



Investigation of the Effect of EMLA Cream, Lidocaine Spray, and Ice Pack on the Arteriovenous Fistula Cannulation Pain Intensity in Hemodialysis Patients

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ABSTRACT

Introduction: Arteriovenous fistula cannulation is one of the problems in hemodialysis patients. Reducing this pain improves their dialysis acceptance and life quality. This study investigated the effect of EMLA cream, Lidocaine spray, and ice pack on arteriovenous cannulation pain intensity in hemodialysis patients. **Materials and Methods:** A total of 40 hemodialysis patients with arteriovenous fistula participated in this quasi-experimental study in Shahid Rahnemoon Hospital in Yazd in 2015. In this study, pain intensity was measured in one group in four states of before intervention and after application of lidocaine spray, EMLA cream, and ice pack using pain intensity numerical scale. The data were analyzed with SPSS16 using ANOVA. **Results:** Our findings suggested that the mean pain score in the four stages of before intervention, and after application of lidocaine spray, ice pack, and EMLA cream were 7.45 ± 0.88 , 4.22 ± 1.33 , 5.38 ± 0.83 , and 2.80 ± 0.70 , respectively. The reduction in mean pain intensity was significantly greater with EMLA cream compared to lidocaine spray and ice pack ($P < 0.001$). The pain score was also significantly different before intervention and after application of the three interventions ($P < 0.001$). **Conclusion:** The results showed that all three methods of intervention were effective in reducing pain intensity, with EMLA cream exerting the greatest effect in decreasing the puncture-related mean pain intensity of arteriovenous fistula cannulation. So, it is recommended that all three methods be used to diminish this type of pain.

Keywords: Hemodialysis, Arteriovenous fistula, Lidocaine, EMLA cream, Cryotherapy, Pain

INTRODUCTION

Hemodialysis is the most important and most-frequently used alternative therapy in kidney disease patients [1]. Almost 150,000 dialysis sessions are performed monthly in Iran on more than 13,000 hemodialysis patients [2]. Statistics show that the population of hemodialysis patients is doubled every 10 years in the USA [3]. It is estimated that the hemodialysis patient population will reach 3,500,000 by 2020 [4]. The growth rate of this disorder in Iran is greater than the average global rate equaling almost 12% [5]. Hemodialysis is the most commonly used line of treatment in ESRD (end-stage renal disease) patients. These patients usually suffer from numerous complications related to either ESRD or to the type of treatment [6]. Experiencing some type of pain is among the discomforts reported by 50% of these patients [7]. They undergo hemodialysis three sessions per week each lasting 3-4 h and experience annually the arteriovenous fistula cannulation pain 300-320 times. This pain continues for the patient's lifetime or till the time of successful kidney transplantation [8-10]. Some studies indicate that 47% of hemodialysis patients are afraid of needles and state the arteriovenous fistula cannulation as the most terrifying stress in the treatment course and the most stubborn concern during hemodialysis [11]. Repeated pain induced by hemodialysis fistula cannulation may lead to depression, reduced quality of life, pain, discomfort, distress, and stress, while controlling the pain

