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Effectiveness of Topical Lidocaine-Prilocaine Cream for Pain Control During Femoral Artery Catheterization in Adult Patients: a Prospective Study

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Abstract

Objective—To test the effectiveness of topical EMLA cream (lidocaine 2.5% and prilocaine 2.5%) for pain control during femoral artery catheterization for neuro-endovascular procedures in adult patients.

Methods—The body habitus overlying the femoral arterial pulsation was graded as: (1) pubic symphysis and iliac crest bone protuberances visualized; (2) Pubic Symphysis and Iliac Crest bone protuberances not seen but easily palpable; (3) Pubic Symphysis and Iliac Crest bone protuberances palpable with considerable difficulty; and (4) abdominal layers fold over the femoral region. The severity of pain at femoral artery catheterization was classified using a numeric rating scale score ranging from 0 (no pain) to 10 (worst pain). The primary endpoints were the proportion of patients with excellent (score of ≤1) and failed pain control (score of ≥8).

Results—The mean (±SD) and median numeric rating scale scores were 2.4 ± 2.7 and 1, respectively, in 186 patients included. The proportion of patients with excellent pain control was 49.4% [95% confidence interval (CI) 42.1%–56.7%] and failed pain control was 6.9% (95% CI 4.1%–11.6%). The body habitus was graded as 1 (n = 31), 2 (n = 61), 3 (n = 48), and 4 (n = 46). In multivariate analysis, grade 4 body habitus [odds ratio (OR) 1.8; 95% CI 1.3–2.9], grade 4 ease of cannulation (OR 2.1; 95% CI 1.2–2.7), and previous femoral artery catheterization (OR 2.5; 95% CI 1.8–4.2) were independent predictors of failed pain control. Grade 1 ease of cannulation (OR 1.6; 95% CI 1.2–3.1) independently predicted excellent pain control.

Conclusion—Topical EMLA cream as an adjunct to local lidocaine infiltration was associated with very low rates of failed pain control during femoral artery catheterization despite a relatively high rate of unfavorable body habitus.

Keywords

Femoral artery catheterization; topical anesthetic; analgesia; pain; lidocaine; prilocaine

Introduction

Femoral artery catheterization using modified Seldinger's technique is the basis of neuro-endovascular procedures [1,2]. The procedure requires percutaneous needle insertion followed by insertion of a wire into the femoral artery. The needle is withdrawn and introducer sheath placed over the wire. Local infiltration of lidocaine in the subcutaneous tissue overlying the artery is the current standard analgesia to reduce local pain during the insertion process [3]. Previous studies have advocated the use of local spray or topical anesthetic creams as adjunct to local lidocaine infiltration to reduce the pain during arterial catheterization predominantly in pediatric population [4–6]. However, despite encouraging results [5,6], such protocols have not been broadly incorporated

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into practice. We performed this prospective study to determine the effectiveness of topical lidocaine 2.5%/ prilocaine 2.5% EMLA cream [7] prior to femoral artery catheterization and factors associated with adequate and inadequate pain control in adult patients undergoing neuro-endovascular vascular procedures.

Methods

A prospective registry was maintained and the protocol for data collection was reviewed and approved by local Institutional Review Board. Informed consent was obtained from the participants. All patients who underwent nonemergent neuroendovascular procedures in awake state at a single institution were registered. EMLA cream (lidocaine 2.5% and prilocaine 2.5%) was applied at least 60 min prior to the procedure on the skin overlying the palpable femoral artery under occlusive dressing over a 5 × 5 cm area. The femoral artery access site catheterization was performed using modified Seldinger's technique by one physician (AIQ). Local infiltration of 10 ml of lidocaine (1% solution) using a 10cc sterile syringe was performed prior to insertion of percutaneous entry thin wall needle (19 Gauge). Each patient received intravenous bolus of 1 mg of midalozam and 50 mg of fentanyl prior to needle insertion.

