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RESEARCH

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The effect of cold packs, lidocaine spray, and flashlights on cannulation pain in patients undergoing hemodialysis: a randomized controlled trial

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Abstract

Background Pain is a frequent and critical problem in daily hemodialysis practice. The pain experienced during arteriovenous fistula cannulation varies from 12% to even 80% in hemodialysis patients depending on the pain assessment tools used. Pain can lead to sleep problems, decreased compliance with hemodialysis therapy, frequent hospital hospitalizations, a decline in quality of life, and high death rates. Despite utilizing several methods as pain relief, it is still unknown in the literature and practice which method is the most effective. The purpose of the study was to compare the effect of lidocaine spray, cold packs, and flashlights on the pain induced by arteriovenous cannulation in hemodialysis patients. This was a prospective randomized open-label controlled trial. Hundred and eight adult patients on regular hemodialysis were recruited and simply randomized into one of four groups (lidocaine spray, cold packs, flashlights, and control) before cannulation.

Results The mean pain severity using visual analog scale was 4.3 (3.3–5.7) in lidocaine group, 4 (3–5.7) in cold packs group, 4.3 (3.3–5.3) in flashlight group, and 4.7 (3–6) in control group. There was a borderline significant difference between groups using Kruskal–Wallis test ($p=0.054$). The post hoc Tukey test showed that only cold packs differ from control group with borderline significance ($p=0.051$).

Conclusion The results showed that cold packs were safe and effective than lidocaine spray or flashlights in reducing cannulation pain. It is suggested to implement this method before cannulation in hemodialysis patients to reduce pain and improve quality of life. Future studies are needed to compare different application times of cold packs and its impact on pain scores to recommend the optimum time needed to achieve maximum analgesic effect.

Trail registration: Clinical trials.gov NCT05822063, REC #194.

Keywords Pain, Hemodialysis, AVF, Lidocaine, Flashlight, Cold pack

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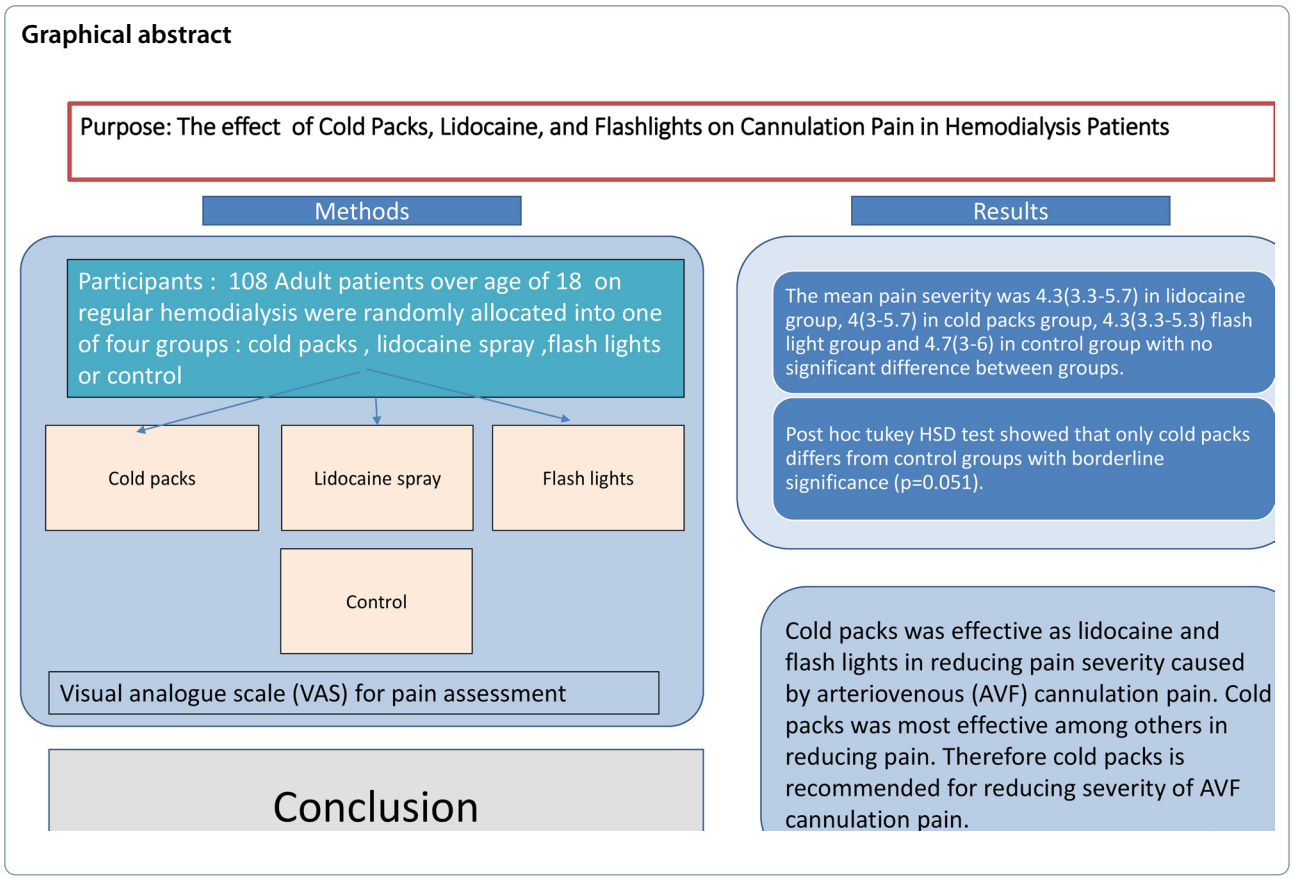

Background

Hemodialysis (HD) patients frequently complain of pain. About 75% of hemodialysis patients suffer from untreated or inadequately treated pain, ranging from moderate to severe [1]. Untreated pain in this population has a detrimental effect on mortality, dialysis adherence, healthcare use, and health-related quality of life [2]. This issue arises for a number of reasons, including the fact that carers are unaware of the problem and worry about the side effects of the analgesic therapy, while patients fear medication side effects, the additional burden of taking daily tablets, and the possibility of addiction if opioid medications are used [3].

