Reducing Pain and Anxiety during Second Trimester Genetic Amniocentesis Using Aromatic Therapy: A Randomized Trial

Tharangrut Hanprasertpong MD*,
Ounjai Kor-anantakul MD*, Roengsak Leetanaporn MD*, Chitkasaem Suwanrath MD*,
Thitima Suntharasaj MD*, Ninlapa Pruksanusak MD*, Savitree Pranpanus MD*

** Department of Obstetrics and Gynecology, Faculty of Medicine, Prince of Songkla University, Hat Yai, Songkhla, Thailand*

Objective: *To evaluate the benefit of aromatic therapy using menthol for decrease pain perception during amniocentesis.*
Material and Method: *A prospective randomized study was conducted to compare pain level between groups of pregnant women who underwent amniocentesis with and without aromatic therapy using menthol. Visual analogue scale (VAS) was used for pain assessment. The participants were asked for their anticipated pain and anxiety level and level of pain before and immediately after the procedure.*
Results: *Three hundred seventeen pregnant women were recruited into the present study, 158 in the menthol group and 159 in the non-menthol group. Mean VAS score of the post-procedure pain and anxiety did not differ significantly between the two groups. Mean VAS score of the anticipated pain influenced the mean VAS score of the pre-procedure anxiety and post-procedure pain and anxiety irrespective of the group. Mean VAS score of the pre-procedure anxiety and post-procedure pain and anxiety increased about 0.3 cm for each 1 cm of increasing mean VAS score of anticipated pain.*
Conclusion: *Aromatic therapy using menthol was not significantly effective in reducing pain and anxiety during second trimester genetic amniocentesis.*

Keywords: *Genetic amniocentesis, Pain, Aromatic therapy, Menthol*

J Med Assoc Thai 2015; 98 (8): 734-8
Full text. e-Journal: *http://www.jmatonline.com*

Second trimester amniocentesis is a prenatal invasive procedure that is commonly performed for abnormal genetic conditions diagnosis at Songklanagarind hospital. Our complication rate was reported around 0.1%[1]. Some pregnant women refused the procedure because they fear or were concerned about pain. Previous study reported that local anesthetic drug through injection or topical application failed to effectively decrease maternal pain perception[2,3]. As an alternative medicine method, the authors found that cryoanalgesia has shown to effectively reduce pain, but music therapy has not shown benefit[4,5].

Menthol is a natural plant compound that is widely used as an alternative medicine for relieving pain, pruritus, and inflammation[6]. Menthol reduces pain sensation via both central and peripheral nervous system by several mechanisms, such as directly affect the spinal cord, blocking voltage-gated Na(+) and Ca(2+) channels, and reducing the neuronal excitability[7]. Menthol has been reported to activate olfactory receptor and trigerminal nerve via smelling and tasting, respectively[8]. The effectiveness of aromatic therapy using menthol for reducing pain and anxiety during the second trimester genetic amniocentesis has not been studied. Therefore, we conducted the present study to evaluate whether aromatic therapy using menthol could reduce the patient's pain and anxiety perception during second trimester genetic amniocentesis.

Correspondence to:
Hanprasertpong T, Department of Obstetrics and Gynaecology, Faculty of Medicine, Prince of Songkla University, Hat Yai, Songkhla 90110, Thailand.
Phone: +66-84-6360055
E-mail: htharang@medicine.psu.ac.th, tharangrut@hotmail.com

Material and Method

Subjects

This prospective computerized randomized controlled trial was conducted on pregnant women scheduled for genetic amniocentesis due to advanced maternal age during 15 and 20 weeks of gestation at the Maternal-Fetal-Medicine Unit, Department of Obstetrics and Gynecology, Faculty of Medicine, Prince of Songkla University, Thailand, between July and September 2013. All participants documented their gestational age by their last menstrual period

(LMP) or ultrasonographic biometric measurement. Exclusion criteria included presence of fetal structural malformation, multiple pregnancy, experience of amniocentesis in the current or a previous pregnancy, more than one attempt of needle insertion, history of smell or taste perception problem, history of upper respiratory tract infection or diagnosed allergic rhinitis within two weeks before the procedure, inability to read or understand the questionnaire, and refusal to enroll in the study.