Data Collected

The body habitus overflying the femoral arterial pulsation was classified [8] as: (1) pubic symphysis and iliac crest bone protuberance visualized on gross examination of femoral region; (2) Pubic Symphysis and Iliac Crest bone protuberances are not seen but easily palpable; (3) Pubic Symphysis and Iliac Crest bone protuberances are not seen but palpable with considerable difficulty; (4) the abdominal layers fold over the femoral region. Ease of cannulation was scored using a 4-point scale, ranging from insertion at first attempt (1), a number of minor adjustments needed (2), a second attempt required (3), or failure of 2 or more attempts (4). Body mass index (BMI) was graded by: underweight-BMI of <17 kg/m^2; normal-BMI of 17–24.9 kg/m^2; grade 1 overweight (overweight)—BMI of 25–29.9 kg/m^2; grade 2 overweight (obesity)—BMI of 30–39.9 kg/m^2; grade 3 overweight (severe or morbid obesity)—BMI greater than or equal to 40 kg/m^2. Technical details regarding the femoral artery catheterization (insertion needle and introducer sheath used) were collected including number of attempts and other adverse events. The severity of pain at femoral artery catheterization was classified using a numeric rating scale score ranging from 0 (np pain) to 10 (most severe pain ever experienced) inquired by one investigator (AIQ) from each of the patient.

Statistical Considerations

The primary endpoints were the proportion of patients with good (numeric rating scale score of 3 or less) and excellent (numeric rating scale score of 1 or less) pain control, and failed pain control (numeric rating scale score of 8 or more). Formal sample size calculations were not performed as part of the study. We wanted to at least include adequate number of patients that allowed detection of expected rates of excellent pain control with local infiltration of lidocaine. We assumed that 5% of patients who receive local infiltration of lidocaine will have excellent pain control based on the study by Spiliopoulos *et al*. [3]. Therefore, a sample size of 164 patients will allow detection of such a rate with a precision of 0.05 [9].

We also calculated the 95% confidence intervals (CIs) for rates of good and excellent pain control and failed pain control using the conservative Clopper–Pearson exact method [10]. In univariate analysis, the Bonferroni method was used for adjustment in multiple comparisons.

We performed two stepwise linear regression analyses to identify predictors of excellent pain control and failed pain control (SPSS Version 20, IBM Corp., Armonk, NY, USA). We entered age strata, gender, obesity grades, ease of cannulation grades, body habitus grades, previous femoral arterial procedure, time interval stata between EMLA application and femoral arterial catheterization (0–79 min vs. ≥80 min), presence of diabetes mellitus, and EMLA application experience (first 50 patients vs. 51–186 patients entered in registry). A p-value of <0.1 was used as entry criterion in the model and $p < 0.05$ was considered significant in the final model.

Results

A total of 186 patients (mean age ± SD, 58.3 ± 16.8; 74 were men) were included in the registry. The mean (±SD) and median numeric rating scale scores were 2.4 ± 2.7 and 1, respectively. The mean time interval (±SD) between application of EMLA cream and femoral artery catheterization was 94.3 ± 63.5 min. The proportion of patients with good and excellent pain control was 70.4% (95% CI 29.3%–36.85%) and 49.4% (95% CI 42.1%–56.7%), respectively. Failed pain control was observed in 6.9% (95% CI 4.1%–11.6%) of patients. Only one patient (0.6%) developed erythema or edema at site of application.