Due to the scarcity of effective non-pharmacological treatments or safe non-opioid pharmaceutical choices, the use of opioids is disproportionately high in this population. In a survey of more than 400,000 end-stage kidney disease patients, more than half had gotten an opioid prescription, which is 3.2 times the prevalence in the US population [4] and 20% were on chronic opioid therapy [5]. Chronic opioid usage in kidney disease patients has been linked, in a dose-dependent way, to an increased risk of disturbed mental status, falls, fractures, hospitalizations, and mortality [6].

The American Society of Nephrology and the US Food and Drug Administration's Renal Health Initiative, a public–private partnership, are working together to promote pain management in renal illness as a key research priority[7]. Furthermore, the National Institutes of Health's Helping to End Addiction Long-term mission and the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) will address pain management and opioid safety in this population through the recently formed Hemodialysis Opioid Prescription Effort (HOPE) Consortium [8].

There are numerous pharmacologic and non-pharmacological pain management techniques. Some of these techniques' are still under debate. Non-pharmacological treatment options include a wide range from psychosocial or behaviorally based interventions (such as cognitive behavioral therapy, acceptance and commitment therapy, relaxation, music therapy, and mindfulness) to physically oriented interventions (such as exercise, physical therapy, yoga, acupuncture, and electrical stimulation) [9], together with the application of heat or cold, lavender oil, virtual reality, and other distraction methods [10–12].

Psychosocial interventions have limited but promising evidence for reducing opioid use and opioid misuse

behaviors. They are effective approaches for reducing pain severity, interference, disability caused by pain, and psychological distress [13, 14]. Physical therapy or exercise-based interventions have been successful in improving pain in the general population [15]. There are few studies that have looked at the effects of exercise, physical therapy, yoga, or acupuncture on pain in hemodialysis patients, but those that have been studied in this population had encouraging findings [16, 17].

Cryotherapy is one of the oldest and most affordable non-pharmaceutical pain management methods which was widely discussed in different studies [18, 19]. Application of cold locally appears to be a recommended and efficient way in reducing pain [20].Oppositely, two studies had reported that thermotherapy as well may be beneficial as pain reduction technique [21, 22]. Also, other studies investigated the use of lavender oil either inhaled or administered to the puncture site seems to have a positive analgesic impact [23–25].

Recently, studies have reported that the discomfort from venous cannulation is less painful after using distraction methods as flashlights from camera. This may be due to the changes in thalamic activity that changes nociceptive input when there is pain, which decreases the perception of pain. A quick flash of light was thought to excite the thalamus, which is an essential part of the light reflex, and as a result minimize the pain related to vein cannulation [26].

The use of local anesthetic drugs in a variety of formulations and dosage forms is the primary focus of pharmacological pain control strategies. Nine trials involving 8 to 75 participants looked at the effects of applying local anesthesia to the puncture sites before cannulation. The majority of trials showed that the most efficient treatment was lidocaine/prilocaine 5% (EMLA cream) application followed by lidocaine spray [20, 27]. A common problem with lidocaine/prilocaine 5% cream is the time of application before dialysis and the allergic reactions [28].

Although several studies have compared different pain methods used [27, 29–33], there is currently no consistent way to decrease arteriovenous fistula cannulation pain in hemodialysis patients and a serious lack of an effective and feasible option to be used as standard procedure in the daily practice of hemodialysis units. Additionally, a thorough assessment of pain in HD patients is necessary, and the multidisciplinary team should also include experts in pain management. Adopting pharmacological or non-pharmacological therapy modalities can reduce HD patients' pain symptoms, which has a substantial positive impact on their quality of life [34].

This study aimed to compare the effectiveness of three different methods (lidocaine spray, cold packs, flashlights) on the pain induced by arteriovenous cannulation in hemodialysis patients that were proven to be effective and feasible with lack of evidence of superiority of either one over other in our target population.

Subjects and methods

Study design and settings

This study was prospective randomized open-label controlled trial in Hemodialysis Units in Ain Shams University Hospital. Data collection was done from April 15 to May 20, 2023.

Subjects

It included 108 patients undergoing hemodialysis three times a week. Eligible patients were adults 18 years and older of both gender who were diagnosed with chronic kidney disease and undergoing hemodialysis with A.V. fistula of upper extremity currently used for hemodialysis which can be radio-cephalic, radio-basilic, or brachio-cephalic.

Exclusion criteria included any known sensitivities or allergies to lidocaine or other local anesthetic or cold therapy, damaged or broken skin at venipuncture location, and previous use of local anesthetic products in previous 24 h.

Ethical consideration

All subjects were informed about the study protocol, potential risks, and purpose and benefits of the study, and a written consent was signed by all enrolled subjects. This study conforms with the principles outlined in the Declaration of Helsinki and was approved by the Faculty of Pharmacy, Ain Shams University Ethical Committee [ACUC-FP-ASU RHDIRB2020110301 REC #194], and was registered in Clinical trials.gov NCT05822063.

Interventions

Patients were assigned to one of four groups using computer generated random numbers. The history of assignments of the entire research work was maintained by a researcher who was not involved in the patients' enrollment, interventions, or data analysis. To ensure that the allocation was effectively concealed, the assigned numbers were placed in sealed opaque envelopes. The present study was an open-label study, because blinding was difficult as methods used were very different.

Eligible patients were randomly allocated to one of the four groups

Group 1: lidocaine group

Two puffs of lidocaine 10% (lidocaine topical aerosol U.SP.38) were sprayed on the skin surface near to the needle insertion point. After ten minutes, the skin

surface was sprayed with 70% alcohol. Then, appropriate hemodialysis needles were put into the vessels of the fistula area by the nurse.

Group 2: "cold packs group"

Cold pack was placed on the fistula site five min before making the puncture. Next, specific hemodialysis needles were inserted in the vessels of fistula area by the nurse after disinfecting the fistula area with 70% alcohol-soaked cotton pads.

Group 3: "flashlights"

The patient's face was photographed. The photograph was taken with a mobile Samsung Note 10 camera 12 MP, f/2.1, 52mm (telephoto), 1/3.6", 1.0 µm, phase detection auto focus, optical image stabilization, 2× optical zoom, LED flash, auto-high dynamic range, panorama.

