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Original Research

Easing the Pain: Lignocaine Spray in Mid-Trimester Amniocentesis – A Randomized Double-Blind, Placebo-Controlled Trial

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Abstract

Background: To evaluate the effect of lignocaine spray on maternal pain perception during mid-trimester amniocentesis compared to placebo.
Methodology: This was a double-blinded, prospective, randomized controlled trial conducted at a tertiary teaching hospital in Western Rajasthan. Singleton pregnancies between 15- and 24-weeks' gestation undergoing amniocentesis were included. Participants were randomly assigned to receive either lignocaine spray or placebo (normal saline). Pain was assessed using the Visual Analogue Scale (VAS), Verbal Rating Scale (VRS), and Numerical Rating Scale (NRS). A total of 138 women were enrolled, with 69 receiving lignocaine spray and 69 receiving placebos.
Results: Pain perception measured by VAS showed no significant difference between the lignocaine and placebo groups ($p = 0.412$). VRS and VAS demonstrated a positive correlation ($r = 0.692$, $p < 0.001$). Median VAS scores at 30 minutes post-procedure were significantly lower in the lignocaine group ($p = 0.008$). The Kappa agreement between VAS and VRS was found to be 59.20%. No significant difference in procedure-related complications was observed between groups.
Conclusion: The study demonstrates no significant difference in VAS scores or secondary outcomes between the lignocaine and placebo groups, suggesting that lignocaine spray may not provide additional benefit for pain relief in amniocentesis.

Keywords: Amniocentesis; Lignocaine Spray; Pain Perception; Pregnancy.

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Quick Response Code:

Introduction

Amniocentesis is a cornerstone of prenatal diagnosis, yet the associated pain and discomfort remain a concern for patients and practitioners. This procedure is often conducted without anaesthesia, as the discomfort is generally mild and transient, which most patients can manage. However, it is crucial to acknowledge that some patients experience notable discomfort and anxiety due to procedural pain. Maternal movement caused by this discomfort can complicate the procedure and increase risks for the fetus. In addition to the potential risks of miscarriage or abnormal results, many women anticipate that amniocentesis will be painful and uncomfortable. Consequently, it is common for patients to expect the administration of local anaesthesia before the procedure, as they believe it will significantly reduce their pain experience. This expectation is valid, as local anaesthesia effectively numbs the treatment area and can considerably alleviate discomfort. [1]

While local anaesthesia can reduce pain, it is important to recognise that some mild sensations or discomfort may still be felt, especially if the procedure involves deeper structures or if the anaesthetic has not fully taken effect. Moreover, the factors influencing pain, anxiety, and related elements are not well understood. Current pain management techniques primarily depend on the operator's skill and patient counselling, with limited use of local anaesthetics. [2]

Although topical lignocaine has demonstrated effectiveness in various minimally invasive procedures, its role in amniocentesis remains underexplored. This study aimed to determine the effect of local anaesthesia (Lignocaine spray) on maternal pain perception during amniocentesis compared to placebo (normal saline spray).

Material and Methods

Study Design and Participants:

This was a single-centre, randomized, double-blind, placebo-controlled trial conducted at a tertiary-level teaching hospital in Western Rajasthan between September 2020 and February 2022. The trial adhered to the CONSORT guidelines and was registered prospectively before the participants were enrolled. Women with a singleton pregnancy and a gestational age of 15-24 weeks, determined by a reliable last menstrual period and sonographic biometry during the first trimester of pregnancy (11 weeks to 13 weeks 6 days) undergoing amniocentesis, were included in the trial. Women who refused to participate in the study, those with a history of Lignocaine allergy and women with abnormal sensory function based on medical history were excluded from the study.

Ethical approval from the Institutional Ethics Committee (Certificate Reference number: AIIMS/IEC/2020/3144) and registration with the Clinical Trial Registry of India (CTRI/2020/10/028469) were obtained.

Randomization and Blinding:

A total of 138 eligible pregnant women were randomly assigned to either the intervention group (Group A) or the control group (Group B). The block randomization method was employed, using blocks of six participants. Computer-generated random sequences were created using online software. These sequences were then used to prepare 138 identical, opaque, sealed envelopes by an individual who had no role in assessing eligibility or recruiting participants. Each time an eligible patient provided written consent for the study, this individual selected one sealed envelope from the corresponding block immediately before the procedure. This envelope was then handed over to the investigator. Based on the code inside the envelope, the patient was assigned to either group A or group B.