There appeared to be lower rates of excellent or good pain control and higher rates of failed pain control in

Table 1. Demographic and clinical characteristics of adult patients included in the study according to strata defined by pain control during femoral artery catheterization

	Excellent pain control *N* = 92	Good pain control *N* = 131	Failed pain control *N* = 13
Age strata	12 (13.0)	19 (14.5)	5 (38.4)
<45 years	36 (39.1)	44 (33.5)	5 (38.4)
45–64 years	36 (39.1)	52 (39.6)	2 (15.3)
65–79 years	8 (8.8)	16 (12.4)	1 (7.6)
≥80 years			
Gender	37 (40.2)	42 (32.0)	5 (38.4)
Men	55 (59.8)	89 (68.0)	8 (61.5)
Women			
Obesity*	2 (1.6)	3 (2.3)	0
Underweight	21 (23.3)	26 (20.1)	0
Normal	28 (30.2)	48 (36.5)	3 (23.1)
Obesity (type I)	29 (31.6)	38 (28.9)	6 (46.1)
Obesity (type II)	12 (13.3)	16 (12.2)	4 (30.8)
Morbid obesity (type III)			
Ease of cannulation*	45 (48.9)	67 (51.1)	1 (7.6)
Grade 1	32 (34.7)	39 (29.7)	3 (23.0)
Grade 2	13 (14.1)	19 (14.5)	5 (38.4)
Grade 3	2 (2.3)	6 (4.5)	4 (30.7)
Grade 4			
Body habitus*	22 (23.9)	27 (20.6)	1 (7.6)
Grade 1	39 (42.3)	53 (40.4)	2 (15.3)
Grade 2	27 (29.3)	38 (29.0)	6 (46.1)
Grade 3	4 (4.2)	13 (10.0)	4 (30.7)
Grade 4			
Previous femoral arterial procedure*	31 (33.6)	51 (38.9)	8 (61.5)
Introducer sheath	78 (84.7)	103 (78.6)	8 (61.5)
5 F	14 (15.3)	28 (21.4)	5 (38.4)
Others			
Diabetes mellitus	21 (22.8)	35 (26.7)	5 (38.4)
Time interval between EMLA application and femoral	53 (57.6)	78 (59.6)	8 (61.5)
artery catheterization	39 (42.4)	53 (40.4)	5 (38.4)
0–79 min			
≥80 min			
EMLA application experience	21 (42)	33 (66)	7 (14)
0–50	71 (52.2)	98 (74.8)	6 (4.4)
51–186			

*Statistically significant.

patients aged <45 years. The ease of cannulation was rated as grade 1 (n = 61), 2 (n = 89), 3 (n = 23), and 4 (n = 13). The proportion of patients with good and excellent pain control according to ease of cannulation is provided in Table 1. There was a significantly higher rate of failed pain control in patients with higher grades (most difficult) of ease of cannulation ($p < 0.001$). The body habitus was graded as 1 (n = 31), 2 (n = 61), 3 (n = 48), and 4 (n = 46). The primary endpoints were significantly different according to strata defined by body habitus are presented in Table 1. There was a significantly higher rate of failed pain control in patients with higher grades of body habitus. There was a significantly higher rate of excellent and good pain control in patients with lower body habitus with no patient experiencing failed pain control in patients with grade 1. The rate of failed pain control was significantly higher among patients with types II and III obesity. The time interval strata between EMLA application and femoral artery catheterization were 0–79 min (n = 86) and ≥80 min (n = 58). There appeared to be a slightly lower rate of failed pain control when the EMLA application and femoral artery cannulation was ≥80 min. The rate of failed pain control was nonsignificantly higher in first 50 patients compared with later 136 patients (14% vs. 4.4%).

In the multivariate analysis, grade 4 body habitus [odds ratio (OR) 1.8; 95% CI 1.3–2.9], grade 4 ease of cannulation [OR 2.1; 95% CI 1.2–2.7], and previous femoral arterial procedure [OR 2.5; 95% CI 1.8–4.2] were independent predictors of failed pain control. Grade 1 ease of cannulation (OR 1.6; 95% CI 1.2–3.1) independently predicted excellent pain control.