Group 4: control group: routine care without additional intervention

The patients was cannulated by hemodialysis needles which was inserted in the vessels of fistula area by the ward nurse after disinfecting the fistula area with 70% alcohol-soaked cotton pads.

Outcome measurement

All patients underwent full physical examination by a senior nephrologist. A thorough history was obtained from the participating patients (age, gender, weight, height, occupation, cause of illness, duration of HD onset, and comorbidities) through interviews by clinical pharmacist and from patient files. Patients were briefed about the study medicines and how to use the visual analog scale (VAS) for pain evaluation before the first intervention. Baseline pain assessment was done initially without any intervention, and pain score was assessed after venipuncture by a junior nephrologist who was blinded about patient assigned study group. Each patient was asked to grade the pain on the VAS, a 10-cm line marked 0 at one end and 10 at other end (0 = no pain, 10 = worst pain). In the three consecutive dialysis sessions, each patient randomly received one of the interventions only once before venipuncture and average of three VAS scores was taken for each patient. Patients were questioned about any unfavorable side effects they had experienced, and the cannulation site was checked for local skin responses by a clinical pharmacist.

Sample size calculation

In the study of Mirzaei et al. [27], the difference in the VAS score between lidocaine spray and ice pack managed groups was 1.16 with pooled standard deviation of 1. Based on these findings, a minimal sample size of 23 subjects in each group is required at an alpha level of 0.0125 and power of 90%. To compensate for dropouts, the sample will be increased by 15% to be 27 subjects in each group of the four groups with a total sample size of 108 subjects. Sample size was estimated using PS (Power and Sample Size Program), version 3.1.2.

Data analysis

Statistical analysis was performed using IBM SPSS® Statistics, version 26 (IBM® Corp., Armonk, NY, USA). Numerical data were expressed as mean and standard deviation or median and range as appropriate. Qualitative data were expressed as frequency and percentage. Pearson's Chi-square test or Fisher's exact test was used to examine the relation between qualitative variables. Comparison of quantitative data between four groups was made using either analysis of variance (ANOVA) for normally distributed data or Kruskal–Wallis test (non-parametric ANOVA) for not normally distributed one. All tests were two-tailed. A p-value < 0.05 was considered significant. Spearman's correlation test was conducted for correlation tests. A post hoc honestly significant difference (HSD) test was conducted to investigate the difference between groups.

Results

A total of 108 patients on regular hemodialysis were enrolled in the study. Flow diagram of patients is shown in Fig. 1.

The mean age of patients was 43.7 ± 15.6 years, 55 participants were males (50.9%), and 53 were females (49.1%). The mean frequency of hemodialysis is three times per week. Other clinical characteristics of the study groups are shown in Table 1. There were no significant differences between studied groups regarding age, weight, gender, and dialysis duration.

On the other side, height ($p < 0.001$) and BMI ($p = 0.011$) were significantly different among groups. The control group had higher BMI values than three other groups. Education levels were also significantly different among studied groups ($p = 0.004$) with high uneducated participants in lidocaine spray group (81.5%).

Comorbidities such as atrial fibrillation, heart failure, diabetes, and rheumatic heart diseases differ in cold packs group than other three studied groups ($p = 0.002$). Table 2 presents factors that may affect pain perception such as diabetes mellitus and gender. There were no differences between males and females visual analog scale pain scores ($p = 0.411$) or between diabetic and non-diabetic patients ($p = 0.441$).

The mean visual analog scale (VAS) scores were comparable between control and three test groups ($p = 0.054$) as shown in Fig. 2. Based on the results of post hoc Tukey