improves the patients' acceptance of hemodialysis and their quality of life [12]. Considering the significance of pain, analgesia relief must be considered as one part of treatment in these patients [11]. Presently, there is no uniform method to be used for relieving arteriovenous fistula cannulation pain in patients undergoing hemodialysis [13]. There are various pharmacologic and nonpharmacologic modalities for pain relief. The effectiveness of some of these methods in relieving pain is still in under question [5]. Some of the puncture-related pain relief methods reported in literature include the application of heat or cold, EMLA local anesthesia creams, distraction methods, lidocaine gel, and lavender aroma inhalation [14-16]. In this regard, the use of local anesthetics is one of the methods used to diminish injection pain. Ice pack and EMLA cream are two examples of local anesthetics which are readily applicable by the patients themselves [17]. Ice is cheap and easily available with rapid and simple use which decreases pain by attenuating the signals of pain sensation, increasing perception of cold sensation instead of pain, and reducing the speed of neural transmission with pain neural fibers [18]. Lidocaine is one of the important common agents used as a local anesthetic [19]. Lidocaine spray is one of the common formulations used clinically with moderate-term effect to induce local anesthesia in mucous membranes and skin. Depending on the site of application, anesthesia is usually induced during 1-5 min lasting for 10-15 min [5,19]. The EMLA cream as a local anesthetic contains lidocaine 25 mg/g and prilocaine 25 mg/g with little complications like slight redness of the site [20]. It produces anesthesia of 5 mm depth [21]. The theory behind pain reduction by lidocaine is the blocking of active and inactive sodium channels resulting in blockade of conduction and absence of stimulation followed by impaired or reduced pain transmission [22]. The results of the study by Benini, et al., aimed at investigating the effect of EMLA cream on controlling pediatric arteriovenous fistula cannulation pain during hemodialysis demonstrated that it was effective in decreasing this pain in children [23]. However, the findings by Turkmen, et al., suggested that the ointment containing lidocaine 2.5% exerted no significant effect in reducing cannulation pain in hemodialysis children with chronic renal failure [24]. Moreover, some studies compared the anesthetizing effects of ice pack and lidocaine-containing ointment on injection-induced pain. Among them, the study by Elibol on pain induced by botulinum injection and the study by Sabzi on pediatric phlebotomy pain brought about controversial results [25]. Considering the contradictory results of these studies and regarding the importance of pain control in hemodialysis patients, this study explored the effect of lidocaine-containing compounds and ice pack on the intensity of pain induced by arteriovenous cannulation in hemodialysis patients.

METHODOLOGY

A population of hemodialysis patients in Shahid Rahmehoon Hospital in Yazd, central Iran, participated in this quasi-experimental study. Considering the results of Shin Mi, et al. study with two-tailed significance level ($\alpha=0.05$) and test power of 90%, also given the pain score SD of 1.38 at the time of fistula catheterization, and a predicted change in mean pain score of 1.55, the sample volume was estimated as 35 patients in each group [26]. Considering a subject attrition rate of 20%, a total of 42 patients participated as study samples.

$$N = [2(Z_{1-\alpha/2} + Z_{1-\beta})^2 \delta^2] / d^2$$

$$Z_{1-\alpha/2} = 1.96 \quad (1-\beta) = 0.90$$

The participants who met the inclusion criteria entered the study using convenient sampling after obtaining their consent. The inclusion criteria were: age of over 18 years, at least a 3-month history of hemodialysis, being conscious, and easy access to vessels. Also, the exclusion criteria were: intolerance and lack of sensation of cold, vascular diseases of upper limbs such as Reynaud syndrome, paralysis of upper extremities, allergy to cold like incidence of rashes, allergy to lidocaine ingredients, peripheral vessels damage, failed cannulation in the first attempt, and repeated needle punctures. Two patients were excluded from the study since they discontinued their participation and finally, the data on 40 patients were analyzed. The data collection instruments included a questionnaire and checklist consisting of two parts. The first part included demographic information such as age, gender, marital status, occupation, history of disease, education level, hemodialysis duration, and duration of fistula use. The second part related to assessing pain severity in the patient which was measured using a numeric pain assessment scale ranging between 0 and 10 in which 0=no pain and 10=the most severe pain experienced by the patient. The validity and reliability of the numeric pain intensity measurement scale were established by Williamson and Hoggart in 2005 approved by several previous studies. To perform the interventions, first the patients were asked to state their experienced pain on the basis of