Discussion

We observed a very high rate of excellent pain control in our cohort of patients treated with EMLA cream prior to femoral arterial catheterization despite a relatively high rate of unfavorable body habitus. The 95% CI of rates of excellent pain control in our EMLA-treated cohort (42.1%–56.7%) did not overlap with 95% CI described in the previous study (0.0–6.3%) [3]. The 95% CI of rates of failed pain control in our EMLA-treated cohort (4.1%–11.6%) did overlap with 95% CI described in the previous study (4.1%–15.9%) [3]. We identified certain factors that were associated with excellent and failed

pain control during femoral arterial cannulation including body habitus, ease of cannulation, and previous femoral arterial catheterization. Increasing grades of body habitus and difficulties in cannulation were associated with increased rates of failed pain control. The mean period between EMLA cream application and femoral arterial catheterization was approximately 90 min which is consistent with recommendations of previous studies demonstrating the analgesic effect after 60 min of cutaneous application and possible incremental effectiveness with 90 and 120 min of application [11–13]. There was a decrease in the rate of failed pain control in later group of patients compared with the first 50 patients treated with the protocol which may be secondary to increased familiarity of use within nurses preparing the patients.

There are some considerations relevant to local analgesia prior to femoral arterial catheterization. There are several nerves that supply the area overlying the common femoral artery region which include the iliohypogastric nerve, ilioinguinal nerve with the genital and femoral branches, and infrequently the lateral femoral cutaneous nerve [14–16]. The skin is innervated by small-myelinated nociceptive nerves which terminate in the epidermis of the skin [17–20] with highest density of nerve fibers in the epidermal tissue [21,22]. Lidocaine is a voltage-gated sodium channel inhibitor, which blocks sodium channels in the dermal nociceptors of small-myelinated nerves, thereby reducing the number of discharges upon stimulation of the innervated skin [23–25]. The EMLA cream can provide anesthesia on skin up to a depth of 3–6 mm after application [11,12] with the effect observed for 30 min after a 90-min application and up to 60 min after a 120-min application of EMLA cream. Application of EMLA for a period of 60 min or longer was found to provide effective local anesthesia in one study [13]. There is minimal systemic resorption through draining veins in cutaneous tissue [26]. The femoral artery is located between 1 and 3 cm below the skin [27–30]. Therefore, the EMLA cream is not expected to penetrate deep enough to reach the subcutaneous tissue overlying the femoral artery. The subcutaneous tissue has multiple layers consisting of fatty tissue and loose multiple laminar structures [31]. The superficial adipose layer is contained within organized, compact fascial septa which fuse with the underlying muscle fascia at particular anatomic locations. The deep layer is contained by the subcutaneous fascia above and the muscle fascia [32]. There are several cutaneous nerve fibers and anastomosing rami most prominent among the layers below the dermis and reduced innervation (and pain generation) within the deeper layers of subcutaneous tissue.

Our study has certain limitations which should be considered prior to interpretation. We did not have a control group [33]. Therefore, the estimate of effectiveness of the EMLA cream application might be higher due to nonspecific effects of treatment (placebo response) [34] as patients are unlikely to doubt whether they have been given an active treatment [35]. However, the frequency of pain perception with femoral artery cannulation is relatively well understood from previous studies and placebo effects are minimal because patients do not perceive the cream as active intervention. We used verbally administered numeric rating scale to measure the pain intensity that has been validated in previous studies for both its ability to identify clinical responsiveness and comparability to visual analog scale [36,37]. Several studies have recommended numeric rating scale on the basis of higher compliance rates, better responsiveness and ease of use, and good applicability relative to visual analog scales [38]. The EMLA cream was placed by nurses over palpable femoral artery in the femoral region. Since the application was focused on anticipated site of femoral arterial catheterization, a higher response could be expected if interventional physicians identified the site of EMLA application but such approach may not be practical.

Application of EMLA cream prior to femoral arterial catheterization appeared to very high rate of excellent pain control. EMLA cream is cheap and readily available and was not associated with any major adverse consequences and could be easily incorporated into preparatory routine in patients undergoing femoral artery catheterization for any indication.

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