Int. J Med. Pharm. Res. (P-ISSN: 2958-3675 | E-ISSN: 2958-3683)
Available on: https://ijmpr.in/

International Journal
of Medical and Pharmaceutical Research

ORGINAL ARTICLE **OPEN ACCESS**

10% Lignocaine Spray Versus Eutectic Mixture of 2.5% Lignocaine With 2.5% Prilocaine for Attenuating Venous Cannulation Pain in Adults: A Clinical Comparitive Study

Dr. Nanda, K. S[1]*, Dr. Mamatha, H. K[2], Dr. Muhammad Shabeer[1]

[1]Post Graduate, Department of Anesthesiology, SSSIMS &RC, Davangere, Karnataka, India
[2]Associate Professor, Department of Anesthesiology & Critical Care, SSSIMS &RC, Davangere, Karnataka, India

OPEN ACCESS

***Corresponding Author**
Dr. Nanda, K. S

Post Graduate, Department of Anesthesiology, SSSIMS &RC, Davangere, Karnataka, India

Received: 26-09-2024
Accepted: 21-11-2024
Available online: 25-11-2024

A B S T R A C T

Background*:** Venous cannulation is a common yet painful procedure in healthcare settings. This study aimed to compare the efficacy of 10% Lignocaine spray with EMLA cream for pain attenuation during venous cannulation in adults.Methods***: A prospective, randomized, comparative study was conducted on 88 adult patients undergoing elective surgeries. Patients were randomly allocated to receive either 10% Lignocaine spray (n=44) or EMLA cream (n=44) prior to venous cannulation. Pain scores were assessed using a visual analog scale (VAS), and hemodynamic parameters were recorded before and after the procedure.***Results***: The mean pain scores were 2.98 ± 1.45 for the Lignocaine spray group and 3.22 ± 1.38 for the EMLA cream group ($p = 0.4287$), indicating no significant difference in analgesic efficacy. Hemodynamic parameters, including heart rate, blood pressure, and mean arterial pressure, showed no significant differences between the groups at any time point ($p > 0.05$ for all comparisons).***Conclusion***: 10% Lignocaine spray demonstrated comparable efficacy to EMLA cream in reducing venous cannulation pain, with the advantage of a significantly shorter application time. Both methods maintained similar hemodynamic stability and safety profiles.

Keywords: Venous cannulation, pain management, topical anesthetics, Lignocaine spray, EMLA cream, hemodynamic parameters.

INTRODUCTION

Peripheral venous cannulation is one of the most frequently performed invasive procedures in modern healthcare settings, serving as a crucial gateway for the administration of medications, fluids, and blood products [1]. Despite its ubiquity, this procedure often causes significant discomfort and anxiety for patients, particularly adults who may have heightened awareness and anticipation of pain [2]. The pain associated with venous cannulation, while typically brief, can have far-reaching consequences, including increased patient distress, elevated heart rate and blood pressure, and potential difficulty in securing vascular access due to patient movement or vein constriction [3].

The importance of effectively managing pain during venous cannulation extends beyond immediate patient comfort. Inadequate pain management can lead to a cascade of physiological responses, including the activation of the sympathetic nervous system, which may result in tachycardia, hypertension, and increased myocardial oxygen consumption [4]. These effects are particularly concerning in patients with pre-existing cardiovascular conditions or those at risk of perioperative complications. Furthermore, negative experiences with venous cannulation can contribute to the development of needle phobia or heightened anxiety during subsequent medical procedures, potentially impacting long-term healthcare engagement and outcomes [5].

Recognizing the need for effective pain mitigation strategies, various approaches have been developed and refined over the years. Among these, topical anesthetic preparations have gained prominence due to their non-invasive

nature and ability to provide localized analgesia without systemic effects [6]. The eutectic mixture of local anesthetics (EMLA) cream, containing 2.5% lidocaine and 2.5% prilocaine, has long been considered the gold standard for topical anesthesia prior to venous cannulation [7]. EMLA cream's effectiveness in reducing pain scores and improving patient satisfaction has been well-documented in numerous clinical trials and meta-analyses [8].

However, despite its proven efficacy, EMLA cream has several limitations that have prompted the search for alternative options. The primary drawback is its prolonged onset of action, typically requiring 45-60 minutes of application time to achieve optimal anesthetic effect [7]. This extended waiting period can be impractical in busy clinical settings, emergency situations, or when rapid vascular access is required. Additionally, the occlusive dressing needed for EMLA application can be cumbersome and may interfere with vein visibility or skin preparation procedures [9].

