplete products of conception, which was performed during the same clinic visit without complication.

Our pain scores were distributed in a non-normal fashion, and thus, we compared median scores using a nonparametric approach. We did not find a difference in injection pain between buffered and plain lidocaine when evaluating median VAS scores for PCB injection [30.0 (interquartile range (IQR) 15.3–64.5); 44.5 (IQR 18.3–65), respectively, p = .32] (Fig. 2). We found no significant differences in pain when analyzed by provider type, level of menstrual symptoms, previous uterine aspiration or parity.

When evaluating median pain scores at other time points during the procedure, we also found no differences in scores between the groups (Fig. 3). Participants provided a wide range of pain scores at each time point with a standard deviation of 27.3 for pain immediately after PCB injection. We found no difference in overall satisfaction with pain control between plain lidocaine and buffered lidocaine [77.0 (IQR 45.8–96.8); 70.0 (IQR 41.8–93.3), respectively, p = .36].

4. Discussion

This randomized, double-blind, placebo-controlled trial demonstrated that using buffered lidocaine for PCBs in first-trimester outpatient surgical

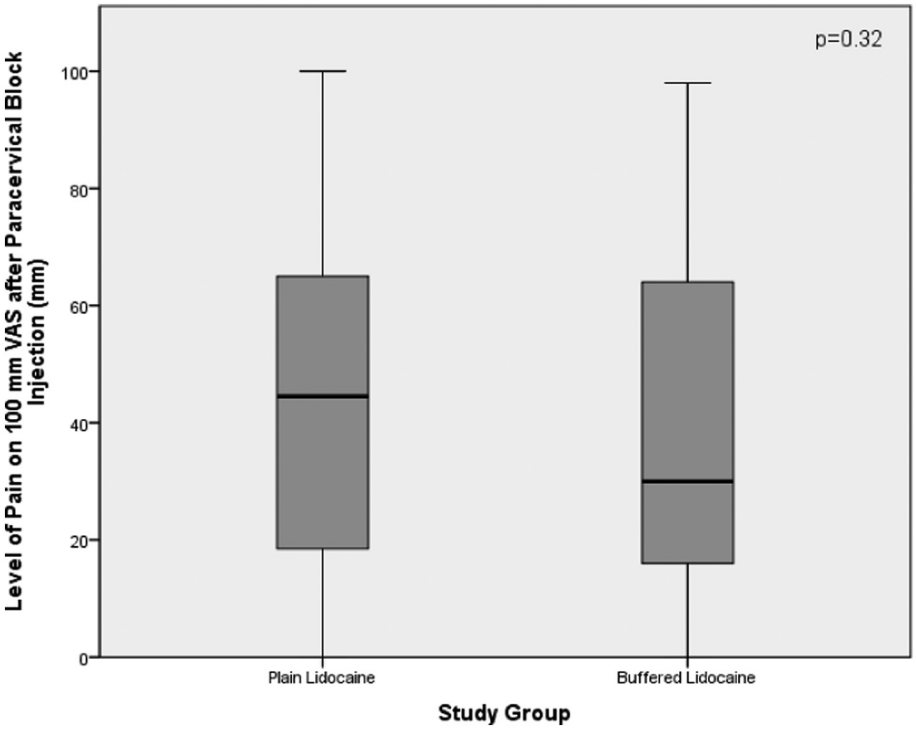

Fig. 2. Median pain scores immediately after paracervical block injection among participants seeking uterine aspiration for pregnancies up to 13 weeks and 6 days of gestation.

