Original Article

Reducing Pain after Second Trimester Genetic Amniocentesis by Postprocedural Cryotherapy: A Randomized Controlled Trial

Orawee Kuemanee MD[1], Densak Pongrojpaw MD[1], Athita Chanthasenanont MD[1], Sawanya Benchahong MD[1], Junya Pattaraarchachai PhD[2], Kornkarn Bhamarapravatana PhD[3], Komsun Suwannarurk MD[1]

[1] Department of obstetrics and gynecology, Faculty of medicine Thammasat University, Pathum Thani, Thailand

[2] Chulabhorn International College of Medicine, Thammasat hospital, Pathum Thani, Thailand

[3] Department of preclinic science, Faculty of medicine, Thammasat University, Pathum Thani, Thailand

Objective: To evaluate the effectiveness of cryotherapy on pain reducing after the second trimester genetic amniocentesis.

Materials and Methods: A prospective randomized controlled trial was performed at Maternal-Fetal-Medicine (MFM) Unit at Thammasat University Hospital, Thailand between December 2019 and March 2020. The participants were pregnant women who underwent amniocentesis for genetic evaluation during the study period were divided into two groups, study and control. After finishing amniocentesis, study and control groups received jelly pack at temperature 4-degree Celsius and room temperature, respectively. The pain measurement was 10-cm visual analog scale (VAS) before, during, and 15 and 30 minutes after amniocentesis. Demographic characters and VAS score were recorded and evaluated.

Results: Two hundred forty pregnant women between 15 and 22 weeks of gestation were recruited and equally allocated into two groups. There were no differences between the two group in demographic data, indication, anticipated, and actual pain scores (p=0.327 and 0.401, respectively). Median pain score at 15 and 30 minutes after the procedure in the study group were 1 and 0 (p=0.202) while in the control group it was 2 and 1 (0.039). Patients' satisfaction after finishing the procedure was not significantly different.

Conclusion: Cryotherapy was effective in decreasing maternal pain perception after amniocentesis.

Keywords: Pregnancy; Amniocentesis; Cold pack; Cryotherapy; Pain

Received 18 December 2020 | Revised 3 March 2021 | Accepted 12 March 2021

J Med Assoc Thai 2021;104(8):1235-40

Website: http://www.jmatonline.com

Second-trimester genetic amniocentesis is the most common invasive prenatal procedure. Indications were pregnant women with advanced maternal age, parenteral chromosome abnormalities, and previous offspring with chromosome abnormalities or prior diagnosis of fetal malformations using ultrasonography[1]. Even though amniocentesis was only an aspiration of amniotic fluid via a tiny spinal needle, some pregnant women refused to undergo the needed procedure. The reason for refusing the procedure was mostly the fear of pain both during and after the procedure[2]. Many women might request a pain controller to avoid experiencing pain during this invasive procedure. Aromatic therapy, music listening, cryoanalgesia, local lidocaine application, lidocaine infiltration, and oral paracetamol consumption were different pain relief methods used during amniocentesis[3-10].

Cryotherapy is one of the most widely used non-pharmacological intervention for pain control in musculoskeletal injury, gynecologic surgery, and vaginal delivery[5,11-13]. Blockage of nerve sensation conduction and decreasing soft tissue inflammation were the consequence of tissue temperature reduction. Since local anesthesia was not routinely used before amniocentesis, cryoanalgesia was a simple method to relieve the pain during the process. The aim of the present study was to evaluate the pain relieving efficacy of cryotherapy in amniocentesis procedure.

Materials and Methods

The present study was a prospective randomized

Correspondence to:

Pongrojpaw D.

Department of obstetrics and gynecology, Thammasat hospital, Pathum Thani, 12120, Thailand.

Phone: +66-81-9878817, Fax: +66-2-9269485.

Email: pongrojpaw@gmail.com

How to cite this article:

Kuemanee O, Pongrojpaw D, Chanthasenanont A, Benchahong S, Pattaraarchachai J, Bhamarapravatana K, et al. Reducing Pain after Second Trimester Genetic Amniocentesis by Postprocedural Cryotherapy: A Randomized Controlled Trial. J Med Assoc Thai 2021;104:1235-40.

doi.org/10.35755/jmedassocthai.2021.08.12338

controlled trial. It was conducted at the Maternal-Fetal Medicine Unit, Department of Obstetrics and Gynecology, Faculty of Medicine, Thammasat University Hospital, Pathum Thani, Thailand. The period of study was between December 2019 and March 2020.