Study procedures

The present study was approved by the Ethics Committee of Faculty of Medicine, Prince of Songkla University. Firstly, our hospital pre-procedural counseling for second trimester genetic amniocentesis was routinely conducted by a maternal fetal medicine midwife and the patient was asked to consent to the procedure. Then, we informed them of the details of our study and all participants were asked to provide written consent if they agreed to join the study. An interview questionnaire was used to obtain patient's demographic data, which included maternal age, body mass index (BMI), education level, religion, occupation, and history of previous abdominal surgery. The participants were then asked to indicate their pre-procedure anxiety and anticipated pain levels before undergoing the procedure using a visual analog scale (VAS). The VAS is is a 10-centimeter horizontal line that is used to assess a degree of pain. The zero (left hand end) was numbered as "no pain" and as the pain gradually increased up to right hand end (10 cm), which was numbered as the "worst possible pain". After that, all participants were randomly assigned to either the aromatic therapy group or the non-aromatic therapy group.

The study provided aromatic therapy using menthol. A menthol candy and menthol soaked mask were given to the participants in the aromatic therapy group, while the participants in the non-aromatic therapy group received only a mask without menthol. After group assignment, all participants underwent ultrasonographic examination for fetal life, fetal number, placental location, biometry, and amount of amniotic fluid assessment. Participants in the aromatic therapy group took the candy during the ultrasonographic scan and stopped at the time of antiseptic skin preparation. Participants in both groups started to put the mask on their faces at the beginning of ultrasonographic scan and removed it at the end of the needle removal process. All amniocentesis was performed under continuous ultrasonographic examination, free-hand technique, using a 23-guage spinal needle performed by the maternal fetal medicine physician who has been qualified by the Royal Thai College of Obstetricians and Gynecologists. No local anesthetic or other pain relief method was used during the procedure. Routinely, 16 to 20 mL of amniotic fluid was withdrawn and the fetal cardiac activity was checked after the procedure. Then all participants rested for at least 30 minutes before discharge from the Maternal Fetal Medicine Unit. Immediately after the procedure, each participant was asked to mark the VAS score of their post-procedure pain and anxiety perception.

Statistical analysis

Statistical analysis was performed with STATA version 10 software (StataCorp, College Station, TX). Descriptive data were presented as numbers, percentages, median, ranges, and means, standard deviations (SD). Chi-square test, Wilcoxon-Rank Sum test, Wald test, and t-test were applied to detect the differences between groups as appropriate. A p-value <0.05 was considered as statistically significant. A mixed effects random intercept linear regression module was constructed to identify the effect of menthol treatment and other effect influencing pain score.

Results

Three hundred seventeen pregnant women were recruited in the present study, 158 and 159 randomly assigned to aromatic and non-aromatic therapy groups, respectively. No participants discontinued before the end of the study. The procedure was completed in all participants with a one-time needle puncture. Table 1 showed the patient's demographic characteristics. Maternal age, BMI, education, occupation, religion, and history of previous abdominal surgery were comparable in the two groups. No complication was found during, immediately after, or two weeks after the procedure. Mean VAS score of the pre-procedural and anticipated pain and anxiety were comparable between both groups (2.75±3.40 vs. 3.06±3.19 and 5.21±1.87 vs. 5.14±2.09, respectively) and mean VAS score of the post-procedure pain and anxiety were also not significantly different (3.49±2.30 vs. 3.53±2.27, $p = 0.90$) (Table 2).

Table 3 shows the result of regression modeling of pain VAS score. There was no evidence from the treatment effect but a higher level of

Table 1. Patients' characteristics

	Menthol (n = 158)	Non-menthol (n = 159)	*p*-value
Age (years)			
Mean ± SD	37.10±2.10	37.54±2.56	0.968
Range	34-42	34-45	
BMI (kg/m^2)			
Mean ± SD	24.1±4.0	23.7±3.5	0.129
Range	16.4-36.7	17.3-35.0	
Education, n (%)			0.561
Less than primary school	59 (37.34)	62 (38.99)	
Primary school-bachelor	98 (62.03)	94 (59.12)	
Higher than bachelor	1 (0.63)	3 (1.89)	
Occupation, n (%)			0.821
Housewife	26 (16.46)	23 (14.47)	
Agriculture	13 (8.23)	12 (7.55)	
Government officer	42 (26.58)	38 (23.90)	
Other	77 (48.73)	86 (54.09)	
Religion, n (%)			0.551
Buddhist	135 (85.44)	134 (84.28)	
Muslim	22 (13.92)	25 (15.72)	
Other	1 (0.63)	0	
Previous abdominal surgery			0.160
Yes	73 (46.2)	86 (54.09)	
No	85 (53.8)	73 (45.91)	