Both the participants and the clinician performing the amniocentesis remained unaware of which agent was sprayed on the abdomen. This was accomplished using similar dispensers for both drugs during the spraying process. Additionally, it was ensured that the drugs were monitored for their expiry dates and maintained in a sterile condition.

Intervention:
Before the procedure, the participants were asked to provide a baseline pain score using a 10-cm visual analogue scale (VAS). This scale is calibrated with "no pain" at one end and "extreme pain" at the other. Each participant marked a perpendicular line on the scale, and the distance to the base of the line was measured in centimetres. Concurrently, a verbal rating scale (VRS) and numerical rating scale (NRS) were employed. This baseline pain scoring was done to familiarise the participants with the rating process after the procedure.

All participants underwent the amniocentesis procedure using 22-gauge needles while adhering to standard protocol.Before the needle (22 gauge spinal needle) puncture at the identified site, the 10% lignocaine/placebo was sprayed on the abdominal wall at the planned puncture site according to the randomised code in the dose of 8 puffs (equal to 80 mg of 10% Lignocaine spray) or 8 puffs of sterile normal saline (placebo) respectively, and then the clinician waited for 1 minute before needle puncture. The procedure was then performed by experienced operators using a standardised technique.

Outcome Measures:
Primary Outcome: Pain perception immediately after the procedure was assessed using a 10-cm Visual Analog Scale (VAS) (0 = no pain, 10 = extreme pain). Additionally, pain perception was analysed using the Numerical Rating Scale (NRS)and the Verbal Rating Scale (VRS).

Secondary outcomes: Included agreement between the different types of pain scores, patient-reported discomfort and anxiety levels using a predefined questionnaire, other factors like number of needle pricks or transplacental entry and procedure-related complications (e.g., bleeding, leakage of amniotic fluid, infection).

Statistical Analysis

Sample size estimation assumed a mean difference of 1.0 in VAS scores between groups with a standard deviation of 2.0, providing 80% power at a 5% significance level based on a previous study by Homkrun et al. [1]. Using these parameters and taking $Z_{(1-\alpha/2)}$ =1.96; $Z_{(1-\beta)}$ = 0.842, μ_d = 1.0 and applying formula n $=\frac{[1.96+\ 0.842]^2\ (2)(4)}{1}$= 62.8 ≅ 63 sample size in each group was calculated. After accounting for a 10% attrition rate, the final sample size was 138 patients with 69 in each group.

Data were collected, coded, and then entered in an IBM-compatible computer using SPSS (Statistical Package for Social Sciences) version 23. Quantitative variables were expressed as a proportion and median with IQR (interquartile range) or mean with standard deviations. Mann-Whitney U test, Pearson's correlation, and chi-square tests were applied, with $p < 0.05$ considered significant.

Results

A total of 138 women were enrolled and randomly assigned to two groups, wherein 69 received lignocaine spray (Group A) and 69 received normal saline spray (Group B). **Figure 1** illustrates the CONSORT diagram detailing the recruited patients.