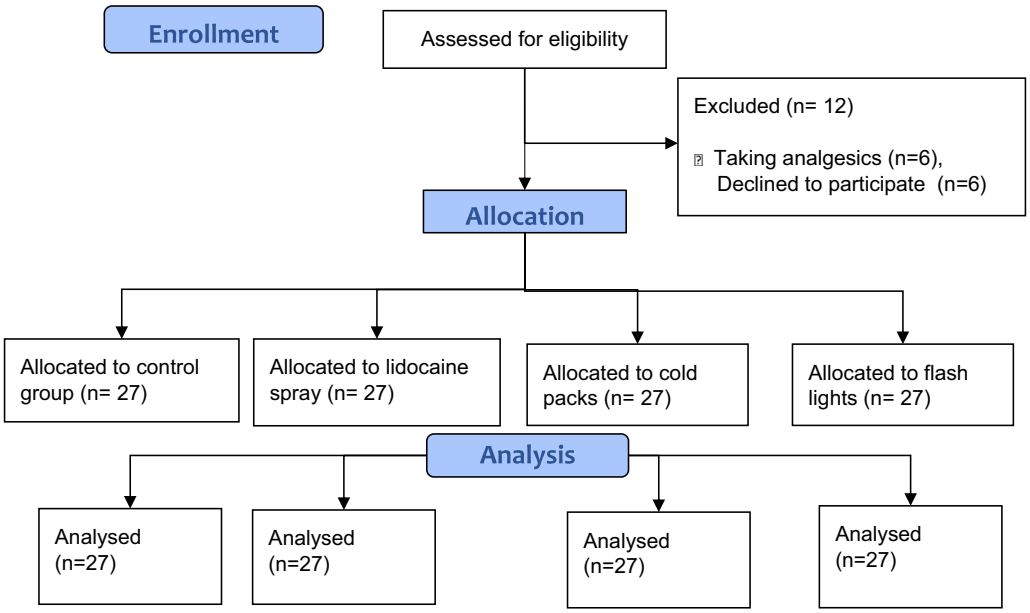

Fig. 1 Flow diagram of patients

Table 1 Baseline characteristics

Baseline characteristics			Group				Total	Test	*p*-value
			Control group	Lidocaine spray	Cold packs	Flashlight			
Age (years)		Mean ± SD	46.1 (15.9)	47.9 (15)	43.7 (15.6)	45.8 (15.6)		0.33[a]	0.804
Weight (kg)		Mean ± SD	77.3 (7.5)	79.6 (9.1)	76.7 (8.8)	77 (10.7)		0.581[a]	0.629
Height (cm)		Mean ± SD	158.4 (6.2)	165.8 (5.6)	165.2 (5.3)	166.7 (5.5)		11.941[a]	< 0.001*
BMI (kg/cm2)		mean ± SD	30.88 (3.36)	29.03 (3.79)	28.11 (3.16)	27.77 (4.23)		3.931[a]	0.011*
Gender	Male	*N* (%)	14 (51.9%)	13 (48.1%)	17 (63%)	11 (40.7%)	55 (50.9%)	2.779 ß	0.427
	Female	*N* (%)	13 (48.1%)	14 (51.9%)	10 (37%)	16 (59.3%)	53 (49.1%)		
Education	Bachelor	*N* (%)	6 (22.2%)	1 (3.7%)	4 (14.8%)	5 (18.5%)	16 (14.8%)	23.19#	0.004*
	Diploma	*N* (%)	2 (7.4%)	0 (0%)	9 (33.3%)	6 (22.2%)	17 (15.7%)		
	Ungraduated	*N* (%)	7 (25.9%)	4 (14.8%)	5 (18.5%)	5 (18.5%)	21 (19.4%)		
	Uneducated	*N* (%)	12 (44.4%)	22 (81.5%)	9 (33.3%)	11 (40.7%)	54 (50%)		
Etiology	DM	*N* (%)	2 (7.4%)	5 (18.5%)	1 (3.7%)	3 (11.1%)	11 (10.2%)	18.381#	0.076
	HTN	*N* (%)	12 (44.4%)	11 (40.7%)	11 (40.7%)	4 (14.8%)	38 (35.2%)		
	Others	*N* (%)	4 (14.8%)	2 (7.4%)	6 (22.2%)	9 (33.3%)	21 (19.4%)		
	Reflux	*N* (%)	4 (14.8%)	0 (0%)	1 (3.7%)	2 (7.4%)	7 (6.5%)		
	Unknown	*N* (%)	5 (18.5%)	9 (33.3%)	8 (29.6%)	9 (33.3%)	31 (28.7%)		
Comorbidities	No	*N* (%)	10 (37%)	12 (44.4%)	21 (77.8%)	8 (29.6%)	51 (47.2%)	14.675 ß	0.002*
	Yes	*N* (%)	17 (63%)	15 (55.6%)	6 (22.2%)	19 (70.4%)	57 (52.8%)		
Dialysis duration (years)		Median (Min–Max)	6 (2–25)	6 (1–15)	8 (1–23)	5 (2–23)		2.538 α	0.468

[a] Done by one-way ANOVA; ß by Chi-square test; α Kruskal–Wallis test; # Fisher's exact test, *Statistical significance $p < 0.05$

honestly significant difference (HSD) test, only cold packs differ from control groups with borderline significance ($p = 0.051$), while neither lidocaine spray and flashlights significantly differ from control. Table 3 shows that the changes in pain scores did not correlate with age, BMI, and dialysis duration ($p > 0.05$). There were no side effects

Table 2 Factors affect pain perception scores

			N	Mean ± SD	Median (Min–Max)	Test	*P* value
Mean. VAS	Gender	Male	55	4.4 ± 0.7	4.7 (3–6)	1325	0.411
		Female	53	4.3 ± 0.7	4.3 (3–6)		
	DM	Yes	11	4.5 ± 0.5	4.3 (4–5.3)	458.5	0.441
		NO	97	4.4 ± 0.8	4.3 (3–6)		

Mann–Whitney test, *N*, number, VAS, visual analog scale, DM, diabetes mellitus

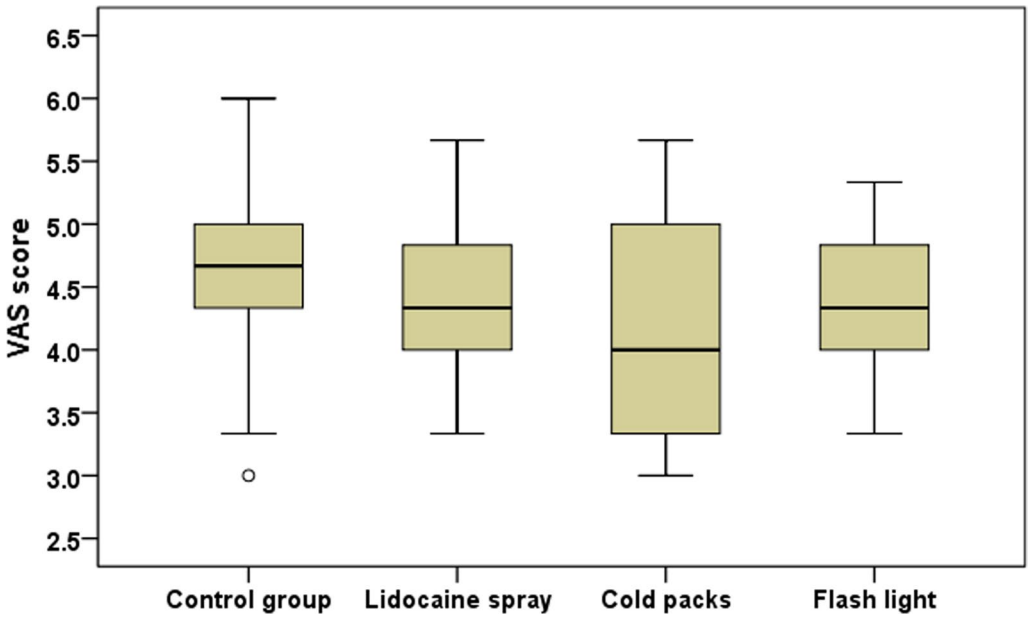

Fig. 2 Visual analog scale in four studied groups done by Kruskal–Wallis test

Table 3 Correlations between visual analog scale scores and parameters affect pain

		Mean. VAS	Age
Spearman's rho			
Age	Correlation Coefficient	− 0.064	
	p-value	0.511	
	N	108	
Dialysis duation	Correlation Coefficient	− 0.118	0.066
	p-value	0.224	0.498
	N	108	108
BMI	Correlation Coefficient	0.131	
	p-value	0.178	
	N	108	

reported in lidocaine or flashlight groups. Only three patients in cold packs group reported itching and minor hypersensitivity relieved ten minutes after removing the cold pack.

