Perineal infiltration with levobupivacaine or placebo for episiotomies or second-degree tears: A double-blind randomized study

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Abstract

Introduction: The purpose of this study was to investigate whether a single perineal infiltration of levobupivacaine administered immediately before repairing a perineal second-degree tear or episiotomy decreased pain in women after delivery.

Materials and methods: This randomized controlled double-blind study included women at low risk with spontaneous (unassisted) or vacuum-assisted vaginal delivery at Foch University Hospital, Suresnes, France. The treatment group (L) (n=54) received a perineal infiltration of 10 mL levobupivacaine (5 mg/mL) (Chirocaine®) and the placebo control group (P) (n=50) a perineal infiltration of 10 mL saline solution (0.9%) immediately before perineal repair of a second-degree tear or an episiotomy after delivery. The primary outcome variable was the mean resting numeric rating scale (NRS) for pain intensity at 8 hours. The secondary outcome variables were mean resting NRS for pain intensity at 2, 4, 12, 24, 36, and 48 hours, and in motion, the safety of levobupivacaine, analgesic consumption, and patient satisfaction scores. At 1 month, the women received a questionnaire to assess pelvic pain and its repercussions, analgesic use, and complications.

Results: The study included 104 women. Demographic data were comparable for the experimental and control groups. The NRS pain scores were low and did not differ between the groups; nor did the groups differ for mean pain intensity, patient satisfaction, or analgesic use either during the 48 hours after delivery or at 1 month.

Conclusions: Levobupivacaine infiltration into an episiotomy wound or perineal tear did not appear to reduce pain significantly among women at low risk.

Abbreviations: NRS: Numeric Rating Scale

Key Message: Levobupivacaine infiltration into an episiotomy wound or perineal tear did not appear to reduce pain significantly among women at low risk (that is, a spontaneous or unassisted vaginal delivery or vacuum extraction) receiving oral analgesics and anti-inflammatory agents.

Introduction

Postpartum perineal pain is not rare. An Australian study published in 2012 showed that 37% of 215 women with a vaginal delivery reported moderate to severe perineal pain in the 72 hours afterwards [1]. While this pain peaks in the immediate postpartum period, discomfort or even intense pain can persist for several weeks after delivery [2]. The principal causes of perineal pain are tears or lacerations and episiotomies [3]. The intensity of pain is correlated with the extent of the injury, as shown in a Canadian study where 60% of women with first- and second-degree lacerations complained of pain on day 7 after delivery, 71% of those with episiotomies, and 91% with third- or fourth-degree lacerations; pain was still present at 6 weeks for respectively 4%, 13% and 20% [4]. Episiotomy is the most common surgical procedure for parturients [5]. The recommendation of a restrictive episiotomy policy by recent clinical practice guidelines has led to a decrease in the use of this procedure [6]. Nonetheless, the episiotomy rate in France in 2010 was still 44.4% for nulliparas and 14.3% for multiparas [7]. Studies of obstetric analgesia have focused on pain during labor or after a cesarean delivery, with less attention paid to analgesia after vaginal delivery [8]. Nonetheless beyond the physical discomfort it causes, postpartum pain can have multiple consequences, disrupting breastfeeding and both caring for and bonding with the baby [9]. Over the longer term, it can also affect the mother’s sexual life [10]. Postpartum pain management is based principally on oral drugs: paracetamol and non-steroidal antiinflammatory drugs (NSAIDs) [11]. Very small quantities of NSAIDs pass into breast milk, but their use is often limited in time (e.g., a single administration) [12]. Any ineffectiveness is a problem, since the next choice-morphine-does transfer into breast milk and has adverse effects.
The analgesic efficacy of infiltration before suturing has been shown in many types of surgery [13,14]. Infiltration is defined as the injection of an analgesic agent (most often a long-acting anesthetic) in a subcutaneous space near the surgical site. Unlike regional blocks, it does not require identification of nerve locations, and is thus an easy procedure that can be performed by midwives, obstetricians, and anesthesiologists. It acts by blocking distal nerve endings. It also helps to break the “pain inflammation” loop and thus provides better control of secondary hyperalgesia [15]. This explains its effectiveness on parietal pain, for several days beyond its theoretical duration of action [14,16,17]. This technique therefore seems interesting for the management of perineal pain after episiotomy or tears. Thus far, very few studies have looked at this subject, and their results are contradictory [18-21]. The purpose of this study was to investigate whether a perineal single infiltration of levobupivacaine immediately before repairing a perineal tear or episiotomy could decrease pain in women 8 hours after delivery. We performed a randomized, double-blind, controlled study.