In response to these challenges, attention has turned to faster-acting topical anesthetic formulations, with 10% lignocaine spray emerging as a promising alternative. Lignocaine (also known as lidocaine) is a well-established local anesthetic agent with a rapid onset of action and a favorable safety profile [10]. The spray formulation offers several potential advantages, including ease of application, quicker onset of anesthesia, and the ability to cover a larger surface area without the need for occlusive dressings [3].

The comparative efficacy of 10% lignocaine spray versus EMLA cream for attenuating venous cannulation pain in adults represents a critical area of investigation. While both agents have demonstrated analgesic properties, their relative effectiveness, onset time, duration of action, and impact on procedural success rates may differ significantly. Understanding these differences is crucial for clinicians to make informed decisions about the most appropriate topical anesthetic for specific clinical scenarios and patient populations.

This study aims to bridge the gap in current knowledge by directly comparing 10% lignocaine spray and EMLA cream in a controlled clinical setting. By evaluating pain scores, hemodynamic parameters, and potential adverse effects, we seek to provide comprehensive data to guide clinical practice. The primary objective is to determine whether 10% lignocaine spray offers comparable or superior pain relief to EMLA cream during venous cannulation in adults, with a particular focus on the speed of onset and overall efficacy.

Additionally, this research will explore the practical implications of using each anesthetic method, including ease of application, cost-effectiveness, and impact on workflow efficiency. These factors are increasingly important in modern healthcare environments, where resource optimization and patient throughput must be balanced with the delivery of high-quality, patient-centered care.

The findings of this study have the potential to significantly influence clinical practice guidelines for venous cannulation procedures. If 10% lignocaine spray demonstrates non-inferiority or superiority to EMLA cream, it could offer a valuable alternative for scenarios where rapid onset of anesthesia is crucial. Conversely, if EMLA cream maintains its superior efficacy despite its longer application time, it may reinforce its position as the gold standard for elective procedures where time allows for optimal preparation.

Furthermore, this research contributes to the broader field of pain management in medical procedures. As healthcare continues to evolve towards more patient-centric models, the importance of minimizing procedural pain and discomfort cannot be overstated. Identifying the most effective and efficient methods for pain relief during common procedures like venous cannulation aligns with global initiatives to improve patient experiences and outcomes.

In conclusion, this study addressing the comparative efficacy of 10% lignocaine spray versus EMLA cream for attenuating venous cannulation pain in adults represents a critical step in optimizing patient care. By rigorously evaluating these two topical anesthetic options, we aim to provide clinicians with evidence-based guidance for choosing the most appropriate method in various clinical contexts. The results of this research have the potential to enhance patient comfort, improve procedural efficiency, and contribute to the ongoing refinement of pain management strategies in healthcare settings.

Aims and Objectives

The primary aim of this study was to compare the efficacy of 10% Lignocaine spray versus the eutectic mixture of local anesthetics (EMLA) cream for attenuating pain during venous cannulation in adult patients. The specific objectives were to evaluate and compare the pain scores using the visual analog scale (VAS) between the two groups, to assess the hemodynamic parameters (heart rate, mean arterial pressure, systolic blood pressure, and diastolic blood pressure) before and after venous cannulation, and to document any adverse effects associated with the use of either analgesic method.

Materials and Methods

Study Design and Setting

This prospective, randomized, comparative clinical study was conducted at our tertiary care hospital from January 2024 to June 2024. The study protocol was approved by the Institutional Ethics Committee, and written informed consent was obtained from all participants prior to enrollment.

Sample Size and Randomization

A total of 88 adult patients, aged between 18 and 60 years, scheduled for elective surgeries under general anesthesia, were included in the study. The sample size was determined based on previous studies and statistical power calculations to detect a clinically significant difference in pain scores between the two groups. Patients were randomly allocated into two groups of 44 each using a computer-generated randomization sequence. Group A received 10% Lignocaine spray, while Group B received EMLA cream for topical anesthesia prior to venous cannulation.

Inclusion and Exclusion Criteria

The study included adult patients of both genders, aged 18 to 60 years, with American Society of Anesthesiologists (ASA) physical status I or II, who were scheduled for elective surgeries under general anesthesia. Patients were excluded if they refused to participate, had a history of chronic pain, local skin infection at the site of cannulation, were taking antiarrhythmic agents, had known allergies to local anesthetics, or required more than one attempt for successful cannulation. Additionally, patients with cognitive impairment that could affect pain assessment, pregnant women, and those with a body mass index (BMI) greater than 35 kg/m^2 were also excluded from the study.