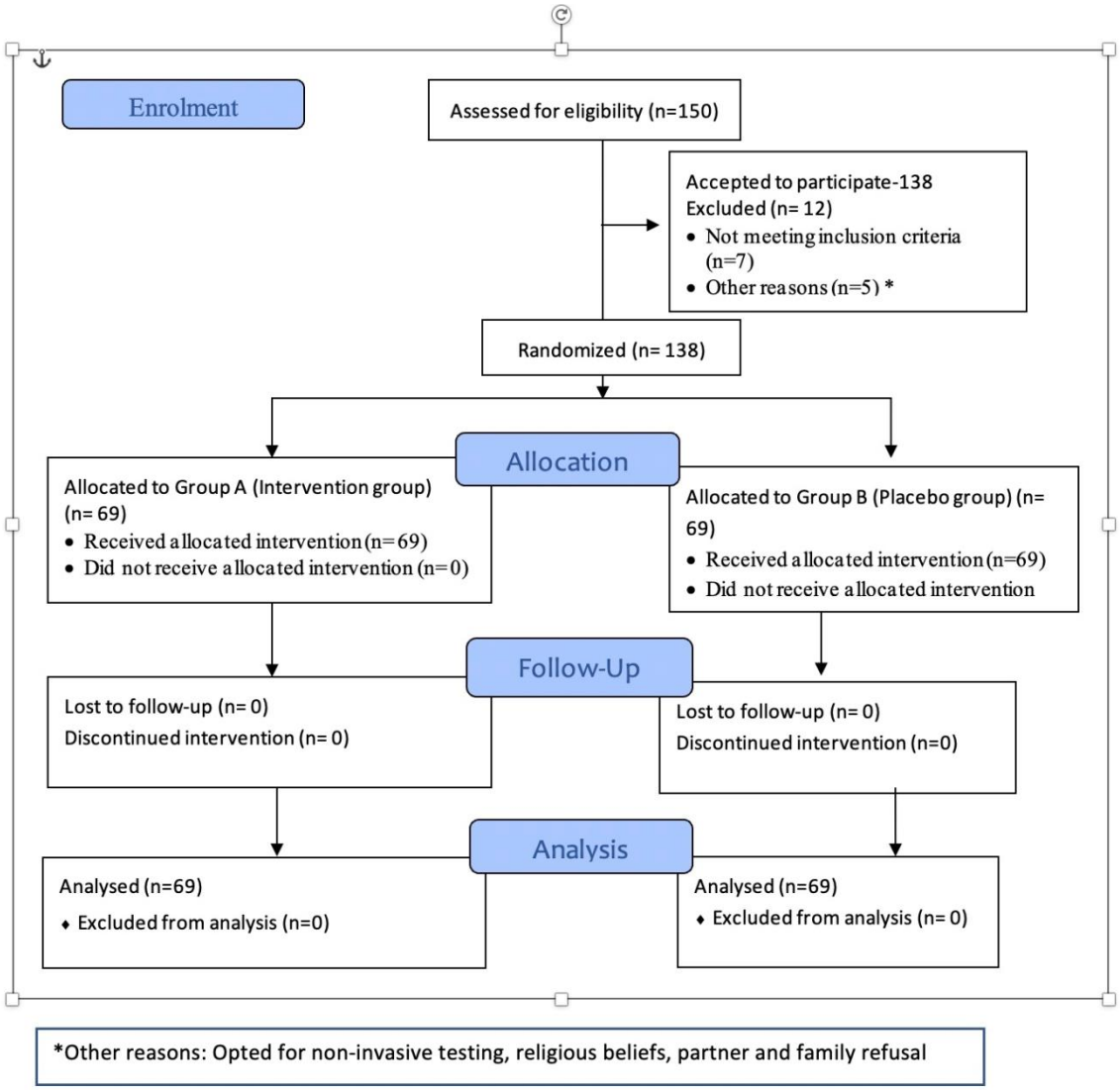

Figure 1: CONSORT Diagram for the recruited patients

Baseline Characteristics: The two groups (n=69 each) were comparable in terms of age, gestational age, and indication for amniocentesis. [Table 1]

Table 1: Baseline characteristics of subjects in the lignocaine and placebo groups

Baseline Characteristics	Group A (Lignocaine spray)	Group B (Placebo)	Significance
Age			
(Mean ± 2SD) years	29.30±5.02	28.65 ±5.04	*P= 0.448*
Socioeconomic Status			
Lower	4(5.80)	6(8.70)	*P=0.729*
Lower middle	41(59.42)	43(62.32)	
Upper lower	20(28.99)	16(23.19)	
Upper middle	4(5.80)	3(4.35)	
Upper	0	1(1.45)	
Education			
Primary	14 (20.29)	12 (17.39)	*P=0.174*
Secondary	7 (10.14)	6 (8.70)	
Higher Secondary	13 (18.84)	13 (18.84)	
Graduate	23 (33.33)	34 (49.28)	
Postgraduate	12(17.39)	4(5.80)	
Gestational age			
Mean±SD	17.56 ±2.48	17.62±3.13	*P*=0.120
Parity			
0	26(37.68%)	27(39.13)	*P=0.990*
1	27(39.13)	26(37.68)	
2	10(14.49)	11(15.94)	
3	3(4.35)	2(2.90)	
4	3(4.35)	3(4.35)	

The mean age in Group A was 29.30 ± 5.02 years, while in Group B, it was 28.65 ± 5.04 years. The majority of the subjects came from an urban background, with 58 participants (84.06%) in Group A and 59 participants (85.51%) in Group B (P = 0.812).