**Material and methods**

Women were included from January 2011 to September 2014 in the obstetrics department of Foch University Hospital, in Suresnes, France. It was approved by the appropriate ethics committee and registered (ClinicalTrials.gov, NCT02905695). Women received written information about the trial during prenatal care and provided written informed consent at the last visit for prenatal care before delivery or at the beginning of labor. Inclusion criteria were vaginal delivery, spontaneous or vacuum-assisted vaginal delivery, with a mediolateral episiotomy or second-degree perineal tear requiring three planes suturing, singleton fetus in a vertex position, maternal age of 18–45 years, effective epidural labor analgesia, and coverage by a national health insurance fund. For practical reasons, the women had to understand and write the French language. Exclusion criteria were delivery with ineffective or no epidural analgesia, contraindication to local anesthetics or levobupivacaine, multiple pregnancy, breech delivery with ineffective or no epidural analgesia, contraindication to levobupivacaine (5 mg/mL) or placebo (saline prepared in strict similarity), tear of the first degree) between patients with levobupivacaine and placebo treatment. Baseline characteristics of the patients were used to conduct the stratified analysis on the type of lesion (episiotomy

The primary outcome was analyzed for both the intention-to-treat (ITT) and per protocol (PP) populations. The secondary outcomes were analyzed only in the ITT population. The ITT population comprised all women who were included and randomized. The PP population excluded those with no episiotomy or perineal tear, who did not have an effective epidural, or a singleton pregnancy in cephalic presentation, who did not give birth by spontaneous or vacuum-assisted delivery, or who did not receive either treatment, or who did not receive the allocated treatment. The missing measurements were imputed by the "last observation carried forward (LOCF)" method. The data were analyzed using multiple imputations for a sensitivity analysis. The Van Elteren test was used to assess the difference between the groups in pain intensity at 8 hours after delivery.
after suture (primary outcome). The secondary criteria were assessed with the Cochran-Mantel-Haenszel test for qualitative data and with the Van Elteren test for quantitative data. Subgroup analyses to test for interactions compared the women with an episiotomy to those with a second-degree tear and those with spontaneous delivery to those with vacuum-assisted delivery with vacuum extractor according to treatment group. A $p$ value $\leq 0.05$ was considered significant.

**Results**

The study randomized 105 women. Six were excluded: 1 for duplicate randomization, 2 for erroneous randomization, 2 who did not meet the inclusion criteria (ineffective epidural analgesia and a continuous suture) and one who did not receive any treatment (Figure 1). Table 1 summarizes the demographic data. The levobupivacaine group (L) and the placebo or control group (C) did not differ for baseline characteristics, labor, or delivery. All episiotomies and tears healed uneventfully. NRS at 8 hours did not differ between the two groups (mean for group L: 1 [0.0; 2.0]/mean for group P: 1.6 [0.0; 3.0], $P = 0.8$). Pain intensity was low during the first 48-h study period, with no difference between groups. The mean resting NRS for pain intensity at 2, 4, 12, 24, 36, 48 hours and in motion were equivalent (Figure 2 and 3). Antalgic consumption, was similar (Table 2). Maternal satisfaction for perineal pain relief during the first 48 hours was similar in the two group (median NRS 2 [2.0; 3.0] = good in the two groups, $P = 0.93$). Levobupivacaine appeared to be safe, and no adverse effects were reported. We found two immediate complications for one patient in the placebo group: a third-stage hemorrhage and a breach of the dura mater, neither attributable to the protocol. We found one scar dehiscence in the control group and 2 in the levobupivacaine group. None required surgical revision. Subgroup analyses for the principal criterion sought to determine the existence of any interactions between the treatment effect and one or more variables. No difference was observed in the following subgroups: episiotomy (NRS L/C: 1.54/1.98 $P = 0.328$), tears (1.89/0.86 $P = 0.401$), spontaneous delivery (NRS L/C: 1.89/1.6 $P = 0.99$) and vacuum extraction (NRS L/C: 1/1.62 $P = 0.284$).

Overall, 8 women in the levobupivacaine group and 9 in the control group did not respond to the questionnaire at 1 month. We observed no difference in perineal pain or its repercussions or analgesic intake (Tables 2 and 3). No complication attributable to the injection was reported at 1 month.