Discussion

One of the main concerns for hemodialysis patients is the impression of pain from arteriovenous fistula (AVF) cannulation. For the vast majority of HD patients, this discomfort is unbearable [35]. Many of these patients consider the pre-dialysis needle insertion procedure to be the most challenging component of their care. Pain control during AVF needling should therefore be prioritized in terms of dialysis care [32].

The present study was conducted to compare the effects of cold packs, lidocaine sprays, and flashlights on needle insertion pain in HD patients. The cold packs group had lowest pain scores (4.1 ± 0.8) followed by flashlights (4.3 ± 0.8) and then lidocaine spray (4.4 ± 0.7), yet the difference between three interventions and control was borderline significant ($p = 0.054$).

One of the therapies utilized in numerous trials to reduce the discomfort brought on by fistula punctures is cryotherapy. The results from multiple research showed that after cryotherapy, both the experimental group and the control group experienced varying variations in pain intensity linked to fistula puncture [19, 20, 27, 36], which somewhat differ from the results of the present study. One possible justification is the environment and psychological state of each person during needle insertion may have an impact on that person's pain tolerance threshold.

Additionally, the difference in the noticeable changes in pain intensity appears to be due to the different types of instruments used to measure pain. In research carried out by Aghajanloo [35] and Arab [37], visual analog scale was similarly used, while in other studies, numerical rating scale was used, though all instruments were 10 points [38, 39].

Studies looking at how lidocaine spray affected hemodialysis patients' arteriovenous fistula cannulation pain intensity found that it was highly beneficial at lessening the discomfort associated with needle insertion. [40]. Alternative studies' findings, which are congruent with ours, demonstrated that the mean pain intensity during the application of different forms of lidocaine was lower with lidocaine compared to alternative placebo formulations. According to Zempsky et al.'s findings, the amount of pain experienced during the use of powdered lidocaine without a needle was much less than that experienced during the placebo treatment (2.26 vs. 3.19) [41].

Different studies have compared the effects of cold packs and lidocaine in various ways, with varying degrees of success. According to Arab et al. [23], lidocaine cream was not as efficient as cold massage ($p=0.03$). In a different trial conducted by Ghoresyshi et al., cryotherapy was found to be superior to Xyla-P cream ($P=0.001$) [28], and both treatments were superior to a placebo. This was in concordance with our results that cold packs group had lower pain scores (4.1 ± 0.8) than lidocaine spray group (4.4 ± 0.7).

On the other hand, a study by Mirazei et al. revealed that lidocaine spray considerably reduced mean pain levels more than cold packs did. The impact of 2.5% lidocaine on pain intensity during pediatric phlebotomy in chronic renal failure was also investigated in a study by Turkmen, et al. on children who received long-term hemodialysis. They discovered that the 2.5% lidocaine had no impact in reducing the discomfort brought on by hemodialysis needle insertion [27]. Additionally, a study comparing the efficiency of lidocaine cream and cryotherapy for putting a needle into the implanted venous access chemotherapy port revealed that lidocaine cream had the strongest effect, followed by cryotherapy, and that both lower pain levels than the control group [42].

Flashlights may contain a distraction element, which seems to involve rivalry for attention between highly prominent pain sensations and shifts emphasis to another activity involving the processing of information. It has been suggested as a treatment for minimizing cannulation pain in individuals receiving hemodialysis [43, 44]. Also, flashlights were effective in decreasing level of pain during IV cannulation in hospitalized children [45]. This came in agreement with our results that flashlights decreased levels of pain than control group; however, it did not reach statistical significance. This may be explained by either the power of flashlight that was not sufficient or time lag between flashlight and measuring pain scores that may not be optimum. Therefore, the desired time lag for the flashlight to produce antinociception needs to be studied.

Given that no study has so far compared the effect of cryotherapy and flashlights or lidocaine spray on reducing fistula cannulation pain in hemodialysis patients, the results of the present study may guide in choosing the best technique of pain reduction in dialysis unit. Cold packs are safe, cheap, and effective than lidocaine and flashlights in our study population. However, these findings may not be generalized due to small sample size. Also, different populations with different comorbidities may affect their pain perception, so future studies are needed to study the optimum duration needed to apply cold packs in hemodialysis patients.

Pain is a complex issue with many facets that is influenced by many factors such as age, gender, culture, and heredity [37]. The results of the present study showed that there was no relationship between fistula puncture-related pain with age, gender, and duration of hemodialysis same as reported by Arab et al. [37]. On the other side, a study done by Ghods et al. found the duration of hemodialysis is significantly associated with the intensity of pain [25].

Regarding age effect, Li et al. examined the candidates' pain intensity using VAS to record pain scores. They found that elderly adults had lower pain thresholds than younger persons [46]. In contrast to the findings of our study, Sabita et al. found a significant association between older age and female gender and fistula puncture-related discomfort [47]. This was justified by the fact that growing older appears to be linked to higher pain thresholds and dysfunctional endogenous pain suppression pathways [48, 49]. Overall, this suggests that older persons would engage the pain system later than younger adults, exhibiting indicators of pain insensitivity, but that the relative lack of pain inhibition would eventually cause pain to escalate, exhibiting more common pain symptoms [50].

On the other side, Bahrami et al. found that younger persons and women felt more pain during EMG needling than men and older people did. Given that women

made up 61.7% of the patients and men made up 38.3% of the study group, it is possible that this contributed to the greater pain that women reported [51]. According to a different study, women experienced more pain right away following surgery [52]. Contrary to the findings of this trial, Chia et al. found that men required higher dosages of morphine and experienced worse postoperative pain [53].

In a different prospective study conducted by a French team, 58% of the 66 hemodialysis patients reported pain during cannulation, with a quarter of them being classified as having severe levels of discomfort. The prevalence of pain was unaffected by age or sex, just like in our study [20]. Additionally, Taenzer et al. showed that shortly following surgery, men and women perceived pain similarly [54]. Being female or old was not linked to a higher level of pain intensity in a different study conducted by Celik et al. [12] which was similar to our findings.