visual analog scale of pain measurement during the first three sessions after arteriovenous fistula cannulation using the routine method without intervention and the gleaned data were recorded. Then, pain severity was measured in all patients at the time of cannulation during the application of lidocaine spray, EMLA cream (IGI Laboratories Inc. Buena, NJ 08310 USA), and ice pack. Each intervention method was repeated three times for every patient. The order of application of methods was randomly selected for each patient. For lidocaine spray method, the skin site was prepped first and then two puffs of lidocaine (20 mg) were sprayed by the researcher from a 5-cm distance on the dermal surface near the needle insertion point. Five minutes after spraying, the skin surface at the site of arterial needle insertion was disinfected with 70% alcohol-soaked cotton pads and the specific hemodialysis needles were inserted into the vessels of the fistula area by the ward nurse. In the ice pack method, 5 pieces of ice measuring $4 \times 2 \times 2$ cm were placed in latex gloves and covered with material cover. They were placed after the passage of 2 min on the hand at the site of fistula 5 min before making the puncture. Next, specific hemodialysis needles were inserted in the vessels of fistula area by the ward nurse after disinfecting the fistula area with 70% alcohol-soaked cotton pads. Also, in the EMLA cream method, 1.5 g of EMLA cream was applied to nearly 5 cm² of the fistula area 20 min before insertion of the needle by 2-cc syringes and fixed with supportive dressing. Subsequently, the EMLA cream was removed and specific hemodialysis needles were inserted in the vessels of fistula area by the ward nurse after sterilization of the area with 70% alcohol-soaked cotton pads. Two minutes after insertion of arterial needles, pain intensity was measured by the nurse using pain severity numeric scale. All canulae were inserted into the fistula by a skilled hemodialysis ward nurse using the same size needle (hemodialysis needle #16). A 4-week wash out interval was considered between the interventions to assure of absence of interference of the previous intervention. Descriptive statistics including frequency distribution tables, percentages, mean, and SD and also inferential statistics such as Repeated ANOVA were used to analyze the culled data with SPSS16. The required ethical considerations were observed in this study. In so doing, the approval of Committee of Ethics in Human Research at Shahid Sadoughi University of Medical Sciences and permission of the university authorities and hemodialysis ward were obtained and then sampling was initiated. The researchers introduced themselves to the samples and explained the research objectives and procedures, voluntary participation, anonymity, and confidentiality of patient information, and then informed written consent for participation was obtained from each patient.

RESULTS

Of 40 patients participating in this study, 25 (62.5%) were male and 15 (37.5%) were female with a mean age of 55.25 years. The mean hemodialysis time of the patients was 4.98 years and the mean of fistula longevity was 3.74 years. Table 1 displays the results of comparisons among the means of pain intensity at various states during insertion of hemodialysis needles. As shown in the table, the mean pain intensity is less with the EMLA cream method compared to the lidocaine spray and ice pack method.

Table 1 Mean pain score at the time of fistula cannulation before and after intervention

Method	Mean	SD	F	P
No intervention	7.45	0.88	289.1	P<0.001
Ice pack	5.38	0.83		
Lidocaine spray	4.22	1.13		
EMLA cream	2.8	0.7		

Table 2 compares the mean pain score at fistula cannulation using the various methods applied in this study and the results of LSD post hoc test indicating a statistically significant difference between mean pain reduction before and after intervention regardless of the method used. As such, the mean pain score was greater at the time of fistula cannulation in no intervention method compared to the three other methods (P<0.001). Furthermore, our findings indicated a significant difference in mean pain severity among the three groups so that a pair-wise comparison of the groups revealed that the mean pain reduction was significantly greater with EMLA cream compared to lidocaine spray and ice pack (P<0.001). A comparison of lidocaine spray and ice pack demonstrated that the mean pain reduction was significantly far greater with lidocaine spray compared to ice pack (P<0.001). On the whole, our results suggested that EMLA cream was the most effective method to be used for decreasing mean pain score during fistula cannulation.