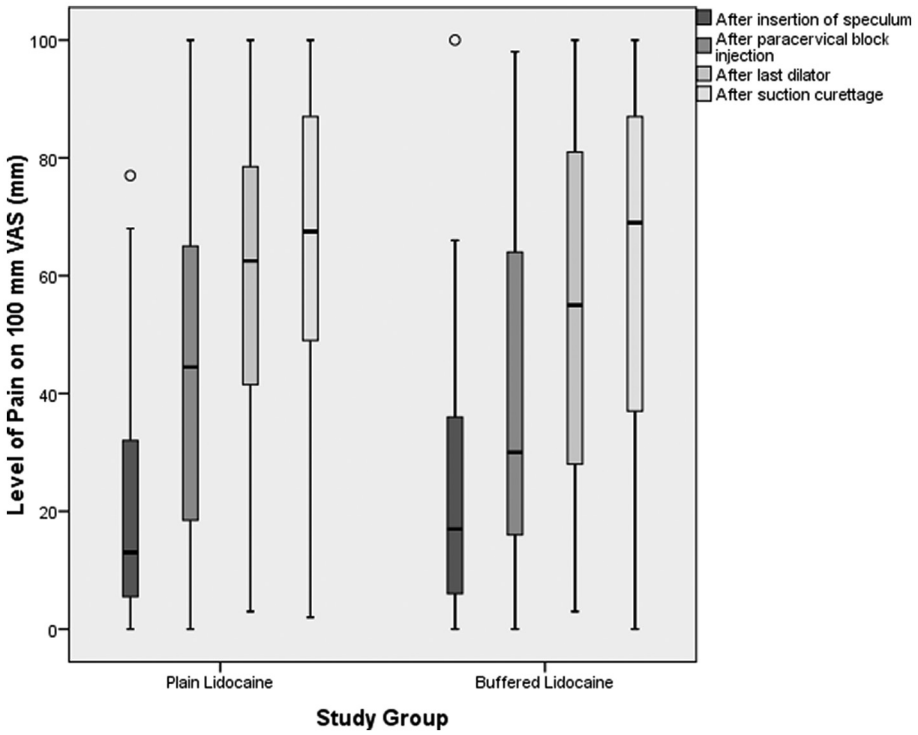

Fig. 3. Median pain scores throughout the dilation and curettage among participants seeking uterine aspiration for pregnancies up to 13 weeks and 6 days of gestation.

abortions did not decrease injection pain as compared to plain lidocaine. Buffered lidocaine did not improve pain at other time points during the procedure, nor did it improve overall satisfaction with pain control for the procedure, although we did not power our study for these secondary outcomes. A total of five patients in our study experienced adverse events; however, we believe these adverse events were unlikely to be related to study participation. We included patients presenting for termination of pregnancy or early pregnancy loss. Previous studies examining pain regimens for aspiration for either indication have found no difference in pain between the two groups [3,17].

Despite the widespread use of PCBs, few studies have examined the difference between buffered lidocaine versus plain lidocaine for injection pain. By creating a more physiologic solution, some providers speculate the injection will be less painful. Theoretically, adding a buffering solution to the acidic local anesthetic will result in a less painful infiltration. Additionally, since lidocaine must be in the nonionized form to enter neurons, neutralizing the acid in lidocaine should promote this and produce a faster onset of action [18]. Other anesthesia studies have shown greater patient satisfaction and more effective anesthesia with buffered lidocaine compared to plain lidocaine, likely due to an increased rate of penetration and a greater amount of lidocaine in the nerve fibers [19]. The only studies that specifically examined buffered lidocaine for PCBs for uterine aspirations did find improvement in dilation pain, aspiration pain and pain at the end of the procedure; however, these studies did not find clinically significant differences in injection pain [11,12].

The main strength of this study was that it was a randomized, double-blind, placebo-controlled study design with a standardized protocol. All people in the procedure room and the data analyst were blinded to study group allocation, and all participants completed the study in the group to which they were allocated. Our study was powered to detect both statistically and clinically significant differences in pain. In addition, we included a variety of providers with different levels of training, which increases our study's generalizability.

One limitation of our study is that we conducted our study at a single clinical site in Hawaii with a unique racial composition. Our median pain scores were 30.0 and 44.5 for buffered and plain lidocaine, respectively. Both of these pain scores are lower than the mean pain score of 54 found in the PCB study conducted by Renner et al. [4]. A previous study conducted on the use of PCBs for laminaria placement in the same office also showed lower pain scores than other studies. We suspect that this difference could be due to differences in patient population or methods of data collection [20]. Another possible limitation is that we calculated our sample size based on a 15-mm difference in pain, which we based on a previous pain study showing that this was the minimal clinically significant difference [13]. However, a more recent study found that a larger minimal difference, 22.6, is necessary to be clinically relevant [21].

We found that buffered lidocaine provides no benefit in pain reduction. Eliminating the need to create a buffered solution for PCBs reduces staff time in preparing the buffered lidocaine solution and cost in purchasing a buffering agent, and increases the shelf life of the solution as buffered lidocaine must be used on the same day it is prepared. Understanding how variations in PCB administration affect pain is important because of the commonality of this intervention for gynecologic procedures.

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Declaration of competing interests

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Dr Kaneshiro receives research support from Contramed Pharmaceuticals (Sebela Pharmaceuticals), Gynuity Health Projects and the National Institutes of Health. She is a consultant for UpToDate. All other authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] Renner RM, Jensen JT, Nichols MD, Edelman AB. Pain control in first-trimester surgical abortion: a systematic review of randomized controlled trials. Contraception. 2010;81(5):372–88.