Many factors may play a role in the differences in pain sensitivity between men and women, some may be related to social conditioning and psychosocial factors, and others may be due to difference in sensitivity and reaction of both males and females to noxious stimuli, suggesting that biological mechanisms may be play a role in these differences. Additionally, sex hormones have an impact on pain sensitivity; in women, menstrual cycle stages affect pain tolerance and threshold. Men and women respond to acute pain differently, in terms of both the spatial pattern and strength of that reaction, according to imaging studies done on men and women brains [55]. Therefore, to fully comprehend these differences, additional descriptive analytical research with bigger sample sizes is needed.

According to studies, a person's ability to tolerate pain is decreased by high glucose levels and/or swift fluctuations in glucose levels. Patients with diabetic neuropathy experience more pain due to a dysfunctional endogenous opioid peptide pathway [56]. In the present study, diabetic and non-diabetics had no difference in their mean pain scores; this was in contrast to what reported that diabetes was associated with more pain on cannulation [20]. This may be explained that our study population had controlled blood glucose levels and did not suffer from peripheral neuropathy.

Conclusion

The results showed that cold packs were safe and effective than lidocaine spray or flashlights in reducing cannulation pain. It is suggested to implement this method before cannulation in hemodialysis patients to reduce pain and improve quality of life. Future studies are needed to compare different application times of cold packs and its impact on pain scores to recommend the optimum time needed to achieve maximum analgesic effect.

Abbreviations

CKD Chronic kidney disease
AVF Arteriovenous fistula
HD Hemodialysis
HSD Honestly significant difference

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Author contributions

KG was involved in investigation and reviewing and editing the manuscript. TS was involved in study conceptualization, methodology, and writing—reviewing and editing the manuscript. SF was involved in study conceptualization, methodology, investigation, formal analysis, data curation, writing original, and reviewing and editing the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

All subjects were informed about the study protocol, potential risks, and purpose and benefits of the study, and a written consent was signed by all enrolled subjects. This study conforms with the principles outlined in the Declaration of Helsinki and was approved by the Ethical Committee of Faculty of Pharmacy, Ain Shams University, Cairo, Egypt (ACUC-FP-ASU RHDIRB2020110301 REC #194**)**, and was registered in Clinical trials.gov NCT05822063.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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References

1. Sadigova E, Ozkurt S, An Yalcin AU (2020) Pain assessment in hemodialysis patients. Cureus 12(2):e6903. https://doi.org/10.7759/cureus.6903
2. Jhamb M, Tucker L, Liebschutz J (2020) When ESKD complicates the management of pain. Semin Dial 33(3):286–296. https://doi.org/10.1111/sdi.12881
3. Weisbord SD, Fried LF, Mor MK, Resnick AL, Unruh ML, Palevsky PM, Levenson DJ, Cooksey SH, Fine MJ, Kimmel PL, Arnold RM (2007) Renal provider recognition of symptoms in patients on maintenance hemodialysis. Clin J Am Soc Nephrol 2(5):960–967. https://doi.org/10.2215/CJN.00990207
4. Daubresse M, Alexander GC, Crews DC, Segev DL, McAdams-DeMarco MA (2019) Trends in opioid prescribing among hemodialysis patients,