Table 2 Pair-wise comparison of interventions using LSD post hoc test

Method	No intervention	Ice pack	Lidocaine spray	EMLA cream
No intervention	-	2.07	3.225	4.65
Ice pack	P<0.001	-	1.158	2.583
Lidocaine spray	P<0.001	P<0.001	-	1.425
EMLA cream	P<0.001	P<0.001	P<0.001	-

DISCUSSION

To overcome the effect of intervening variables such as age, gender, marital status, occupation, history of diseases, education level, hemodialysis duration, and the duration of fistula use, the study was conducted on one group in four states of application of EMLA cream, ice pack, lidocaine spray, and no intervention. Upon determining the pain intensity during fistula cannulation in hemodialysis patients in this study, it was found that there was a statistically significant difference in mean pain intensity score before and after interventions regardless of type of intervention indicating that the interventions have been effective in reducing pain using any of the three methods. Additionally, our findings indicated that the difference in mean pain intensity was significant in the three methods as the pair-wise comparison of the groups showed that the mean pain reduction was significantly greater with EMLA cream compared to lidocaine spray and ice pack. Also, a comparison of lidocaine spray and ice pack showed that the mean pain reduction was significantly greater with lidocaine spray than with ice pack. Many studies have been carried out on the use of different forms and combinations of medicines compared to the use of EMLA cream, ice pack, and lidocaine spray to inhibit the pain sensation in painful medical interventions with results consistent with our findings. Watson et al. explored the effects of EMLA cream and ice pack on fistula cannulation pain intensity in hemodialysis patients compared to placebo inert formulations and their findings demonstrated that EMLA cream reduced needle insertion pain significantly more than placebo ($P<0.01$) [27]. Also, another study investigated the effect of EMLA cream on reducing arteriovenous fistula cannulation pain in hemodialysis patients and the results revealed that EMLA cream was significantly more effective in diminishing fistula cannulation pain compared to placebo [28]. The findings of another study showed that although both EMLA cream and cryotherapy are effective in subcutaneous injection pain reduction, EMLA cream was more effective than local cryotherapy with a significant difference between the two methods [29]. This is consistent with our results. Moreover, another study investigating the effect of lidocaine spray on arteriovenous fistula cannulation pain intensity in hemodialysis patients suggested that this spray was significantly effective in reducing needle insertion pain [30]. The findings of other studies also showed that the mean pain intensity during the application of various forms of lidocaine was smaller with lidocaine compared to other placebo formulations which is consistent with our results. In this regard, the results of the study by Zempsky, et al. demonstrated that the venous cannulation pain intensity during delivery of powdered lidocaine without needle was significantly smaller compared to placebo (2.26 vs. 3.19) [31]. Also, a study on the application of EMLA cream for reducing adult phlebotomy pain indicated that phlebotomy pain decreased significantly even 5 min after the application of EMLA cream [32]. Furthermore, the results of the study by Sundar, et al. investigating the effect of cryotherapy on fistula cannulation pain in hemodialysis patients indicated that the pain score in cryotherapy group significantly diminished ($P<0.001$). This study introduced cryotherapy as a simple non-pharmacological cost-effective method of pain reduction [33]. Elibol, et al. showed in their study that both EMLA cream and cryotherapy were effective in reducing the pain induced by subcutaneous injection of botulinum; yet, the difference between the two was not significant. They believed that the best method for comparing the effects of analgesic effects of various anesthesia techniques and their comparison with no intervention method is to investigate them just in one patient. Thomas, et al. elucidated the effect of anesthesia injection pain in vasectomy and found no significant difference in pain intensity between the EMLA group and control group [34]. The results of these studies are not consistent with our findings since there was no significant difference in phlebotomy pain severity between the EMLA cream group and placebo group while this difference was significant in our study. Given that no study has so far compared the effect of lidocaine spray and EMLA cream on reducing fistula cannulation pain in hemodialysis patients, the results of the studies that explored the effects of lidocaine in other forms and methods on venous cannulation pain intensity indicated the positive effect of lidocaine on reducing cannulation pain intensity. Additionally, the results of some studies showed that hemodialysis patients prefer lidocaine-containing local anesthetic agents over its parenteral form. In this regard, Watson, et al. investigated the effect of local anesthetics on decreasing the fistula cannulation pain intensity in hemodialysis patients and figured out that these patients prefer the use of lidocaine-containing topical