BMI = body mass index

Table 2. Pre-procedure, anticipated, post-procedure median (range) visual analogue scores of pain and anxiety

	Menthol (n = 158)	Non-menthol (n = 159)	*p*-value
Pre-procedure anxiety	0.2 (0, 10)	2.2 (0, 10)	0.094
Anticipated-pain	5 (0, 10)	5 (0, 10)	0.982
Post-procedure pain and anxiety	3 (0, 9.7)	3 (0, 10)	0.799

Table 3. Mixed effects random intercept linear regression module of pain score

Variable	Level	Coefficient	95% CI	*p*-value
Menthol	Before	0[a]	-	0.020
	After	0.75[b]	0.18, 1.32	
Non-menthol	Before	0.34[a,b]	-0.27, 0.95	0.020
	After	0.80[b]	0.19, 1.11	
Treatment effect	Menthol Non-menthol	0.28	-0.52, 1.09	0.490
Anticipated pain (cm)	Per cm test score	0.30	0.18, 0.42	<0.001

[a,b] Coefficients not having a superscript in common differ significantly (*p*-value <0.05; Wald test)

anticipated pain was associated with an overall increase in pain score irrespective of group and time of assessment. Each 1 cm increase in anticipated pain and anxiety VAS score was associated with a 0.3 cm increase in mean VAS score of the pre- and post-procedural pain and anxiety.

Discussion

As far as the authors are ascertained, the present study is the first to evaluate the effectiveness of aromatic therapy for decreasing pain and anxiety during the second trimester genetic amniocentesis. Menthol is inexpensive and available worldwide. Our

study included only pregnant women who underwent second trimester genetic amniocentesis due to advanced maternal age, which was the most common indication for second trimester genetic amniocentesis. It failed to demonstrate that aromatic therapy using menthol could reduce patients' pain and anxiety perception during the second trimester genetic amniocentesis.

Several previous studies have evaluated the effectiveness of various other methods for reducing patients' pain and anxiety perception during the second trimester genetic amniocentesis[2-5]. It was found that only local cryoanalgesia applied to the puncture site could reduce the patients' pain and anxiety perception. The analgesic mechanism of menthol acts by its fresh odor and its induction of a cooling feeling, which is similar to cooling in cryoanalgesia[7]. The cooling effect in cryoanalgesia locally produced to the abdominal wall but the menthol acts centrally via olfactory and taste buds. The authors hypothesize that pain reduction during the second trimester genetic amniocentesis may be more pronounced when it is directly applied to the abdominal wall. Thus, the authors plan further study using menthol gel to elicit a cold sensation.

The authors found that the VAS anticipated pain was associated with the participants' VAS pre-procedure anxiety and post-procedure pain and anxiety in both groups. This finding was similar to our previous report[9]. Moreover, we showed that with each 1 cm increasing of mean VAS anticipated pain, the participants mean VAS pre-procedure anxiety and post-procedure pain and anxiety increase about 0.3 cm.

In conclusion, aromatic therapy using menthol odor and taste did not effectively reduce the pain during second trimester genetic amniocentesis due to advanced maternal age but overall the level of anticipated pain VAS influenced the participants' pre-procedure anxiety and post-procedure pain and anxiety.

What is already known on this topic?

• Amniocentesis related-complication was low.

• Cryoanalgesia has shown to effectively reduce pain during second trimester genetic amniocentesis.

What this study adds?

• Aromatic therapy using menthol odor and taste did not effectively reduce the pain during second trimester genetic amniocentesis.

• Anticipated pain VAS influenced the participants' pre-procedure anxiety and post-procedure pain and anxiety.

Acknowledgements

The authors would like to thank Mr. Leather from the International Affairs Office, Faculty of Medicine, Prince of Songkla University, Songkhla, Thailand for his editorial assistance, and Dr. Alan Geater and Miss Walailuk Jitpiboon from Epidemiology unit, Faculty of Medicine, Prince of Songkla University, Songkhla, Thailand for their help with statistical analysis.

Potential conflicts of interest

None.