The present study was approved by the Human Ethics Committee of Thammasat University (MTU-EC-OB-2-138/62). Thai clinical trial registry identification number was TCTR20191116001.

Two hundred forty pregnant women between 15 to 22 weeks of gestation who underwent genetic amniocentesis were enrolled in the present study. The exclusion criteria were multifetal pregnancy, severe congenital anomaly previously detected by ultrasonography, cases with multiple attempts of needle puncture during the procedure, cases with changing the puncture site due to fetal behavior, maternal psychiatric disorder, those with contraindication to cold therapy, and with refusal to participate in the present study. Subjects were divided into two groups, study and control, by computer generated random number, prior to amniocentesis. The participants received a sealed envelope with label of randomization number. The sealed envelope was opened after finishing the amniocentesis by the assisting nurse. Both groups received standard medical care after the procedure. Jelly pack with room or cold temperature was applied immediately at surgical site after the procedure to the control and study group, respectively.

Pregnant women with indication for second trimester amniocentesis for genetic evaluation had the procedure performed by certified staff of the Maternal-Fetal Medicine Unit, Department of Obstetrics and Gynecology, Thammasat University Hospital. Pre-procedural counseling was performed by a certified nurse in the Maternal-Fetal Medicine Unit. Counseling contents included indication, steps of procedure, post procedural care, and possible complications. Subjects were recruited and randomized into two groups with simple random sampling methods. Inclusion and exclusion criteria were reviewed before written informed consent were signed by the participants. Structural questionnaire was given via interview by certified nurses. Demographic data included age, body weight, height, education, occupation, income, gestational age, parity, previous delivery, history of abortion, underlying illness, previous obstetrical or gynecological surgery, parity, and history of genetic amniocentesis in previous gestation. The visual analog scale (VAS) is a subjective pain measuring method that is recorded by making a mark along a 10-cm horizontal line. Pain level ranged from zero to ten centimeters as no pain to the worst pain. VAS was used for pain evaluation before the procedure to quantify patients' anticipated pain level (T_a). Expected pain before the procedure was estimated by participants and data given during interview. This was used for baseline control by VAS method.

All participants underwent ultrasonography to detect fetal anomalies, amniotic fluid pocket, and placenta location. The genetic amniocentesis procedure was performed by the staff at the Maternal-Fetal Medicine Unit. Amniocentesis was performed by free-handed, aseptic technique under continuous ultrasonographic guidance. A 22-gauge spinal needle (Terumo® Spinal needle, Terumo corp., Japan) was used in this procedure. No local analgesia was used during the procedure. Eighteen to twenty ml amniotic fluid was aspirated and placed for further investigation. Ultrasonography was immediately performed to check fetal cardiac activity certainty after the procedure. The puncture site was then covered with a waterproof occlusive dressing by an assistant nurse. Immediately after the intervention, the participants were interviewed to qualify their pain perception during the amniocentesis (T_0) by using the same VAS. Following the procedure, the patients routinely rested for 30 minutes. VAS after procedure were interviewed at 15 and 30 minutes (T_{15} and T_{30}).

Participants who were assigned as study and control group received jelly pack at –4°C and room temperature, respectively. Ice jelly pack (Siriraj Cold-Hot Pack, Thailand) was kept in the refrigerator at –4°C for at least six hours before using in the study group. A jelly pack was placed on patients' lower abdomen at the puncture site over the waterproof gauze pad for 30 minutes. Post-procedural and cryotherapy complication were observed and recorded by medical team before discharge.

The sample size was calculated from a standard deviation of post-procedure pain and anxiety of the control group (SD 1.58) based on the study of Hanprasertpong et al[5]. The alpha and beta were set at 0.05 and 0.20, respectively. One hundred eight subjects for each group would provide 80% power at the 0.05 significance level. Given a 10% dropout rate, the total participants to be recruited were 120 for each group.