Study Protocol

Upon arrival in the preoperative area, baseline vital signs including heart rate, blood pressure, and oxygen saturation were recorded for all patients. In Group A, three to four sprays of 10% Lignocaine were applied to the chosen venous cannulation site on the dorsum of the hand, covering an area of approximately 2 cm in diameter. The site was then allowed to dry for 5 minutes before cannulation was attempted. For Group B, a thick layer of EMLA cream (containing 2.5% Lignocaine and 2.5% Prilocaine) was applied to a similar area on the dorsum of the hand and covered with an occlusive dressing. The cream was left in place for 45 minutes before removal and subsequent cannulation.

Venous cannulation was performed by experienced anesthesiologists using a 20G intravenous cannula. The procedure was standardized across all patients to minimize variability. Immediately following cannulation, patients were asked to rate their pain experience using a 10-point visual analog scale (VAS), where 0 represented no pain and 10 represented the worst pain imaginable.

Hemodynamic parameters including heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP) were recorded at three time points: before the application of the anesthetic agent (baseline), immediately after venous cannulation, and 5 minutes post-cannulation. These measurements were taken using standard, calibrated monitoring equipment.

The anesthesiologist performing the cannulation and the researcher recording the data were blinded to the group allocation to minimize bias. Patients were observed for any immediate adverse effects such as local skin reactions, allergic responses, or systemic side effects throughout the procedure and in the immediate post-cannulation period.

Data Collection and Analysis

Demographic data including age, gender, weight, and ASA status were collected for all participants. The primary outcome measure was the VAS pain score reported by patients immediately after cannulation. Secondary outcome measures included changes in hemodynamic parameters (HR, SBP, DBP, MAP) from baseline to post-cannulation, and the incidence of any adverse effects.

All data were recorded on standardized forms and later transferred to a secure electronic database for analysis. Statistical analysis was performed using appropriate software, with a p-value of less than 0.05 considered statistically significant. Continuous variables were expressed as mean ± standard deviation, and categorical variables as frequencies and percentages. The independent t-test was used to compare pain scores and hemodynamic parameters between the two groups, while the chi-square test was employed for categorical data.

The study adhered to the principles of the Declaration of Helsinki and followed good clinical practice guidelines throughout its conduct. Patient confidentiality was maintained, and all data were anonymized before analysis.

RESULTS

The study compared the efficacy of 10% Lignocaine spray and EMLA cream for attenuating venous cannulation pain in adults. A total of 88 patients were included in the analysis, with 44 patients in each group. The demographic characteristics of the patients in both groups were comparable, ensuring a balanced comparison.

Pain Score Comparison

The primary outcome measure of the study was the pain score reported by patients immediately after venous cannulation, assessed using a visual analog scale (VAS). As shown in Table 1, the mean pain score for the Lignocaine spray group (Group A) was 2.98 with a standard deviation of 1.45. In comparison, the EMLA cream group (Group B) reported a mean pain score of 3.22 with a standard deviation of 1.38. Statistical analysis of these pain scores yielded a p-value of 0.4287, indicating no statistically significant difference between the two groups. This result suggests that both 10% Lignocaine spray and EMLA cream provided comparable pain relief during venous cannulation.

Hemodynamic Parameters

The study also examined various hemodynamic parameters to assess the physiological response to venous cannulation under the influence of the two analgesic methods. These parameters included heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP), measured before and after the cannulation procedure.

Heart Rate: The pre-cannulation heart rate in Group A (Lignocaine spray) was 76.02 ± 5.48 beats per minute, while in Group B (EMLA cream), it was 76.19 ± 5.21 beats per minute. The difference was not statistically significant ($t = -0.14$, $p = 0.886$). Post-cannulation, the heart rates were 75.38 ± 5.95 and 76.72 ± 4.66 beats per minute for Groups A and B, respectively. Again, this difference did not reach statistical significance ($t = -1.45$, $p = 0.151$).

Systolic Blood Pressure: The pre-cannulation SBP in Group A was 120.32 ± 8.10 mmHg, and in Group B, it was 119.93 ± 7.48 mmHg. This difference was not significant ($t = 0.23$, $p = 0.818$). Post-cannulation, the SBP values were 121.39 ± 8.61 mmHg for Group A and 120.59 ± 7.83 mmHg for Group B, showing no significant difference ($t = 0.52$, $p = 0.603$).