creams over the parenteral lidocaine. They postulated that the factor of patient comfort during the use of topical lidocaine-containing compounds contributes to this preference of the patients [5]. This is consistent with our findings. Though many studies confirm our results, some other studies contradict our findings. The study by Turkmen, et al. surveyed the effect of 2.5% lidocaine on pain severity during pediatric phlebotomy in chronic renal failure children who underwent hemodialysis for a long time. They found that 2.5% lidocaine had no effect on diminishing the pain induced by hemodialysis needle insertion. Of course, they asserted that factors such as psychological parameters, skin puncture technique, and needle size should also be considered along with the use of local and topical anesthetics [4]. The study by Qane, et al. on the effect of EMLA cream on lumbar puncture pain revealed that the use of this cream was not effective in pain reduction. They mentioned that their study differed from other studies in that they used no dressing to support the EMLA cream and asserted that the use of dressing may be effective in relieving pain with this cream [35]. This is not consistent with the results of the present study. Contrary to our findings on the efficacy of lidocaine in cannulation pain reduction, the results of the study by McNikolas in 2012, investigating the effects of 2% lidocaine gel on pain reduction before cervical IUD placement indicated that topical or intracervical 2% lidocaine gel did not reduce pain before IUD placement [36]. Moreover, Alizadeh suggested that the use of 2% lidocaine gel and intracervical lubricant gel 1 min before placing tenaculum on the cervix was ineffective on decreasing the total pain of IUD placement [37].

CONCLUSION

Considering the results of the present study and similar studies, it could be concluded that all three methods of the use of EMLA cream, ice pack, and lidocaine spray are effective in reducing fistula cannulation pain in hemodialysis patients. Hence, a painless stress-free experience can be provided for hemodialysis patients through educating the personnel and the patients. However, our findings suggested that EMLA cream was the most effective method to be used for reducing mean pain score in fistula cannulation. Therefore, considering the severe pain of fistula cannulation in hemodialysis patients, this method is recommended as a safe and easy method for these patients.

Limitations of the Study

The first limitation was the inability of the researcher to blind the study due to awareness of patients of the interventions which was out of control of the researcher. Another limitation was the patients' previous experiences and their mental status at the time of fistula cannulation and changes in their psychological status during interventions that affected the sensation of pain severity and was out of control of the researcher.

DECLARATIONS

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Conflict of Interest

The authors and planners have disclosed no potential conflicts of interest, financial or otherwise.

REFERENCES

- [1] Efstratiadis, G., et al. "Interventional Nephrology: a new subspecialty of Nephrology." *Hippokratia*, Vol. 11, No. 1, 2007, p. 22.
- [2] Ekrikpo, Udeme E., et al. "Haemodialysis in an emerging centre in a developing country: a two-year review and predictors of mortality." *BMC Nephrology*, Vol. 12, No. 1, 2011, p. 50.
- [3] Collins, Allan J., et al. "The state of chronic kidney disease, ESRD, and morbidity and mortality in the first year of dialysis." *Clinical Journal of the American Society of Nephrology*, Vol. 4, Supplement 1, 2009, pp. S5-S11.
- [4] Mirzaei, S., et al. "Efficacy of application of eutectic mixture of local anesthetics and lidocaine spray in pain management of arteriovenous fistula cannulation in hemodialysis patients." *Journal of Renal Injury Prevention*, Vol. 6, No. 4, 2017, pp. 269-74.