2007–2014. Am J Nephrol 49(1):20–31. https://doi.org/10.1159/000495353
5. Dowell D, Haegerich TM, Chou R (2016) CDC guideline for prescribing opioids for chronic pain-United States. JAMA 315(15):1624–1645. https://doi.org/10.1001/jama.2016.1464
6. Kimmel PL, Fwu CW, Abbott KC, Eggers AW, Kline PP, Eggers PWO (2017) Opioid prescription, morbidity, and mortality in United States dialysis patients. J Am Soc Nephrol 28(12):3658–3670. https://doi.org/10.1681/ASN.2017010098
7. Flythe JE, Hilliard T, Lumby E, Castillo G, Orazi J, Abdel-Rahman EM, Pai AB, Rivara MB, St Peter WL, Weisbord SD, Wilkie CM, Mehrotra R (2019) Kidney health initiative prioritizing symptoms of ESRD patients for developing therapeutic interventions stakeholder meeting participants. Fostering innovation in symptom management among hemodialysis patients: paths forward for insomnia, muscle cramps, and fatigue. Clin J Am Soc Nephrol 14(1):150–160. https://doi.org/10.2215/CJN.07670618
8. NIDDK (2020) Hemodialysis opioid prescription effort (HOPE) consortium [Internet]. [cited 2020 May 29]. https://www.niddk.nih.gov/research-funding/research-programs/hemodialysis-opioid-prescription-effort-consortium
9. Kassim MAK, Pantazi AC, Nori W, Tuta LA, Balasa AL, Mihai CM, Mihai L, Frecus CE, Lupu VV, Lupu A, Andrusca A, Iorga AM, Litrin RM, Ion I, Ciciu E, Chirila SI, Chisnoiu T (2023) Non-pharmacological interventions for pain management in hemodialysis: a narrative review. J Clin Med 12(16):5390. https://doi.org/10.3390/jcm12165390
10. Shivashankar A, Nalini KB, Rath P (2018) The role of nonpharmacological methods in attenuation of pain due to peripheral venous cannulation: a randomized controlled study. Anesth Essays Res 12(1):7–10. https://doi.org/10.4103/aer.AER_172_17
11. Alzaatreh MY, Abdalrahim MS (2020) Management strategies for pain associated with arteriovenous fistula cannulation: an integrative literature review. Hemodial Int 24(1):3–11. https://doi.org/10.1111/hdi.12803
12. Çelik G, Özbek O, Yılmaz M, Duman I, Özbek S, Apiliogullari S (2011) Vapocoolant spray vs. lidocaine/prilocaine cream for reducing the pain of venipuncture in hemodialysis patients: a randomized, placebo-controlled, crossover study. Int J Med Sci 8:623
13. Williams ACC, Fisher E, Hearn L, Eccleston C (2020) Psychological therapies for the management of chronic pain (excluding headache) in adults. Cochrane Database Syst Rev 8(8):CD007407. https://doi.org/10.1002/14651858.CD007407.pub4
14. Brintz CE, Cheatle MD, Dember LM, Heapy AA, Jhamb M, Shallcross AJ, Steel JL, Kimmel PL, Cukor D (2021) HOPE consortium. Nonpharmacologic treatments for opioid reduction in patients with advanced chronic kidney disease. Semin Nephrol 41(1):68–81. https://doi.org/10.1016/j.semnephrol.2021.02.007
15. Searle A, Spink M, Ho A, Chuter V (2015) Exercise interventions for the treatment of chronic low back pain: a systematic review and meta-analysis of randomised controlled trials. Clin Rehabil 29(12):1155–1167. https://doi.org/10.1177/0269215515570379
16. Painter P, Carlson L, Carey S, Paul SM, Myll J (2000) Physical functioning and health-related quality-of-life changes with exercise training in hemodialysis patients. Am J Kidney Dis 35(3):482–492. https://doi.org/10.1016/s0272-6386(00)70202-2
17. Kim KH, Lee MS, Kim TH, Kang JW, Choi TY, Lee JD (2016) Acupuncture and related interventions for symptoms of chronic kidney disease. Cochrane Database Syst Rev 6:CD009440. https://doi.org/10.1002/14651858.CD009440.pub2
18. Garcia C, Karri J, Zacharias NA, Abd-Elsayed A (2021) Use of cryotherapy for managing chronic pain: an evidence-based narrative. Pain Ther 10(1):81–100. https://doi.org/10.1007/s40122-020-00225-w
19. Jafari-Koulaee A, Moosazadeh M, Bagheri Nesami M, Goudarzian AH (2020) Effect of cryotherapy on arteriovenous fistula puncture-related pain in hemodialysis patients: a systematic review and meta-analysis. Complement Ther Med Mar 49:102326. https://doi.org/10.1016/j.ctim.2020.102326
20. Kosmadakis G, Amara I, Costel G (2021) Pain on arteriovenous fistula cannulation: a narrative review. Semin Dial 34(4):275–284. https://doi.org/10.1111/sdi.12979
21. Tapia González I, Esteve Simó V, Moreno Guzman F, Fulquet Nicolás M, Duarte Gallego V, Saurina Solé A, Pou Potau M, de Arellano R, Serna M (2019) Thermotherapy: improving the vascular access cannulation procedure. J Vasc Access 20(4):386–391. https://doi.org/10.1177/1129729818809013
22. Ali Madadi ZA, Azimian J, Falahatpishe F, Heidari MA (2017) Effect of warm footbath with vibration on arteriovenous fistula puncture-related pain in hemodialysis patients. Int J Res Med Sci 5(2):631–635. https://doi.org/10.18203/2320-6012.ijrms20170165
23. Bagheri-Nesami M, Espahbodi F, Nikkhah A, Shorofi SA, Charati JY (2014) The effects of lavender aromatherapy on pain following needle insertion into a fistula in hemodialysis patients. Complement Ther Clin Pract 20(1):1–4. https://doi.org/10.1016/j.ctcp.2013.11.005
24. Taşan E, Ovayolu O, Ovayolu N (2019) The effect of diluted lavender oil inhalation on pain development during vascular access among patients undergoing haemodialysis. Complement Ther Clin Pract 35:177–182. https://doi.org/10.1016/j.ctcp.2019.02.010
25. Ghods AA, Abforosh NH, Ghorbani R, Asgari MR (2015) The effect of topical application of lavender essential oil on the intensity of pain caused by the insertion of dialysis needles in hemodialysis patients: a randomized clinical trial. Complement Ther Med 23(3):325–330. https://doi.org/10.1016/j.ctim.2015.03.001
26. Shivashankar A, Nalini KB, Rath P (2018) The role of nonpharmacological methods in attenuation of pain due to peripheral venous cannulation: a randomized controlled study. Anesth Essays Res 12(1):7–10. https://doi.org/10.4103/aer.AER_172_17.PMID:29628545;PMCID:PMC5872897
27. Mirzaei S, Javadi M, Eftekhari A, Hatami M, Hemayati R (2018) Investigation of the effect of EMLA cream, Lidocaine spray, and ice pack on the arteriovenous fistula cannulation pain intensity in hemodialysis patients. Int J Med Res Health Sci 7:51–57
28. Bahar E, Yoon H (2021) Lidocaine: a local anesthetic, its adverse effects and management. Medicina (Kaunas) 57(8):782. https://doi.org/10.3390/medicina57080782
29. Ghoreyshi Z, Amerian M, Amanpour F, Ebrahimi H (2018) Evaluation and comparison of the effects of Xyla-P cream and cold compress on the pain caused by the cannulation of arteriovenous fistula in hemodialysis patients. Saudi J Kidney Dis Transpl 29(2):369–375. https://doi.org/10.4103/1319-2442.229265
30. Nasirzadeh A, Mircheraghi SF, Ghodrati M, Shareinia H (2019) Comparing the effect of guided visualization and virtual reality techniques on cannulation pain in hemodialysis patients. J Res Med Dent Sci 7(3):55–62
31. Matsumoto T, Chaki T, Hirata N, Yamakage M (2018) The eutectic mixture local anesthetics (EMLA) cream is more effective on venipuncture pain compared with lidocaine tape in the same patients. J A Clin Rep 4(1):73. https://doi.org/10.1186/s40981-018-0210-1
32. Khosravi Pour A, Hejazi S, Kameli A, Hoseini Azizi T, Armat MR, Eshghi M (2023) Cooling spray or lidocaine spray and needle insertion pain in hemodialysis patients: an open-label cross-over randomized clinical trial. BMC Anesthesiol 7(23(1)):69. https://doi.org/10.1186/s12871-023-02028-w
33. ÇÇelik G, Özbek O, Yılmaz M, Duman I, Özbek S, Apiliogullari S (2011) Vapocoolant spray vs lidocaine/prilocaine cream for reducing the pain of venipuncture in hemodialysis patients: a randomized, placebo-controlled, crossover study. Int J Med Sci 8(7):623–627. https://doi.org/10.7150/ijms.8.623
34. Dos Santos PR, Mendonça CR, Noll M, Borges CC, Alves PM, Dias NT, de Sousa Romeiro AM, Barbosa MA, Porto CC (2021) Pain in hemodialysis patients: prevalence, intensity, location, and functional interference in daily activities. Healthcare (Basel) 9(10):1375. https://doi.org/10.3390/healthcare9101375.PMID:34683055;PMCID:PMC8544358
35. Aghajanloo A, Ghafourifard M, Haririan H, Gheydari PS (2016) Comparison of the effects of cryotherapy and placebo on reducing the pain of arteriovenous fistula cannulation among hemodialysis patients: a randomized control trial. J Nurs Midwifery Sci 3(1):59–65
36. Dumbre D (2019) Astudy to assess the effectiveness of cryotherapy on pain during puncture of arteriovenous fistula among patients on Haemodialysis in selected hospital. Int J Curr Res 8:37201–37203. https://doi.org/10.13140/RG.2.2.33518.56645
37. Arab V, Bagheri-Nesami M, Mousavinasab SN, Espahbodi F, Pouresmail Z (2017) Comparison of the effects of hegu point ice massage and 2% lidocaine gel on arteriovenous fistula puncture-related pain in hemodialysis patients: a randomized controlled trial. J Caring Sci 6(2):141–148

