The Efficacy of Lidocaine-Prilocaine Cream to reduce Pain in Genetic Amniocentesis

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Objective: *Evaluate whether local anesthesia by lidocaine-prilocaine cream decreases maternal pain during mid-trimester genetic amniocentesis.*

Material and Method: *This randomized controlled study of mid-trimester genetic amniocentesis was conducted between 1 October 2006 and 30 April 2007.Pregnant women were randomized to receive lidocaine-prilocaine cream or placebo cream 30 minutes prior to amniocentesis. Patients, blinded to allocation, recorded anticipated and actual pain before and after the procedure. The visual analog score (VAS) was evaluated, using a 0-10 scale.*

Results: *One hundred and twenty women participated in the present study. Sixty women were randomized to lidocaine-prilocaine group. The two groups were similar with respect to clinical correlations and procedure characteristics. Anticipated pain was 6.1 $\pm$ 2.0 in the lidocaine-prilocaine group and 6.3 $\pm$ 2.3 in the placebo group (p = 0.61). Actual pain was 2.3 $\pm$ 2.2 in the lidocaine-prilocaine group and 2.9 $\pm$ 2.5 in the placebo group (p = 0.16).*

Conclusion: *Lidocaine-prilocaine cream does not decrease pain during mid-trimester genetic amniocentesis.*

Keywords: *Pain, Amniocentesis*

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Mid-trimester genetic amniocentesis is increasingly being used as a prenatal diagnosis procedure for genetic disorders in pregnant women who have advanced aged, suspected fetal chromosome abnormalities or abnormal maternal serum markers. Amniocentesis is an emotional situation and most women are apprehensive undergoing the procedure. Apart from fear of complication such as miscarriage, abnormal chromosome, many expect the procedure to be painful. There are reported data on the sensory or affective nature of pain that is associated with mid-trimester genetic amniocentesis or clinical characteristics that are associated with increased pain[1-3].

There were many studies about decreasing pain in mid-trimester genetic amniocentesis by using local infiltration of lidocaine, subfreezing needles or light pressure effleurage[4-7]. All studies reported a similar outcome compared to the controlled group. The authors were interested in the study of Van Schoubroeck et al[4] and Gordon et al[7] about local infiltration of lidocaine. Because local infiltration can cause the pain sensation to the pregnant women, the outcome of pain perception can be confounded by this infiltration. Lidocaine-prilocaine cream was studied in many medical procedures to decrease pain such as venous cannulation, prostatic biopsy with successful outcome[8,9]. In the authors' practice, local anesthesia is not routinely used in mid-trimester genetic amniocentesis. The aim of the present study was to evaluate whether the use of local lidocaine-prilocaine cream does decrease pain experience in mid-trimester genetic amniocentesis.

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Material and Method

All pregnant women, who were participated in the present study, had been referred for genetic counseling in the second trimester of pregnancy and had consented to have amniocentesis at the Maternal -

Fetal Medicine Unit, Thammasat University Hospital, Pathumthani, Thailand between 1 October 2006 and 30 April 2007.The present study was approved by the ethic committee of Faculty of Medicine, Thammasat University and received grant support from Thammasat University as well. Exclusion criteria were multiple pregnancy or severe congenital anomaly after sonographic detection, known or suspected allergy for lidocaine-prilocaine, psychiatric disease, more than one attempt of needle insertion, and changing the puncture site where the cream was applied due to fetal behavior. Informed consent was obtained beforehand. Patients were interviewed following the questions in the case record before the procedure that assessed age, parity, weight, height, history of previous amniocent-esis and abdominal surgery. The visual analog score (VAS) was used to subjectively quantify the patient's pain and anxiety. The patients were asked to indicate a point along a 10 cm horizontal continuous line from 0 to 10 (0 = no pain or anxiety and 10 = the worst imaginable pain or anxiety). The anticipated pain and anxiety before the procedure and the actual pain immediately after the procedure were recorded. All amniocentesis were performed by staff of the Maternal - Fetal Medicine Unit. After ultrasonography was performed for anomaly scan, the location of needle insertion was selected to avoid puncturing through placenta without causing fetal trauma. If the placental puncture was inevitable, the location with minimal placental thickness was chosen. The lidocaine-prilocaine cream or placebo cream 1 gm was applied at the puncture site in 3 x 3 cm^2 covered with an occlusive dressing by the assistant nurse. The patients were asked to rest for 30 minutes then amniocentesis was performed using a 22 gauge spinal needle with continuous ultrasound guidance. Approximately 18-20 mL of amniotic fluid was obtained. After the procedure, the patients routinely rested for about 15 minutes then fetal cardiac activity was checked.