**Discussion**

Three potent and therefore long-acting local anesthetic agents are available: bupivacaine (Marcaine®), ropivacaine (Naropein®),
Table 1. Characteristics of the study population.

| Characteristic                      | Group P N = 50 | Group L N = 54 | P-value |
|-------------------------------------|---------------|----------------|---------|
| Gravida n (%)                       |               |                |         |
| 1                                   | 25 (51.02%)   | 39 (100%)      | 0.386*  |
| 2                                   | 15 (30.61%)   | 13 (38.89%)    |         |
| 3                                   | 3 (6.12%)     | 4 (11.76%)     |         |
| 4                                   | 6 (12.24%)    | 0 (0%)         |         |
| Parity n (%)                        |               |                |         |
| 1                                   | 4 (21.05%)    | 10 (29.76%)    | 0.767*  |
| 2                                   | 24 (78.95%)   | 20 (60.24%)    |         |
| 3                                   | 4 (21.05%)    | 20 (58.82%)    |         |
| 4                                   | 24 (78.95%)   | 13 (38.89%)    |         |
| Previous vaginal delivery n (%)     |               |                |         |
| 1                                   | 11 (22.45%)   | 13 (24.53%)    | 0.985*  |
| 2                                   | 28 (56.82%)   | 36 (107.69%)   |         |
| 3                                   | 5 (10.20%)    | 12 (35.29%)    |         |
| 4                                   | 1 (2.04%)     | 0 (0%)         |         |
| Genital mutilation n (%)            | 0 (0%)        | 0 (0%)         | 1*      |
| Weight before pregnancy (kg) Median | 5 [4.5-6.5]   | 5 [5.5-6.9]    | 0.604*  |
| Gestational age at birth (week) Median | 38 [37-38] | 38 [37-38.8]  | 0.618*  |
| Working time (min) Median           | 390 [300-490] | 360 [300-540] | 0.578*  |
| Full expansion time (min) Median    | 105 [60-130]  | 76.5 [51-131.2]| 0.414*  |
| Amount of epidural levobupivacaine (mg) Median | 75 [54.7-106.8] | 75 [55.6-96.9] | 0.604*  |
| Vaccum extraction n (%)             | 10 (20.41%)   | 12 (22.22%)    | 0.767*  |
| Tear length (cm) n < 3cm            | 19 (38.00%)   | 14 (41.18%)    | 0.651*  |
| Tear length (cm) ≥ 3cm              | 24 (48.00%)   | 20 (58.82%)    |         |
| Episiotomy length (cm) n < 3cm      | 32 (63.93%)   | 32 (94.12%)    | 0.21*   |
| Episiotomy length (cm) ≥ 3cm        | 12 (24.49%)   | 15 (28.35%)    | 0.634*  |
| Hemorrhoids n (%)                   | 2 (4.08%)     | 2 (4.08%)      |         |
| Birth weight (kg) Median            | 3.4 [3-3.7]   | 3.3 [3.1-3.5]  | 0.201*  |
| Cephalic perimeter (cm) Median      | 34 [33.5-35]  | 34.8 [34.5-35] | 0.657*  |

n = number of data items entered, (%) = percentage of data entered, IQR = Interquartile range

Table 2. Analgesic use.

| Analgesic use | Group P n (%) | Group L n (%) | p-value^c |
|---------------|---------------|---------------|-----------|
| n (0-2) (%) / n (m1) (%) | 43 (100%) / 39 (100%) | 46 (100%) / 40 (100%) | 0.83 / 0.54 |
| Paracetamol   |               |               | 0.99      |
| d0            | 34 (79%)      | 36 (78.2%)    | 1         |
| d1            | 39 (80.7%)    | 43 (83.5%)    |           |
| d2            | 34 (79%)      | 35 (76.1%)    |           |
| d3            | 7 (17.9%)     | 8 (17.78%)    |           |
| Ketoprofen    |               |               | 1         |
| d0            | 23 (53.5%)    | 22 (41.3%)    | 1         |
| d1            | 28 (65.1%)    | 27 (54.7)     |           |
| d2            | 22 (51.1%)    | 19 (36.5)     |           |
| d3            | 3 (6.12%)     | 0             |           |
| Nefopam       |               |               | 1         |
| d0            | 34 (69.39%)   | 39 (72.22%)   | 0.21*     |
| d1            | 34 (69.39%)   | 39 (72.22%)   |           |
| d2            | 3 (6.12%)     | 5 (10.20%)    |           |
| d3            | 0             | 0             |           |
| Tramadol      |               |               | 1         |
| d0            | 0             | 0             |           |
| d1            | 0             | 1 (2.04%)     |           |
| d2            | 0             | 0             |           |
| d3            | 0             | 0             |           |

n = number of data items entered, c = Cochran-Mantel-Haenszel test, d = day, m = month