Diastolic Blood Pressure: The pre-cannulation DBP for Group A was 81.39 ± 5.88 mmHg, and for Group B, it was 81.48 ± 6.02 mmHg. The difference was not statistically significant ($t = -0.07$, $p = 0.946$). After cannulation, the DBP values were 81.54 ± 6.76 mmHg and 81.75 ± 5.45 mmHg for Groups A and B, respectively, again showing no significant difference ($t = -0.17$, $p = 0.862$).

Mean Arterial Pressure: The pre-cannulation MAP in Group A was 94.37 ± 7.19 mmHg, while in Group B, it was 94.29 ± 7.11 mmHg. This difference was not significant ($t = 0.05$, $p = 0.960$). Post-cannulation, the MAP values were 94.98 ± 7.96 mmHg for Group A and 94.78 ± 6.66 mmHg for Group B, showing no significant difference ($t = 0.15$, $p = 0.883$).

The analysis of hemodynamic parameters revealed no statistically significant differences between the two groups at any time point. Both pre-cannulation and post-cannulation measurements of HR, SBP, DBP, and MAP were comparable between the Lignocaine spray and EMLA cream groups. These findings suggest that both analgesic methods had similar effects on the patients' cardiovascular responses to venous cannulation.

Adverse Effects

Throughout the study, patients were monitored for any adverse effects related to the use of either 10% Lignocaine spray or EMLA cream. No significant adverse events were reported in either group. Minor local reactions, such as transient erythema at the application site, were observed in a small number of patients in both groups, but these were self-limiting and did not require any intervention.

In summary, the results of this study demonstrate that 10% Lignocaine spray and EMLA cream provide comparable pain relief during venous cannulation in adults. Both methods were associated with similar pain scores and showed no significant differences in their effects on hemodynamic parameters. The absence of significant adverse effects in both groups further supports the safety profile of these topical analgesic methods for venous cannulation.

Table 1: Pain Score Comparison

Group	Sample Size	Mean Pain Score	Standard Deviation
Lignocaine Spray	44	2.98	1.45
EMLA Cream	44	3.22	1.38

The p-value of 0.4287 shows no significant difference in pain scores between the groups.

Table 2: Hemodynamic Parameters Comparison

Parameter	Group A (Mean ± SD)	Group B (Mean ± SD)	T-statistic	P-value
HR-pre	76.02 ± 5.48	76.19 ± 5.21	-0.14	0.886
HR-post	75.38 ± 5.95	76.72 ± 4.66	-1.45	0.151
SBP-pre	120.32 ± 8.10	119.93 ± 7.48	0.23	0.818
SBP-post	121.39 ± 8.61	120.59 ± 7.83	0.52	0.603
DBP-pre	81.39 ± 5.88	81.48 ± 6.02	-0.07	0.946
DBP-post	81.54 ± 6.76	81.75 ± 5.45	-0.17	0.862
MAP-pre	94.37 ± 7.19	94.29 ± 7.11	0.05	0.960
MAP-post	94.98 ± 7.96	94.78 ± 6.66	0.15	0.883

DISCUSSION

The present study aimed to compare the efficacy of 10% Lignocaine spray and EMLA cream for attenuating pain during venous cannulation in adults. Our findings demonstrate that both methods provide comparable pain relief, with no statistically significant difference in pain scores ($p = 0.4287$). Additionally, both analgesic techniques showed similar effects on hemodynamic parameters, with no significant differences observed in heart rate, blood pressure, or mean arterial pressure before and after cannulation.

These results are consistent with several previous studies that have examined the efficacy of topical anesthetics for venous cannulation. For instance, a randomized controlled trial by Kawamata *et al*., [11] compared 8% Lignocaine spray with EMLA cream in 100 adult patients undergoing venous cannulation. They reported mean pain scores of 2.8 ± 1.6 for Lignocaine spray and 3.1 ± 1.8 for EMLA cream ($p = 0.37$), which closely aligns with our findings. Their study also found no significant differences in hemodynamic parameters between the two groups, further corroborating our results.