The most common reason for amniocentesis in this study was 'high-risk results for aneuploidy 'on first trimester combined screening (FTCS) or second-trimester biochemical screening (55.07%) followed by detecting ultrasonographic abnormalities at 21.01% and single gene disorders in the family at 11.59%. Most fetuses were found to be euploid, with 132 (95.65%) showing a normal karyotype. The incidence of aneuploidy was 4.34%. Among those with aneuploidy, 4 cases (5.50%) were identified as Down syndrome, 1 case (1.45%) as Edwards syndrome, and another case (1.45%) as Turner syndrome. Additionally, one foetus was diagnosed with thalassemia major, and another was found to have Niemann-Pick syndrome. In both cases, the parents opted for medical termination of pregnancy.

Primary Outcome:

Pain score on the Visual Analogue Scale (VAS)

The pain scores anticipated by both groups were not significantly different. The median Visual Analog Scale (VAS) score for Group A was 3.2 cm (IQR 2.3-3.8), while Group B had a median score of 3.4 cm (IQR 2.4 -3.9) [P - 0.412]

Pain score on the Numerical rating scale (NRS)

In our study, lower scores were observed when maternal pain perception was measured by the mean NRS score in Group A compared to Group B [3.71±1.40 vs 3.89 ±1.48, *P*=0.503], but the difference was not statistically significant.

Pain score on the Verbal rating scale (VRS)

Amniocentesis was reported as mildly painful by 63.8% of women in Group A and 40.58% in Group B. In addition, 33.33% of Group A and 56.52% of Group B found it moderately painful. No women in Group A described it as extremely painful, while 1.45% in Group B did. These findings were statistically significant (P=0.009).

Secondary outcomes

In the present study, the pain experienced during amniocentesis was comparable to that during venipuncture for blood sampling in 34.78% of cases. Additionally, 34.06% of participants reported feeling less pain during amniocentesis than during blood sampling, while 31.16% found it more painful, (P=0.037), indicating statistical significance.

Moreover, our study revealed that the pain experienced during amniocentesis was less than that experienced during tetanus toxoid (TT) immunization for 34.78% of the participants. In contrast, 35.51% reported feeling more pain during amniocentesis than during TT immunization, and another 35.51% felt the pain was comparable (P = 0.050).

Almost 97.1% of the participants stated that they would be willing to undergo amniocentesis again if necessary (P = 0.843). Notably, 82.61% of women reported experiencing less pain than they had anticipated during the procedure, 15.94% felt the same level of pain, and only 1.45% experienced more pain than expected. However, the difference between these groups was not statistically significant (P = 0.748). Anxiety levels were comparable between the two groups (mean Likert score 3.1 vs. 3.2, p = 0.42).

Overall, the experience during the procedure was rated as good by 83.35% of women, with 13% reporting an average experience and 3.6% describing their experience as poor. The Chi-square test indicated no statistically significant difference between the two groups (P = 0.520).

In the current study, 53.6% of women had an anterior placenta, while 46.4% had a posterior placenta. The Mann-Whitney U test revealed no significant correlation between the Visual Analog Scale (VAS) scores and the transplacental entry (P = 0.634). Additionally, no statistically significant association was found between VAS scores and the number of needle pricks (P = 0.07).

There is a positive and significant correlation between VAS and VRS. The Pearson correlation coefficient r = 0.692, with a P-value of <0.001). The Kappa agreement between VAS and VRS is 59.20% (see Table 2). There was a significant correlation between pain scores measured by VAS and NRS, with a Pearson correlation coefficient of r = 0.970, as seen in Figure 2.