Authors, greater efficacy than ropivacaine [22,23]. Moreover, we are currently using levobupivacaine in our epidural analgesia. Accordingly we chose this anesthetic agent for the local infiltrations, although it has never been studied in episiotomies. When good practice guidelines are followed and the toxic dose is not exceeded, complications are rare: an aspiration test was routinely performed before injection to avoid intravascular injection, which is the leading cause of adverse effects; the injection was slow and fractionated with monitoring of vital signs and clinical state in the minutes after injection. No serious accident attributable to parietal infiltration has been reported in our series or in the literature. Nor did we find more scar dehiscence at 1 month attributable to levobupivacaine, as others have reported [24]. The maximum recommended dose in a single injection is 150 mg, which corresponds to 30 mL as a 5 mg/mL solution. Moreover the maximum recommended dose over a 24-hour period is 400 mg [25]. We therefore chose to inject 10 mL as a 5 mg/mL solution to remain below the toxic dose. Pain was assessed for the first 48 hours at rest and while moving. Although the potential effect of long-acting local anesthetics peaks in the first 12 hours, studies show that an effect continues in the hours and even days that follow [14,16,17]. We note in our series that the mean pain scores were low with nonetheless considerable analgesic intake. Although women were asked not to take treatment routinely or spatulas as well as third- and fourth-degree perineal lacerations, and levobupivacaine (Chirocare'). Bupivacaine is more toxic and has a shorter period of action than the others and accordingly has no marketing authorization for local infiltrations. The toxicity of ropivacaine is lower than for both the others. Levobupivacaine appears to have an intermediate level of toxicity, but also, according to some authors, greater efficacy than ropivacaine [22,23]. Moreover, we are currently using levobupivacaine in our epidural analgesia. Accordingly we chose this anesthetic agent for the local infiltrations, although it has never been studied in episiotomies. When good practice guidelines are followed and the toxic dose is not exceeded, complications are rare: an aspiration test was routinely performed before injection to avoid intravascular injection, which is the leading cause of adverse effects; the injection was slow and fractionated with monitoring of vital signs and clinical state in the minutes after injection. No serious accident attributable to parietal infiltration has been reported in our series or in the literature. Nor did we find more scar dehiscence at 1 month attributable to levobupivacaine, as others have reported [24]. The maximum recommended dose in a single injection is 150 mg, which corresponds to 30 mL as a 5 mg/mL solution. Moreover the maximum recommended dose over a 24-hour period is 400 mg [25]. We therefore chose to inject 10 mL as a 5 mg/mL solution to remain below the toxic dose. Pain was assessed for the first 48 hours at rest and while moving. Although the potential effect of long-acting local anesthetics peaks in the first 12 hours, studies show that an effect continues in the hours and even days that follow [14,16,17]. We note in our series that the mean pain scores were low with nonetheless considerable analgesic intake. Although women were asked not to take treatment routinely but only in cases of pain with NRS > 3, we cannot be certain that these oral analgesics were not used more routinely, consistent with general practices in the department (Figure 3).

We sought to study a uniform population with the least possible bias. Accordingly, we excluded operative vaginal deliveries with forceps or spatulas as well as third- and fourth-degree perineal lacerations,
Perineal infiltration with levobupivacaine was not more effective than placebo in decreasing episiotomy or laceration pain after delivery. This result is consistent with the results of a randomized controlled trial by Schinkel et al. [18], which study compared pain after infiltration of 15 mL of ropivacaine 0.75%, another long-acting anesthetic, lidocaine 1%, and a placebo for pain after episiotomy in women without operative vaginal deliveries. It showed no difference during the first 24 hours postpartum. These findings are not consistent from previous literature in other fields. Analgesic infiltrations have proved their effectiveness in reducing postoperative pain in surgery of the anal canal and the deep branches of the pudendal nerve. They are part of multimodal pain management and thus promote early rehabilitation [29].