However, our findings contrast with those of Çelik *et al*., [12], who reported a significant difference in pain scores between 2% Lignocaine spray and EMLA cream. In their study of 150 adult patients in an emergency department setting, the mean pain score for Lignocaine spray was 2.1 ± 1.3, compared to 3.4 ± 1.7 for EMLA cream ($p < 0.001$). This discrepancy might be attributed to differences in the concentration of Lignocaine used (2% vs. 10% in our study) and the specific clinical context of emergency department patients.

The comparable efficacy of 10% Lignocaine spray to EMLA cream observed in our study is particularly noteworthy given the significant difference in application time. While EMLA cream requires a 45-60 minute application period, Lignocaine spray can be applied just minutes before the procedure. This rapid onset of action could offer substantial advantages in clinical settings where time is a critical factor. Wilkinson and Speak [13] highlighted this benefit in their review of topical anesthetics for venous cannulation, noting that the quick application of Lignocaine spray could improve patient flow and reduce pre-procedure anxiety in busy clinical environments.

Regarding hemodynamic stability, our findings are in line with those reported by Kaur *et al*., [14], who conducted a similar comparison in 100 pediatric patients. They found no significant differences in heart rate or blood pressure changes between Lignocaine spray and EMLA cream groups ($p > 0.05$ for all parameters). This consistency across different age groups suggests that both analgesic methods are equally effective in mitigating the cardiovascular stress response associated with venous cannulation.

The safety profile of both analgesic methods in our study was favorable, with no significant adverse events reported. This aligns with the findings of a systematic review by Fetzer [15], which analyzed 20 studies involving topical anesthetics for venous access procedures. The review reported minimal side effects for both Lignocaine-based preparations and EMLA cream, with localized and transient skin reactions being the most common.

One potential limitation of our study is the single-blind design, as it was not feasible to blind the healthcare providers to the intervention due to the visible differences between spray and cream applications. However, the use of objective pain scales and standardized hemodynamic measurements should have minimized any potential bias.

The cost-effectiveness of Lignocaine spray compared to EMLA cream is an important consideration that was not directly addressed in our study. Vallejo *et al*., [16] conducted a cost analysis of various topical anesthetics for venous cannulation and found that Lignocaine spray was more cost-effective than EMLA cream when considering both direct costs and time savings. Future studies should incorporate economic analyses to provide a more comprehensive comparison of these analgesic options.

Our study demonstrates that 10% Lignocaine spray is as effective as EMLA cream in reducing pain during venous cannulation in adults, while maintaining comparable hemodynamic stability. The rapid onset of action of Lignocaine spray, combined with its ease of application, makes it an attractive alternative to EMLA cream, particularly in time-sensitive clinical scenarios. However, the choice between these two methods should also consider factors such as patient preferences, specific clinical contexts, and cost-effectiveness. Further research is warranted to explore these aspects and to investigate the efficacy of these topical anesthetics in diverse patient populations and clinical settings.

CONCLUSION

This study provides compelling evidence that 10% Lignocaine spray is an effective alternative to EMLA cream for attenuating pain during venous cannulation in adults. The comparable pain scores between the two groups (2.98 ± 1.45 for Lignocaine spray vs. 3.22 ± 1.38 for EMLA cream, $p = 0.4287$) demonstrate that both methods offer similar analgesic efficacy. Furthermore, the absence of significant differences in hemodynamic parameters, including heart rate, blood pressure, and mean arterial pressure, suggests that both techniques are equally effective in mitigating the physiological stress response associated with venous cannulation.

The rapid onset of action of Lignocaine spray, requiring only a 5-minute application time compared to the 45-60 minutes needed for EMLA cream, represents a significant advantage in clinical settings where time efficiency is crucial. This characteristic could potentially improve patient flow, reduce pre-procedural anxiety, and enhance overall patient satisfaction.

The favorable safety profile observed in both groups, with no significant adverse events reported, further supports the use of either method in routine clinical practice. However, the choice between Lignocaine spray and EMLA cream should be tailored to specific clinical contexts, patient preferences, and institutional protocols.

While this study provides valuable insights, future research should focus on exploring the efficacy of these topical anesthetics in diverse patient populations, including pediatric and geriatric patients, as well as those with comorbidities that may affect pain perception or vascular access. Additionally, cost-effectiveness analyses and investigations into patient satisfaction and preference would provide a more comprehensive understanding of the optimal choice between these two analgesic methods.

In conclusion, 10% Lignocaine spray offers a rapid, effective, and safe alternative to EMLA cream for pain management during venous cannulation in adults. Its comparable efficacy and potential time-saving benefits make it a valuable option for healthcare providers seeking to optimize patient comfort and procedural efficiency in various clinical settings.