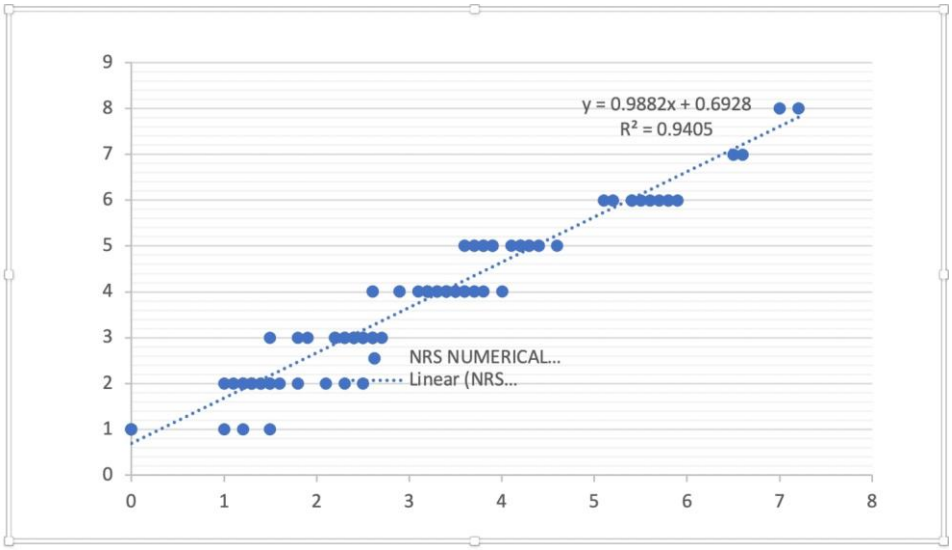

Figure 2: Correlation/Agreement between VAS and NRS

No significant difference in procedure-related complications was observed between groups. The rates of abortion and incidence of amniotic fluid leakage in this study were both recorded at 2.17%.

Table 2: Correlation between VAS and VRS

	VRS							
	None	**Mild**	**Moderate**	**Severe**	**Total**	***P* value**	**Kappa agreement**	
VAS	None	1	4	0	0	5	<0.001	59.20%
	Mild	1	49	5	0	55		
	Moderate	0	19	55	0	74		
	Severe	0	0	2	2	4		
	Total	2	72	62	2	138		

Discussion

Amniocentesis is known to produce only slight, temporary pain; however, it can still cause concern and distress for some women. There is currently insufficient data to recommend a preferred strategy for pain management during this procedure.

Lignocaine is one of the most effective anesthetic agents commonly used in medical procedures. The use of lignocaine spray is a practical and straightforward method for alleviating pain in the skin or mucosa. Numerous studies have investigated the efficacy of lignocaine spray in reducing pain during obstetric and gynaecological procedures, such as loop electrosurgical excision, intrauterine device insertion, endometrial sampling, and first-trimester surgical abortion. However, literature on its use in amniocentesis is sparse. It is important to note that pain perception is highly subjective and can be influenced by various factors, including the patient's age, pre-procedure anxiety, education, and socioeconomic status.

In our study, we evaluated 138 women, of whom seventy-seven had a gestational age between 15 and 16+6 weeks with 38 (55.07%) in Group A and 39 (56.52 %) in group B. This finding aligns with Van Schoubroeck et al. [2], which reported a mean gestational age of 15.9 ± 1.3 weeks in the local anaesthesia group and 15.8 ± 1.4 weeks in the control group. The early gestational ages observed in our study may be attributed to early screening conducted at 11 to 13.6 weeks. Although chorionic villus sampling (CVS)is routinely offered if results are positive on FTCS, most women opted for amniocentesis due to concerns about potential pain and complications during CVS. High risk for aneuploidy (55.07%) was the most common reason, followed by ultrasonographic abnormality and single-gene disorders. This finding is consistent with Karasahin E et al. [3], where the most common reason was a positive result to a screening test in 42.18%, followed by age risk.

In our study in Group A, the median VAS score was 3.2 cm, and in Group B median VAS score was 3.4 cm with a *P*-value of 0.412, which is statistically non-significant and is consistent with findings of some studies [4-6]. However, in few studies like Elimian et al. [7] and Homkuran et al. [1], statistically significant results were obtained between the two groups. For maternal pain perception measured by the NRS, the mean score was 3.71 ± 1.40 for Group A and 3.89 ± 1.48 for Group B (P=0.503). This is similar to Elimian et al, who reported a mean of 15.4 mm in the lignocaine group versus 22.4 mm in the placebo group. Gordon et al. [8] found a mean NRS of 16.0 ± 17 in the local anaesthesia group compared to 19.4 ± 18.6 in the no anaesthesia group.

Regarding the VRS, 52.2% of participants reported mild pain, 44.9% reported moderate pain, and 1.45% reported extreme pain. In contrast, Van Schoubroeck et al. [2] found that 61% of patients in the local anaesthesia group experienced no pain, with 33% reporting mild pain.

This study analysed the correlation between two pain scoring methods, the Visual Analog Scale (VAS) and the Numerical Rating Scale (NRS), to ensure reproducibility and objectivity. We found a strong correlation between VAS and NRS, with a Pearson correlation coefficient of $r = 0.970$ ($p < 0.001$), which aligns with findings from Elimian et al. ($r = 0.85$, $p = 0.01$) and Gordon et al. (2007) ($r = 0.86$, $p < 0.001$). Additionally, VAS and the Verbal Rating Scale (VRS) showed a significant correlation ($r = 0.692$, $p < 0.001$), with a Kappa agreement of 59.20%.