The pain associated with episiotomy or perineal tears or lacerations thus appears to be a good candidate for infiltration of local long-acting anesthetics. Preliminary studies showed its potential interest for episiotomy. In a before-and-after study of a small number of women with and without operative vaginal deliveries, Sillou et al. [20] showed that an infiltration of 10 mL ropivacaine 0.75% effectively reduced pain in the first 24 hours postpartum. But this study was neither randomized nor blinded and combined deliveries with and without operative vaginal deliveries. Gutton et al. [19] also conducted a before-and-after study of 102 women to compare 20 mL of lidocaine and 20 mL of ropivacaine 0.75% after episiotomy in a population with and without operative vaginal deliveries. They found a significant difference in favor of ropivacaine for the pain scores during the first 48 hours. In a randomized, prospective single-blinded study of 92 women, Bolandard et al. [21] also assessed the utility of perineal infiltration with 20 mL of lidocaine 1%, or ropivacaine 0.2% and 0.75% for postpartum perineal pain management. Although perineal infiltration with ropivacaine in the two doses before perineorrhaphy did result in an absence of postpartum pain in 25% of the cases on average versus 6% in the lidocaine group and also delayed the first intake of analgesics by 10 hours, this study failed to show a significant difference in terms of pain in the different groups. Unfortunately, we had little information about this series, published only as a conference abstract. Beyond the poorer quality of the studies favoring ropivacaine, other factors may explain the non-superiority of the long-acting local anesthetic in our study. The 10-mL quantity of levobupivacaine might have been inadequate, especially because of the strong reabsorption in this area, which explains the lesser effectiveness of wound infiltration compared with plexus blocks (for the obturator nerve). Moreover, perineal pain after delivery is not localized to the area of the episiotomy but affects the entire genital area; accordingly, reducing the wound/incision pain may also be inadequate. Finally, the lack of a difference in pain between rest and motion is further support for the conclusion that levobupivacaine is ineffective in this situation. Finally, still another factor might influence these results. The studies reporting positive effects of long-acting local anesthetics included operative vaginal deliveries and had higher mean NRS scores than the studies not including such deliveries [18-21]. A low overall level of pain decreases the likelihood of detecting differences between treatment groups. Excluding patients who required an instrumental delivery, such as forceps or spatulas, may have selected patients likely to experience low levels of perineal pain after delivery. Such deliveries cause more maternal trauma and therefore more pain than spontaneous vaginal and vacuum deliveries [30]. Standard analgesia with an NSAID and oral paracetamol is not effective in 33% of women with post-episiotomy pain [31] and in 78% of women with forceps delivery [32]. Accordingly, although infiltration of long-acting local anesthetics did not appear very beneficial in a population with spontaneous or vacuum-assisted vaginal deliveries, it might merit study specifically for the populations with operative deliveries by forceps or spatulas, where it might be more useful.

### Table 3. NRS 1-month pain

|                        | Group P (N = 50) | Group L (N = 54) | P valuev |
|------------------------|-----------------|-----------------|----------|
| Pain right now         | 2 [2-3]         | 2 [2-3]         | 0.70     |
| Worst pain in the last 8 days | 1 [0-3] | 1 [0-2] | 0.44 |
| Pain during the last 8 days | 0 [0-1] | 0 [0-2] | 0.98 |
| Effect of pain on mood | 0 [0-2.5]       | 0 [0-2]         | 0.72     |
| Effect of pain on walking | 0 [0-2.5] | 0 [0-2] | 0.69 |
| Effect of pain on child care tasks | 0 [0-2] | 0 [0-2] | 0.72 |
| Effect of pain on usual chores | 0 [0-2.5] | 0 [0-2] | 0.72 |

Figure 2. Median [range] NRS for resting pain assessment during the first 48 h after suturing.

Figure 3. Median [range] NRS for mobilization pain assessment during the first postoperative 48 hours.

Associated anterior lacerations, and breech and twin pregnancies that induced maneuvers that could cause additional pain. We also excluded cases which used continuous sutures with one thread and one knot for all the plans, which reduces postpartum pain [26].

Perineal infiltration with levobupivacaine was not more effective than placebo in decreasing episiotomy or laceration pain after delivery. This result is consistent with the results of the prospective randomized study by Schinkel et al. [18], which study compared pain
Conflict of interest

None.

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