The sample size calculation was based on data from the study of Lekskul N[3]. The present study reported the mean VAS = 2.7 $\pm$ 2.1. The authors calculated that if the mean score difference of 50% was clinically important. The sample size was 60 subjects per group with type I error of 5% and type II error of 10%. Statistical analysis used was performed using SPSS for windows version 14.0 software. Descriptive statistics: range, mean, standard deviation (SD) and 95% confidence interval (95% CI) as well as chi square test and t-tests were used to detect the differences, a probability value of < 0.05 was considered significant.

Results

One hundred and twenty pregnant women entered the present study. Sixty women received lidocaine-prilocaine cream, while sixty women received placebo cream. Seven women in the lidocaine-prilocaine cream group and five women in the placebo cream group were excluded from the present study because of changing of puncture sites or multiple procedures. The patients' characteristics are described in Table1. No significant differences between both groups were detected.

Table 1. Patients' characteristics

	Lidocaine-Prilocaine (n = 60)	Placebo (n = 60)	p-value	95%CI
Age (years)				
Mean $\pm$ SD	36.8 $\pm$ 3.79	36.9 $\pm$ 3.41	0.88	-1.4, 1.2
Range	25-43	27-44		
Gestational age (weeks)				
Mean $\pm$ SD	17.6 $\pm$ 1.6	17.7 $\pm$ 1.5	0.72	-0.6, 0.4
Range	17-20	17-21		
BMI (kg/m^2)				
Mean $\pm$ SD	24.4 $\pm$ 4.2	24.1 $\pm$ 3.6	0.67	-1.1, 1.7
Range	17.1-34.3	18.7-32.4		
Parity				
Mean $\pm$ SD	0.7 $\pm$ 0.8	0.6 $\pm$ 0.7	0.46	-0.1, 0.3
Range	0-3	0-3		

SD: standard deviation, CI: confidence interval, BMI: body mass index

The most indications for amniocentesis were advanced maternal age (93% in the lidocaine-prilocaine group and 95% in the placebo group) (Table 2). The clinical correlates of the patients were similar between both groups (Table 3). All samples of amniotic fluid collected had a clear colour and no complications were reported.

The pre-procedure anxiety mean VAS score were 5.6 $\pm$ 2.5 in the lidocaine-prilocaine group and 5.3 $\pm$ 3.7 in the placebo group (p = 0.60). The anticipated mean VAS of pain were 6.1 $\pm$ 2.0 in the lidocaine-prilocaine group and 6.3 $\pm$ 2.3 in the placebo group (p = 0.61). The post procedure mean VAS of pain were 2.3 $\pm$ 2.2 in the lidocaine-prilocaine group and 2.9 $\pm$ 2.5 in the placebo group (p = 0.16) (Table 4). There were no statistical differences between both groups.

Discussion

Pain is a complex, multidimensional sensation that varies in quality, strength, duration, location, and unpleasantness from one individual to another. The strength and unpleasantness of pain are neither simple nor directly related to the nature and extent of tissue damage. Amniocentesis can be an anxiety-provoking procedure, due to concern about underlying fetal abnormalities and procedure-related fetal loss, as well as pain from the needle. Multiple clinical correlations were purposed to affect maternal pain. Feber et al[1] found that the anticipated pain was nearly double the actual amount of pain experienced and the history of a prior amniocentesis was the variable associated with reducing pain. The study of Harris et al[2] assessed pain from amniocentesis found that 31% of women rated the pain as more than mild and 6.7% of women rated it as distressing or horrible. They concluded that pain was associated with increased maternal anxiety, previous amniocentesis, and insertion of the needle in the lower uterus.

The studies of Van Schoubroeck et al[4] and Gordon et al[7] used local infiltration of lidocaine prior

Table 2. Indication for amniocentesis

	Lidocaine-Prilocaine No. (%)	Placebo No. (%)	p-value
Age risk (> 35 years)	56 (93%)	57 (95%)	0.69
Genetic risk	4 (7%)	3 (5%)	

Table 3. Clinical correlates of the patients

	Lidocaine-Prilocaine No. (%)	Placebo No. (%)	p-value
Previous amniocentesis	1 (0.1%)	3 (0.5%)	0.31
Previous abdominal surgery	20 (33%)	12 (20%)	0.09
Needle insertion through placenta	8 (13%)	14 (23%)	0.15
Needle insertion at lower uterus	16 (26%)	20 (33%)	0.42

Table 4. Visual Analogue score of pain and anxiety

	Lidocaine-Prilocaine (n = 60) Mean $\pm$ SD	Placebo (n = 60) Mean $\pm$ SD	p-value	95%CI
Pre-procedure anxiety	5.6 $\pm$ 2.5	5.3 $\pm$ 3.7	0.60	-0.8, 1.4
Anticipated pain	6.1 $\pm$ 2.0	6.3 $\pm$ 2.3	0.61	-0.9, 0.5
Post-procedure pain	2.3 $\pm$ 2.2	2.9 $\pm$ 2.5	0.16	-1.4, 0.2