References

1. Hanprasertpong T, Kor-anantakul O, Prasartwanakit V, Leetanaporn R, Suntharasaj T, Suwanrath C. Outcome of second trimester amniocentesis in singleton pregnancy at Songklanagarind Hospital. J Med Assoc Thai 2011; 94: 1288-92.
2. Gordon MC, Ventura-Braswell A, Higby K, Ward JA. Does local anesthesia decrease pain perception in women undergoing amniocentesis? Am J Obstet Gynecol 2007; 196: 55-4.
3. Pongrojpaw D, Somprasit C, Chanthasenanont A. The efficacy of lidocaine-prilocaine cream to reduce pain in genetic amniocentesis. J Med Assoc Thai 2007; 90: 1992-6.
4. Hanprasertpong T, Kor-Anantakul O, Prasartwanakit V, Leetanaporn R, Suntharasaj T, Suwanrath C. Efficacy of cryoanalgesia in decreasing pain during second trimester genetic amniocentesis: a randomized trial. Arch Gynecol Obstet 2012; 286: 563-6.
5. Hanprasertpong T, Kor-anantakul O, Leetanaporn R, Suwanrath C, Suntharasaj T, Pruksanusak N, et al. Music therapy to decrease pain during second trimester genetic amniocentesis: a randomized trial. Asian Biomed. In press 2014.
6. Gaudioso C, Hao J, Martin-Eauclaire MF, Gabriac M, Delmas P. Menthol pain relief through cumulative inactivation of voltage-gated sodium channels. Pain 2012; 153: 473-84.
7. Pan R, Tian Y, Gao R, Li H, Zhao X, Barrett JE, et al. Central mechanisms of menthol-induced analgesia. J Pharmacol Exp Ther 2012; 343: 661-72.

8. Renner B, Schreiber K. Olfactory and trigeminal interaction of menthol and nicotine in humans. Exp Brain Res 2012; 219: 13-26.
9. Hanprasertpong T, Kor-anantakul O, Geater A, Suwanrath C, Pruksanusak N, Jitpiboon W. Factors influencing pain senstation during second trimester genetic amniocentesis for advanced maternal age. Asian Bio Med. In press 2014.

การลดความเจ็บปวดและกังวลจากการเจาะตรวจน้ำคร่ำช่วงไตรมาสที่สองของการตั้งครรภ์ด้วยกลิ่นหอม

ธารางรัตน์ หาญประเสริฐพงษ์, อุ่นใจ กออนันตกุล, เรืองศักดิ์ ลีธนาภรณ์, จิตเกษม สุวรรณรัฐ, ฐิติมา สุนทรสัจ, นิลภา พฤกษานุศักดิ์, สาวิตรี พรานพนัส

วัตถุประสงค์: *เพื่อประเมินประโยชน์ของกลิ่นหอมจากเมนทอลต่อการลดการเจ็บปวดและกังวลจากการเจาะตรวจน้ำคร่ำช่วงไตรมาสที่สองของการตั้งครรภ์*

วัสดุและวิธีการ: *การศึกษาแบบไปข้างหน้าเปรียบเทียบระดับความเจ็บปวดที่เกิดจากการเจาะตรวจน้ำคร่ำช่วงไตรมาสที่สองของการตั้งครรภ์ระหว่างการได้รับและไม่ได้รับการระงับปวดด้วยกลิ่นหอมจากเมนทอล โดยประเมินด้วยมาตรวัดความปวดด้วยสายตาก่อนและหลังการเจาะตรวจน้ำคร่ำ*

ผลการศึกษา: *สตรีตั้งครรภ์ 317 คน เข้าร่วมในการศึกษา 158 และ 159 คน ได้รับและไม่ได้รับการระงับปวดด้วยกลิ่นหอมจากเมนทอล ตามลำดับ ระดับความเจ็บปวดและกังวลภายหลังการเจาะตรวจน้ำคร่ำไม่มีความแตกต่างอย่างมีนัยสำคัญระหว่างสตรีตั้งครรภ์ทั้งสองกลุ่ม ค่าเฉลี่ยความเจ็บปวดที่สตรีตั้งครรภ์คาดมีอิทธิพลต่อระดับความเจ็บปวดและกังวลทั้งก่อนและหลังการเจาะตรวจน้ำคร่ำทั้งสองกลุ่ม ระดับความเจ็บปวดก่อนและหลังการเจาะตรวจน้ำคร่ำจะเพิ่มขึ้นประมาณ 0.3 เซนติเมตร ต่อทุก 1 เซนติเมตรของความเจ็บปวดที่สตรีตั้งครรภ์คาด*

สรุป: *กลิ่นหอมจากเมนทอลไม่มีประสิทธิภาพอย่างมีนัยสำคัญในการลดความเจ็บปวดและกังวลจากการเจาะตรวจน้ำคร่ำช่วงไตรมาสที่สองของการตั้งครรภ์*