- [5] Asgari, Mohammad Reza, et al. "Effect of lidocaine spray on the pain intensity during insertion of vascular needles in hemodialysis patients." *Koomesh*, Vol. 14, No. 3, 2013.
- [6] Azimiyan, Jalil. "Effect of warm footbath on arteriovenous fistula puncture-related pain in dialysis patients." *JQUMS*, Vol. 18, No. 6, 2015, pp. 39-45.
- [7] Davison, Sara N. "Pain in hemodialysis patients: prevalence, cause, severity, and management." *American Journal of Kidney Diseases*, Vol. 42, No. 6, 2003, pp. 1239-47.
- [8] Sabitha, P.B., et al. "Effect of cryotherapy on arteriovenous fistula puncture-related pain in hemodialysis patients." *Indian Journal of Nephrology*, Vol. 18, No. 4, 2008, p. 155.
- [9] Bagheri-Nesami, Masoumeh, et al. "The effects of lavender aromatherapy on pain following needle insertion into a fistula in hemodialysis patients." *Complementary Therapies in Clinical Practice*, Vol. 20, No. 1, 2014, pp. 1-4.
- [10] Çelik, Gülperi, et al. "Vapocoolant spray vs lidocaine/prilocaine cream for reducing the pain of venipuncture in hemodialysis patients: a randomized, placebo-controlled, crossover study." *International Journal of Medical Sciences*, Vol. 8, No. 7, 2011, p. 623.
- [11] Park JS. The effect of cutaneous stimulation on AV fistula puncture pain of hemodialysis patients. *Taehan kanho The Korean nurse*, Vol. 33, No. 1-2, 1994, pp. 37-51.
- [12] Hassan, A., et al. "The impact of cryotherapy on pain intensity at puncture sites of arteriovenous fistula among children undergoing hemodialysis." *Journal of American Science*, Vol. 8, No. 12, 2012, pp. 1490-1500.
- [13] Aliasgharpour, Mansooreh, et al. "Comparison the effect of lidocaine gel and inhalation of lavender aromatherapy on pain score of arteriovenous fistula puncture in hemodialysis patients." *Complementary Medicine Journal of faculty of Nursing & Midwifery*, Vol. 4, No. 4, 2015, pp. 1000-11.
- [14] Reis, Evelyn Cohen, and Richard Holubkov. "Vapocoolant spray is equally effective as EMLA cream in reducing immunization pain in school-aged children." *Pediatrics*, Vol. 100, No. 6, 1997, pp. e5-e5.
- [15] Waterhouse, Marie R., Deborah R. Liu, and Vincent J. Wang. "Cryotherapeutic topical analgesics for pediatric intravenous catheter placement: ice versus vapocoolant spray." *Pediatric Emergency Care*, Vol. 29, No. 1, 2013, p. 8.
- [16] Shah, Vibhuti, Anna Taddio, and Michael J. Rieder. "Effectiveness and tolerability of pharmacologic and combined interventions for reducing injection pain during routine childhood immunizations: systematic review and meta-analyses." *Clinical Therapeutics*, Vol. 31, 2009, pp. S104-S151.
- [17] Elibol, Orhan, et al. "Efficacy of skin cooling and EMLA cream application for pain relief of periorbital botulinum toxin injection." *Ophthalmic Plastic & Reconstructive Surgery*, Vol. 23, No. 2, 2007, pp. 130-33.
- [18] Hogan, Mary-Ellen, et al. "A systematic review of vapocoolants for reducing pain from venipuncture and venous cannulation in children and adults." *Journal of Emergency Medicine*, Vol. 47, No. 6, 2014, pp. 736-49.
- [19] Trevor, Anthony J., Bertram G. Katzung, and Susan B. Masters. *Basic & clinical pharmacology*. McGraw-Hill Medical, 2009.
- [20] George, Anisha, et al. "Topical anesthetic versus lidocaine infiltration in arteriovenous fistula cannulation." *Chrismed Journal of Health and Research*, Vol. 1, No. 2, 2014, p. 95.
- [21] Young, Kelly D. "What's new in topical anesthesia." *Clinical Pediatric Emergency Medicine*, Vol. 8, No. 4, 2007, pp. 232-39.
- [22] Farhadi, Abolfazl. "Effect of lidocaine 2% gel on intensity of pain due to penicillin benzathin (1/200/000 U) testing and intramuscular injection." 2010, pp. 39-44.
- [23] Benini, F., et al. "Pain management of arteriovenous fistula cannulation in haemodialysis children: efficacy of EMLA anaesthetic cream." *European Journal of Pain*, Vol. 2, No. 2, 1998, pp. 109-13.
- [24] Rogers, Tanya L., and C. Lynne Ostrow. "The use of EMLA cream to decrease venipuncture pain in children." *Journal of Pediatric Nursing*, Vol. 19, No. 1, 2004, pp. 33-39.