38. Sheha M (2019) Effectiveness of cryotherapy related pain management among patients undergoing hemodialysis at the site of arteriovenous fistula puncture. World J Nurs Sci 5(3):97–103. https://doi.org/10.5829/idosi.wjns.2019.97.103
39. Basal A, Okasha K (2013) Effect of cryotherapy on pain intensityat puncture sites of arteriovenous fistula among adult patients undergoing hemodialysis at Tanta University Hospital. Tanta Sci Nurs J 5(2):27–42
40. Song JM, Park HJ (2016) Effects of 10% lidocaine spray and aroma hand massage on pain, anxiety, blood pressure, and pulse during arteriovenous fistula needling in hemodialysis patients. Korean J Rehabil Nurs 19(1):1–11
41. Zempsky WT, Bean-Lijewski J, Kauffman RE, Koh JL, Malviya SV, Rose JB, Richards PT, Gennevois DJ (2008) 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 121(5):979–987. https://doi.org/10.1542/peds.2007-0814
42. Shin J, Kim GS, Sim H (2022) Comparing the effectiveness of three pain relief methods for inserting a needle into the implanted venous access chemoport: a randomized controlled trial. Int J Nurs Pract 28(4):e12974. https://doi.org/10.1111/ijn.12974
43. Agarwal A, Yadav G, Gupta D, Tandon M, Singh PK, Singh U (2008) The role of a flash of light for attenuation of venous cannulation pain: a prospective, randomized, placebo-controlled study. Anesth Analg 106(3):814–816. https://doi.org/10.1213/ane.0b013e318163fcc6
44. Rahimi M, Makarem J, Rooyan P (2013) Effects of a flash of light in different colors on venous cannulation pain: a randomized, controlled trial. J Clin Anesth 25(1):42–46. https://doi.org/10.1016/j.jclinane.2012.06.006
45. Loitam P (2021) Effectiveness of flash of light as a distraction technique on level of pain among hospitalized children undergoing IV cannulation at selected hospital, Bangalore. Int J Sci Res Publ. https://doi.org/10.29322/IJSRP.11.08.2021.p11680
46. Li SF, Greenwald PW, Gennis P, Bijur PE, Gallagher EJ (2001) Effect of age on acute pain perception of a standardized stimulus in the emergency department. Ann Emerg Med 38(6):644–647. https://doi.org/10.1067/mem.2001.119849
47. Sabitha P, Khakha DC, Mahajan S, Gupta S, Agarwal M, Yadav SL (2008) Effect of cryotherapy on arteriovenous fistula puncture-related pain in hemodialysis patients. Indian J Nephrol 18(4):155–158. https://doi.org/10.4103/0971-4065.45290
48. Lautenbacher S (2012) Experimental approaches in the study of pain in the elderly. Pain Med 13(2):S44–S50. https://doi.org/10.1111/j.1526-4637.2012.01326.x
49. Lautenbacher S, Peters JH, Heesen M, Scheel J, Kunz M (2017) Age changes in pain perception: a systematic-review and meta-analysis of age effects on pain and tolerance thresholds. Neurosci Biobehav Rev 75:104–113. https://doi.org/10.1016/j.neubiorev.2017.01.039
50. González-Roldán AM, Terrasa JL, Sitges C, van der Meulen M, Anton F, Montoya P (2020) Age-related changes in pain perception are associated with altered functional connectivity during resting state. Front Aging Neurosci. 12:116. https://doi.org/10.3389/fnagi.2020.00116
51. Digala LP, Govindarajan R (2021) Topical lidocaine hydrochloride 4% spray on pain perception during the needle electromyography: a prospective study. Clin Neurophysiol Pract 6:170–171. https://doi.org/10.1016/j.cnp.2021.04.001
52. Mattila K, Toivonen J, Janhunen L, Rosenberg PH, Hynynen M (2005) Postdischarge symptoms after ambulatory surgery: first-week incidence, intensity, and risk factors. Anesth Analg 101(6):1643–1650. https://doi.org/10.1213/01.ANE.0000184189.79572.28
53. Chia YY, Hung CC, Liu K, Ger LP, Wang PN (2002) Gender and pain upon movement are associated with the requirements for postoperative patient-controlled iv analgesia: a prospective survey of 2,298 Chinese patients. Can J Anaesth 49(3):249–255. https://doi.org/10.1007/BF03020523
54. Taenzer AH, Clark C, Curry CS (2000) Gender affects report of pain and function after arthroscopic anterior cruciate ligament reconstruction. Anesthesiology 93(3):670–675. https://doi.org/10.1097/00000542-200009000-00015
55. Wiesenfeld-Hallin Z (2005) Sex differences in pain perception. Gend Med 2(3):137–145. https://doi.org/10.1016/s1550-8579(05)80042-7
56. Prakash SB, Shankarappa V, Prabha V (2019) Comparative study of pain thresholds between diabetic neuropathy patients & non diabetic subjects. Int J Physiol. https://doi.org/10.37506/ijop.v7i2.229

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