Statistical analyses were performed by using IBM SPSS Statistics for Windows, version 23.0 (IBM Corp., Armonk, NY, USA). T-test was using for calculated continuous data and illustrated by

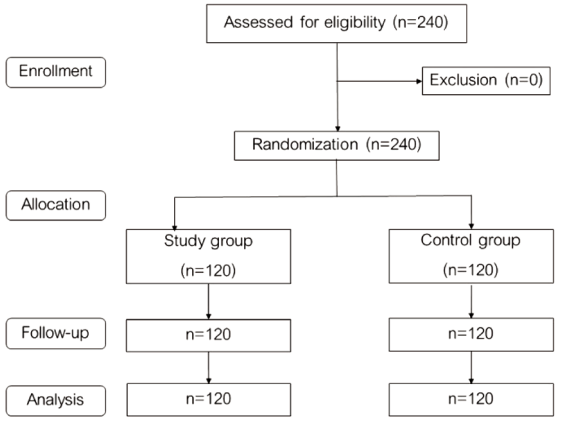

Figure 1. CONSORT flow diagram.

Study: cryotherapy received group, Control: non-cryotherapy received group

mean and standard deviation. The chi-square test and cross tabulation were workout for categorical data as shown in Table 1 and 2. The VAS score was analyzed with the use of the Mann-Whitney U test. The level of statistical significance was set at a p-value of less than 0.05.

The primary outcome was a measurement of VAS before amniocentesis (T_a), immediately (T_0), 15 minutes (T_{15}), and 30 minutes (T_{30}) after the procedure. The secondary outcome was the patient satisfaction score after finishing the procedure and take a rest for 30 minutes with a score of 0 as the lowest 0 and 10 as the highest.

Results

Two hundred forty pregnant women were recruited and divided equally into two groups. The study and the control group participants received cryotherapy and non-cryotherapy after their amniocentesis procedure, respectively. There was no dropout of the participants during the study (Figure 1).

Demographic characters are described in Table 1. Mean age of participants in the present study was around 36 years old. Body mass index (BMI) averaged at 25 kg/m². Most of participants had one living child. Ninety percent of the participants had an education level of less than bachelor's degree. Three-quarter of the participants received a monthly income from either the private or the government sector. Both groups showed no significant differences.

The most indication for amniocentesis in the present study was 89% advanced maternal age of more than 35 years old at estimated delivery date (Table 2). There was no significant difference between both groups.

Table 1. Characteristics of the patients (120 participants per group)

	Study (n=120); n (%)	Control (n=120); n (%)	p-value
Age (years); mean±SD (range)	36.8±3.7 (22 to 45)	36.5±3.9 (18 to 44)	0.518
BMI (kg/m^2); mean±SD (range)	24.9±4.2 (15.6 to 37.9)	24.7±4.1 (16.9 to 43.7)	0.691
Parity; mean±SD (range)	0.8 (0 to 4)	0.8 (0 to 5)	0.742
Education			
< Bachelor	113 (94.3)	108 (90)	0.232
≥ Bachelor	7 (5.7)	12 (10)	
Occupation			
Government officer	14 (11.7)	19 (15.8)	0.721
Business owner	18 (15)	15 (12.6)	
Salaried employee	77 (64.3)	77 (64.7)	
Others	11 (9.2)	9 (7.5)	
Previous surgery	30 (25)	40 (33.3)	0.156

Study=cryotherapy received group; Control=non-cryotherapy received group; BMI=body mass index; Others=housewives, students; Previous surgery=previous abdominal surgery; SD=standard deviation

Table 2. Indication for amniocentesis (120 participants per group)

	Study (n=120); n (%)	Control (n=120); n (%)
Age ≥35 years	109 (90.9)	105 (87.6)
Family history	3 (2.5)	7 (5.8)
Abnormal test	7 (5.8)	4 (3.3)
Patient's need	0 (0.0)	1 (0.8)
Previous abnormality	0 (0.0)	3 (2.5)
Abnormal finding in USG	1 (0.8)	0 (0.0)

Study=cryotherapy received group; Control=non-cryotherapy received group; Family history=family history of chromosome abnormality; Abnormal test=abnormal prenatal screening test; Previous abnormality= previous child with chromosome abnormality; USG=ultrasonography

Before amniocentesis procedure, both groups had median perceived expected pain (T_a) from the procedure at 5.

Immediate pain level (T_0) after procedure of the study and the control groups were 3.5 and 4.0, respectively, without statistical difference. Participants in the study group reported lower pain score level than the control group at 15 and 30 minutes after procedure with statistically significant difference as shown in Figure 2.