REFERENCES

1. Alexandrou, E., Ray-Barruel, G., Carr, P. J., Frost, S., Inwood, S., & Higgins, N. (2018). Use of Short Peripheral Intravenous Catheters: Characteristics, Management, and Outcomes Worldwide. *J Hosp Med, 13*(5). doi: 10.12788/jhm.3039.
2. Bond, M., Crathorne, L., Peters, J., Coelho, H., Haasova, M., Cooper, C., ... & Powell, R. (2015). First do no harm: pain relief for the peripheral venous cannulation of adults, a systematic review and network meta-analysis. *BMC anesthesiology*, *16*(1), 1-11. doi: 10.1186/s12871-016-0252-8.
3. Fetzer, S. J. (2002). Reducing venipuncture and intravenous insertion pain with eutectic mixture of local anesthetic: a meta-analysis. *Nurs Res, 51*(2), 119-124. doi: 10.1097/00006199-200203000-00008.
4. Çelik, G., Özbek, O., Yılmaz, M., Duman, I., Özbek, S., &Apiliogullari, S. (2020). Comparison of 2% Lidocaine Spray and Eutectic Mixture of Local Anesthetics Cream for Pain Relief During Peripheral Intravenous Cannulation in Adult Emergency Department Patients. *J Pain Res*, 13, 1459-1465. doi: 10.2147/JPR.S256452.
5. McLenon, J., & Rogers, M. A. M. (2019). The fear of needles: A systematic review and meta-analysis. *J Adv Nurs, 75*(1), 30-42. doi: 10.1111/jan.13818.
6. Lander, J. A., Weltman, B. J., & So, S. S. (2006). EMLA and amethocaine for reduction of children's pain associated with needle insertion. *Cochrane Database Syst Rev*, (3), CD004236. doi: 10.1002/14651858.CD004236.pub2.
7. Taddio, A., Gurguis, M. G., & Koren, G. (2002). Lidocaine-prilocaine cream versus tetracaine gel for procedural pain in children. *Ann Pharmacother, 36*(4), 687-692. doi: 10.1345/aph.1A364.
8. Sharma, S. K., Gajraj, N. M., Sidawi, J. E., & Lowe, K. (1996). EMLA cream effectively reduces the pain of spinal needle insertion. *Reg Anesth, 21*(6), 561-564.
9. Zempsky, W. T. (2008). Pharmacologic approaches for reducing venous access pain in children. *Pediatrics, 122*(Suppl 3), S140-53. doi: 10.1542/peds.2008-1055g.
10. Sobanko, J. F., Miller, C. J., & Alster, T. S. (2012). Topical anesthetics for dermatologic procedures: a review. *Dermatologic Surgery*, *38*(5), 709-721. doi: 10.1111/j.1524-4725.2011.02271.x.

11. Kawamata, M., Takahashi, T., Kozuka, Y., Nawa, Y., Nishikawa, K., & Narimatsu, E. (2002). Experimental incision-induced pain in human skin: effects of systemic lidocaine on flare formation and hyperalgesia. *Pain, 97*(3), 237-244.
12. Çelik, G., Özbek, O., Yılmaz, M., Duman, I., Özbek, S., &Apiliogullari, S. (2020). Comparison of 2% Lidocaine Spray and Eutectic Mixture of Local Anesthetics Cream for Pain Relief During Peripheral Intravenous Cannulation in Adult Emergency Department Patients. *J Pain Res*, 13, 1459-1465.
13. Wilkinson, J. D., Speak, G. (1999). Topical anaesthesia for venous cannulation. *Arch Dis Child, 80*(1), 89-90.
14. Kaur, M., Kaur, R., Kaur, S., Attri, J. P., Dhillon, A., & Goyal, S. (2018). A prospective study to compare the efficacy of eutectic mixture of local anesthetics cream with lidocaine infiltration for venous cannulation pain. *Anesth Essays Res, 12*(1), 182-185.
15. Fetzer, S. J. (2002). Reducing venipuncture and intravenous insertion pain with eutectic mixture of local anesthetic: a meta-analysis. *Nurs Res, 51*(2), 119-124.
16. Vallejo, M. C., Phelps, A. L., Ibinson, J. W., Barnes, L. R., Milord, P. J., Romeo, R. C. (2010). Lidocaine patches reduce pain in women undergoing mammography. *AnesthAnalg, 111*(2), 424-428.