SD: standard deviation, CI: confidence interval

to amniocentesis and they found no benefit of local infiltration to decrease pain. The study of Van Schoubroeck et al[4] used verbal rating scale 1 to 4 and it was not blinded. In the study of Gordon et al[7], the procedure was performed by Maternal Fetal Medicine staff in 66% of the local anesthesia group and 53% of the controlled group. Moreover, they found that women perceived less pain when the procedure was performed by staff. Because local infiltration caused pain perception to the women, so the outcome can be confounded. The authors would like to evaluate the pain by using the local anesthesia without causing the pain sensation before the procedure. The strength of the present study lies in the proper randomization and blinding of the subjects to the two arms of the present study. The visual analog scale was chosen as the authors' tool for self reporting of pain and anxiety. Unlike a numerical pain scale, in which subjects assign pain intensity to discrete numbers ranging from zero to ten, the visual analog scale permits subjects to select along a continuum of values, which can then be analyzed with parametric statistical tests.

The outcome demonstrated that women's perception of anxiety and pain before genetic amniocentesis were moderate. The clinical correlates of the pain were similar in both groups. No significant differences of VAS scores in pre-procedure anxiety, anticipated pain, and post-procedure pain were found between both groups. The present results indicated no significant benefit of lidocaine-prilocaine cream on pain perception from amniocentesis as measured by the difference between the pre and post procedure VAS pain scores. The authors' finding may be explained in a number of ways. First, amniocentesis was not judged a very painful procedure. Second, local anesthesia reduced pain at the cutaneous level but not at the peritoneum. The major pain perception from this procedure derived from the peritoneum and uterus.

In conclusion, local anesthesia need not be used prior to mid-trimester genetic amniocentesis. Pre-amniocentesis counseling should emphasize the fact that, for most women, the actual pain experienced during the procedure is significantly lower than that expected.

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ประสิทธิภาพของยา lidocaine-prilocaine cream ในการลดความปวดจากการเจาะน้ำคร่ำ ตรวจทางพันธุกรรม

เด่นศักดิ์ พงศ์โรจน์เผ่า, จรินทร์ทิพย์ สมประสิทธิ์, อธิตา จันทเสนานนท์

วัตถุประสงค์: เพื่อศึกษาประสิทธิภาพของยา lidocaine-prilocaine cream ว่าสามารถลดความปวดจากการเจาะน้ำคร่ำตรวจทางพันธุกรรม

วัสดุและวิธีการ: การศึกษาแบบไปข้างหน้าในสตรีตั้งครรภ์ที่มารับการเจาะน้ำคร่ำตรวจทางพันธุกรรม ณ หน่วยเวชศาสตร์มารดาและทารกในครรภ์ โรงพยาบาลธรรมศาสตร์ ตั้งแต่วันที่ 1 ตุลาคม พ.ศ. 2549 ถึงวันที่ 30 เมษายน พ.ศ. 2550 โดยทำการแบ่งแบบสุ่มเป็นสองกลุ่มๆละ 60 ราย กลุ่มแรกได้รับยา lidocaine-prilocaine cream 30 นาทีก่อน ทำการเจาะน้ำคร่ำตรวจทางพันธุกรรม กลุ่มที่สองได้รับยาหลอก

ผลการวิจัย: ข้อมูลจากสตรีตั้งครรภ์ 120 รายที่ยินยอมเข้าร่วมการวิจัย ไม่พบความแตกต่างอย่างมีนัยสำคัญทางสถิติของคะแนนความปวด (VAS) ค่าเฉลี่ยความเจ็บปวดที่คาดไว้ก่อนจากการเจาะน้ำคร่ำ เท่ากับ 6.1 $\pm$ 2.0 ในกลุ่มที่ได้รับยา lidocaine-prilocaine cream และ 6.3 $\pm$ 2.3 ในกลุ่มที่ได้รับยาหลอก ($p = 0.61$) ค่าเฉลี่ยความเจ็บปวดหลังการเจาะน้ำคร่ำ เท่ากับ 2.3 $\pm$ 2.2 ในกลุ่มที่ได้รับยา lidocaine-prilocaine cream และ 2.9 $\pm$ 2.5 ในกลุ่มที่ได้รับยาหลอก ($p = 0.16$)

สรุป: ยา lidocaine-prilocaine cream ไม่ช่วยลดความปวด ในการเจาะน้ำคร่ำตรวจทางพันธุกรรม