Patient satisfaction after finishing the procedure and 30 minutes rest in both groups were the same,

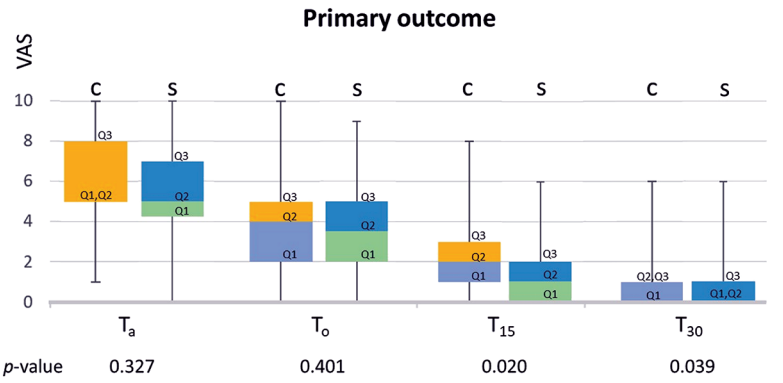

Figure 2. Compare box plot of VAS between control and study group.

VAS: visual analog scale, c: control group, s: study group, Ta: anticipated pain score, T0: actual pain, T15: Pain score at 15 minutes after amniocentesis, T30: Pain score at 15 minutes after amniocentesis, Q1: first quartile, Q2: second quartile, Q3: third quartile

excellent, at median score of 10. There was no significant difference between both groups (Figure 2).

Discussion

Pain is an unpleasant sensation. It varies individually because of experiences. Associated potential tissue damage results in significant suffering. Second-trimester genetic amniocentesis can be a painful procedure that may cause patients' emotional distress and anxiety[12].

Participants with indication for amniocentesis had more concern of possible abnormality for their fetuses. Pain from amniocentesis was a sensation caused by the penetration of a tiny gauge 22 spinal needle through the amniotic cavity to collect amniotic fluid for chromosome study. It was known that anxiety could aggravate the pain more than the actual pain.

The present research explored the use of cryotherapy to alleviate pain sensation subjects normally felt at post amniocentesis procedure. The result showed that cryotherapy, which is a non-pharmacologic application, was well accepted by patients in the study group. Homkrun et al's study (2019) revealed the efficacy of lidocaine spray application before amniocentesis[8]. It was a pharmacological application. The current study utilized a non-pharmacological method with no extra procedure time. The immediate cold application at amniocentesis site reduced post procedure pain for 30-minute's duration with statistical significance. The cold pack could be re-sterilized and reuse with no efficacy reduction.

Elimian et al's work illustrated the efficacy of local injection of lidocaine before amniocentesis[9]. Pain alleviation from the application was effective only for a short period during the procedure. Local infiltration of lidocaine was limited only to the abdominal wall. Amniocentesis procedure caused pain from the needle penetration through skin, subcutaneous fat, subcutaneous tissue, abdominal muscle, parietal, and visceral peritoneum. Amniocentesis fluid collection needle penetration was driven deeper than the needle penetration at lidocaine infiltration site. Pain induced by peritoneum irritation, namely parietal and visceral peritoneum, were not affected by local injection of lidocaine.

Cold therapy was used with amniocentesis in previous literature. Wax et al reported that subfreezing needle for amniocentesis was ineffective for pain relief during amniocentesis[6]. Hanprasertpong et al revealed that cold application at amniocentesis site before the procedure could minimize pain during and immediately after the procedure[5]. However, Hanprasertpong et al did not applied cold compression at amniocentesis site after the procedure. In the current study, amniocentesis was performed, then cold compression was applied at the amniocentesis site right after the procedure. The pain relief effect of cold compression in the present study was felt for a longer duration compared to what reported by Hanprasertpong et al as 30 minutes compared to only immediately after procedure. The cold application at amniocentesis site for five minutes before the procedure as used in Hanprasertpong et al's report was rather inconvenient for the amniocentetic operator. The required five minutes waiting before the procedure could begin, the condition of wet operative site from cold application, and the possibility of the needle penetration site alteration due to normal continuous fetal movement were inconvenience

factors for the amniocentetic process. However, the pain difference among the study and the control group at 15 and 30 minutes was only slightly different at only one point. The cold application immediately applied after the procedure to the amniocentetic site could alleviate and provide satisfaction among the participants. There was no harmful effect, and it is easy to practice.