Various studies have explored the use of different interventions, such as aromatherapy with menthol spray, cryoanalgesia, and music therapy, to alleviate pain and anxiety during amniocentesis. However, these studies found no statistically significant differences in pre-procedural anxiety or pain perception between the two groups. These findings suggest that non-pharmacological approaches, like pre-procedural counselling and effective communication, may be equally, if not more, effective in enhancing the patient experience during amniocentesis. [4,6]

No significant correlation was found between Visual Analog Scale (VAS) scores and the needle crossing the placenta (P=0.634), aligning with Tuaktaew et al. [9] Additionally, our study showed no relationship between VAS scores and the number of needle pricks, similar to the findings by Homkrun et al. [1]

After the procedure, participants completed a questionnaire in a relaxed state, with nearly 97.1% indicating they would be willing to undergo amniocentesis again. There was no statistically significant difference between the groups, supporting results from studies where 97% and 98.65% were willing to undergo the procedure again, respectively. [2,10]

The lack of difference in VAS scores suggests that factors other than localized pain relief, such as patient anxiety, anticipation of pain, and individual pain thresholds, may play a more substantial role in determining overall procedural discomfort.

While lignocaine spray has demonstrated efficacy in other minimally invasive procedures, its application in amniocentesis may be limited due to the deeper and more complex nature of pain associated with this procedure. Additionally, the placebo effect, which is particularly relevant in interventions perceived to provide pain relief, could have influenced patient-reported outcomes.

Secondary outcomes, including anxiety levels and procedural complications, were also similar between the two groups, further supporting the conclusion that lignocaine spray may not offer a significant advantage in this setting.

The primary strength of this study lies in its design as a randomised controlled trial, which minimises potential biases and accounts for various factors that could influence pain scores, such as being a first-time mother (primigravida), puncturing through the placenta and the need for multiple needle insertions. However, the study had some drawbacks. Despite the initiation of the action of lignocaine spray, the one-minute waiting interval before proceeding with the treatment may not have been adequate to induce anaesthesia.

Conclusion:

This randomised, double-blind, placebo-controlled trial demonstrates that lignocaine spray does not significantly reduce pain or improve secondary outcomes during mid-trimester amniocentesis compared to placebo. These findings suggest that the routine use of lignocaine spray may not be necessary in this context. Future research should focus on alternative strategies to enhance patient comfort, such as personalised pre-procedural counselling and the development of less invasive diagnostic techniques.

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References

1. Homkrun P, Tongsong T, Srisupundit K. Effect of Xylocaine spray for analgesia during amniocentesis: a randomized controlled trial. PrenatDiagn. 2019 Dec;39(13):1179-1183.

2. Van Schoubroeck D, Verhaeghe J. Does local anesthesia at mid-trimester amniocentesis decrease pain experience? A randomized trial in 220 patients. Ultrasound Obstet Gynecol. 2000 Nov;16(6):536-8.
3. Karasahin E, Gungor S, Goktolga U, Keskin U, Gezginc K, Baser I. Anticipated and perceived pain from mid-trimester amniocentesis. Int J Gynaecol Obstet. 2008 Jun;101(3):290-4.
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 Dec;99(12):1272-6.
5. Albazee E, Sayad R, Alnifise M, Al-Anzi A, Alshammari F, Rasheed G, Samy A, Al-Jundy H, Bintalib MG, Abu-Zaid A. Efficacy of lidocaine local anesthesia on pain perception during amniocentesis: A meta-analysis of randomized controlled trials. Turk J Obstet Gynecol. 2022 Dec 13;19(4):327-332. doi: 10.4274/tjod.galenos.2022.99404.
6. 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 Aug;98(8):734-8.
7. 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. PrenatDiagn. 2013 Dec;33(12):1158-61.
8. Gordon MC, Ventura-Braswell A, Higby K, Ward JA. Does local anaesthesia decrease pain perception in women undergoing amniocentesis? Am J Obstet Gynecol. 2007 Jan;196(1):55.e1-4.
9. 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 Nov;38(8):1078-1082.
10. Telapol K, Bumrungphuet S, Ayudhya NI. Effect of Ethyl Chloride Spray for Pain Reduction during Amniocentesis: A non–blinded randomised controlled trial. Thai Journal of Obstetrics and Gynaecology. 2018 Jun 30:75-82.