[2] White KO, Jones HE, Lavelanet A, Norman WV, Guilbert E, OLichtenberg ES, et al. First-trimester aspiration abortion practices: a survey of United States abortion providers. Contraception. 2019 Jan;99(1):10–5.

[3] Ndubisi C, Danvers A, Gold MA, Morrow L, Westhoff CL. Auricular acupuncture as an adjunct for pain management during first trimester abortion: a randomized, double-blinded, three arm trial. Contraception. 2019 Mar;99(3):143–7.

[4] Renner RM, Nichols MD, Jensen JT, Li H, Edelman AB. Paracervical block for pain control in first-trimester surgical abortion: a randomized controlled trial. Obstet Gynecol. 2012 May;119(5):1030–7.

[5] Kizer NT, Zhao Q, Peipert JF, Ioffe Y, Massad LS. A randomized trial of buffered versus nonbuffered lidocaine with epinephrine for cervical loop excision. J Low Genit Tract Dis. 2014 Jan;18(1):8–12.

[6] Villavicencio JC, Kulkarni A, Luis C, Mendez H, Raker C, Cronin B, et al. Sensation of pain using buffered lidocaine for infiltration before vulvar biopsy: a randomized controlled trial. Obstet Gynecol. 2020 Mar;135(3):609–14.

[7] Welch MN, Czyz CN, Kalwerisky K, Holck DE, Mihora LD. Double-blind, bilateral pain comparison with simultaneous injection of 2% lidocaine versus buffered 2% lidocaine for periocular anesthesia. Ophthalmology. 2012 Oct;119(10):2048–52.

[8] Narváez J, Wessels I, Bacon G, Chin VR, Baqai WK, Zimmerman GJ. Prospective randomized evaluation of short-term complications when using buffered or unbuffered lidocaine 1% with epinephrine for blepharoplasty surgery. Ophthal Plast Reconstr Surg. 2010 Jan-Feb;26(1):33–5.

[9] Hobeich P, Simon S, Schneiderman E, He J. A prospective, randomized, double-blind comparison of the injection pain and anesthetic onset of 2% lidocaine with 1:100,000 epinephrine buffered with 5% and 10% sodium bicarbonate in maxillary infiltrations. J Endod. 2013 May;39(5):597–9.

[10] Harreld TK, Fowler S, Drum M, Reader A, Nusstein J, Beck M. Efficacy of a buffered 4% lidocaine formulation for incision and drainage: a prospective, randomized, double-blind study. J Endod. 2015 Oct;41(10):1583–8.

[11] Wiebe ER. Comparison of the efficacy of different local anesthetics and techniques of local anesthesia in therapeutic abortions. Am J Obstet Gynecol. 1992 Jul;167(1):131–4.

[12] Wiebe ER, Rawling M. Pain control in abortion. Int J Gynaecol Obstet. 1995 Jul;50(1):41–6.

[13] Todd KH, Funk KG, Funk JP, Bonacci R. Clinical significance of reported changes in pain severity. Ann Emerg Med. 1996 Apr;27(4):485–9.

[14] Methods for estimating the due date. Committee opinion no. 700. American College of Obstetricians and Gynecologists. Obstet Gynecol. 2017;129:e150–4.

[15] Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap) — a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform. 2009 Apr;42(2):377–81.

[16] Harris PA, Taylor R, Minor BL, Elliott V, Fernandez M, O'Neal L, et al. REDCap Consortium. The REDCap Consortium: building an international community of software partners. J Biomed Inform. 2019 May;9.

[17] Wilson SF, Gurney EP, Sammel MD, Schreiber CA. Doulas for surgical management of miscarriage and abortion: a randomized controlled trial. Am J Obstet Gynecol. 2017;216(1):44.e1–44.e6.

[18] Best CA, Best AA, Best TJ, Hamilton DA. Buffered lidocaine and bupivacaine mixture — the ideal local anesthetic solution? Plast Surg (Oakv). 2015;23(2):87–90.

[19] Gormley WP, Hill DA, Murray JM, Fee JP. The effect of alkalinization of lidocaine on axillary brachial plexus anesthesia. Anesthesia. 1996;51(2):185–8.

[20] Soon R, Tschann M, Salcedo J, Stevens K, Ahn HJ, Kaneshiro B. Paracervical block for laminaria insertion before second-trimester abortion: a randomized controlled trial. Obstet Gynecol. 2017 Aug;130(2):387–92.

[21] Danoff JR, Goel R, Sutton R, Maltenfort MG, Austin MS. How much pain is significant? Defining the minimal clinically important difference for the visual analog scale for pain after total joint arthroplasty. J Arthroplasty. 2018;33(7S):S71–5 e2.