Tuaktaew et al's pharmacological intervention showed that oral paracetamol at one hour before amniocentesis could reduce pain perception during and thereafter the procedure for two hours[10]. Pre-amniocentesis counseling and pre-medication were needed for the participants to take oral paracetamols at adequate time prior to the procedure. Alternative pain treatments using psychotherapy were reported. Aromatherapy and music therapy were effective in calming and relaxing amniocentesis participants. However, both therapies were ineffective for pain reduction before, during, and after the amniocentesis procedure[3,4].

Conclusion

Cryotherapy is a simple, cost-effective non-pharmacological method for pain management in amniocentesis patients. The outcome of the current study demonstrated that cryotherapy could successfully reduce pain after amniocentesis for 30 minutes.

What is already known on this topic?

Second-trimester genetic amniocentesis is the most common invasive prenatal procedure. Amniocentesis is only an aspiration of amniotic fluid via a tiny spinal needle. Fear of pain both during and after the procedure were the major reason for refusal of this procedure. Cryotherapy is one of the most widely used non-pharmacological intervention for pain control in musculoskeletal injury, gynecologic surgery, and vaginal delivery. Blockage of nerve sensation conduction and decreasing soft tissue inflammation were the consequence of tissue temperature reduction. Cryoanalgesia is a simple method to relief the pain during the process.

What this study adds?

Cryotherapy is simple and easy applicable to reduce pain after amniocentesis for 30 minutes post procedure.

Acknowledgments

The present study was supported by Thammasat University Research Fund in year 2019. The authors would like to thank all the nurses of the Maternal-Fetal Medicine Unit, Department of Obstetrics and Gynecology, Faculty of Medicine, Thammasat University Hospital for their assisting in the present study.

Conflicts of interest

The authors declare no conflict of interest.

References

1. Cunningham FG, Leveno KJ. Prenatal diagnosis. In: Cunningham FG, Lenovo KJ, editors. Williams obstetrics. 25th ed. New York: McGraw-Hill Education; 2018. p. 277-99.
2. Sadlecki P, Grabiec M, Walentowicz P, Walentowicz-Sadlecka M. Why do patients decline amniocentesis? Analysis of factors influencing the decision to refuse invasive prenatal testing. BMC Pregnancy Childbirth 2018;18:174.
3. Hanprasertpong T, Kor-anantakul O, Leetanaporn R, Suwanrath C, Suntharasaj T, Pruksanusak N, et al. Reducing pain and anxiety during second trimester genetic amniocentesis using aromatic therapy: A randomized trial. J Med Assoc Thai 2015;98:734-8.
4. Hanprasertpong T, Kor-anantakul O, Leetanaporn R, Suwanrath C, Suntharasaj T, Pruksanusak N, et al. Music listening to decrease pain during second trimester genetic amniocentesis: A randomized trial. J Med Assoc Thai 2016;99:1272-6.
5. 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.
6. Wax JR, Pinette MG, Carpenter M, Chard R, Blackstone J, Cartin A. Reducing pain with genetic amniocentesis-A randomized trial of subfreezing versus room temperature needles. J Matern Fetal Neonatal Med 2005;18:221-4.
7. 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.
8. Homkrun P, Tongsong T, Srisupundit K. Effect of Xylocaine spray for analgesia during amniocentesis: a randomized controlled trial. Prenat Diagn 2019;39:1179-83.
9. Elimian A, Goodman JR, Knudtson E, Wagner A, Wilson P, Williams M. Local anesthesia and pain perception during amniocentesis: a randomized double blind placebo-controlled trial. Prenat Diagn 2013;33:1158-61.
10. Tuaktaew T, Sudjai D, Pattanavijarn L. Oral paracetamol premedication effect on maternal pain in amniocentesis: a randomised double blind placebo-

controlled trial. J Obstet Gynaecol 2018;38:1078-82.
11. Piana LE, Garvey KD, Burns H, Matzkin EG. The cold, hard facts of cryotherapy in orthopedics. Am J Orthop (Belle Mead NJ) 2018;47.
12. Chumkam A, Pongrojpaw D, Chanthasenanont A, Pattaraarchachai J, Bhamarapravatana K, Suwannarurk K. Cryotherapy reduced postoperative pain in gynecologic surgery: A Randomized Controlled Trial. Pain Res Treat 2019;2019:2405159.
13. East CE, Begg L, Henshall NE, Marchant PR, Wallace K. Local cooling for relieving pain from perineal trauma sustained during childbirth. Cochrane Database Syst Rev 2012;(5):CD006304.