- [25] Farnia, F., et al. "Comparison of the effect of Emla cream and cold compress on the pain intensity of enoxaparin injection." *Community Health Journal*, Vol. 8, No. 2, 2014, pp. 39-46.
- [26] Shin, Mee-Ok, et al. "A comparison of pain reducing effects of topical EMLA cream and subcutaneous lidocaine in hemodialysis patients." *Journal of Korean Academy of Fundamentals of Nursing*, Vol. 2, No. 1, 1995, pp. 37-43.
- [27] Watson, A.R., Pat Szymkiw, and A.G. Morgan. "Topical anaesthesia for fistula cannulation in haemodialysis patients." *Nephrology Dialysis Transplantation*, Vol. 3, No. 6, 1988, pp. 800-802.
- [28] Nam, Sun Hee, Yong Hee Kim, and Ji Yun Choi. "The Effects of Lidocaine/Prilocaine Cream on Pain and Anxiety before Intravenous Cannulation." *Nursing*, Vol. 1, 2016, p. 2.
- [29] Kuwahara, Raymond T., and Robert B. Skinner. "EMLA versus ice as a topical anesthetic." *Dermatologic Surgery*, Vol. 27, No. 5, 2001, pp. 495-96.
- [30] Song, Ji Mi, and Hye Ja Park. "Effects of 10% Lidocaine Spray and Aroma Hand Massage on Pain, Anxiety, Blood Pressure, and Pulse During Arteriovenous Fistula Needling in Hemodialysis Patients." *The Korean Journal of Rehabilitation Nursing*, Vol. 19, No. 1, 2016, pp. 1-11.
- [31] Zempsky, William T., et al. "Needle-free powder lidocaine delivery system provides rapid effective analgesia for venipuncture or cannulation pain in children: randomized, double-blind Comparison of Venipuncture and Venous Cannulation Pain After Fast-Onset Needle-Free Powder Lidocaine or Placebo Treatment trial." *Pediatrics*, Vol. 121, No. 5, 2008, pp. 979-87.
- [32] Nott, M.R., and J.L. Peacock. "Relief of injection pain in adults EMLA cream for 5 minutes before venepuncture." *Anaesthesia*, Vol. 45, No. 9, 1990, pp. 772-74.
- [33] Sundar, S. Benin, DR P. Mangala Gowri, and DRS Aruna. "assess the effectiveness of cryotherapy on arterio venous fistula puncture site pain among patients on haemodialysis." *International Journal of Pharma and Bio Sciences*, Vol. 8, No. 3, 2017, pp. 69-76.
- [34] Thomas, Anil A., et al. "Topical anesthesia with EMLA does not decrease pain during vasectomy." *The Journal of Urology*, Vol. 180, No. 1, 2008, pp. 271-73.
- [35] Qane, M., et al. "The efficacy of the EMLA analgesic cream in compare with placebo in pediatric oncology lumbar puncture." *Iranian Journal of Pediatric Hematology and Oncology*, Vol. 2, No. 2, 2012, pp. 44-48.
- [36] McNicholas, Colleen P., et al. "Cervical lidocaine for IUD insertional pain: a randomized controlled trial." *American Journal of Obstetrics & Gynecology*, Vol. 207, No. 5, 2012, p. 384-e1.
- [37] Mohammad-Alizadeh-Charandabi, S., S. Seidi, and F. Kazemi. "Effect of lidocaine gel on pain from copper IUD insertion: a randomized double-blind controlled trial." *Indian Journal of Medical Sciences*, Vol. 64, No. 8, 2010, p. 349.