Acta Biomed 2024; Vol. 95, N. 3: e2024105 DOI: 10.23750/abm.v95i3.15266

Original article

Effectiveness of tattoo cream on children's pain and fear during venipuncture procedure: a randomized controlled trial

Sherzad Khudeida Suleman[1], Nizer Yahya[2], Stefan Nilsson[3, 4, 5], Karin Enskär[1]

[1]Department of Women's and Children's Health, University of Uppsala, Uppsala, Sweden; [2]Department of Pediatric Medicine, University of Duhok, Duhok, Iraq; [3]Institute of Health and Care Sciences, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden; [4]Centre for Person-Centered Care, University of Gothenburg, Gothenburg, Sweden; [5]Queen Silvia Children´s Hospital, Sahlgrenska University Hospital, Gothenburg, Sweden

Abstract. *Background and aim:* The venipuncture procedure causes significant discomfort, fear, and pain in children. This study aimed to evaluate the effectiveness of TKTX cream, also known as tattoo cream, in reducing pain and fear during venipuncture in children. *Methods:* In this parallel randomized controlled trial, children aged 6–12 years were randomly assigned to either an intervention group or a control group. The intervention group (n = 44) received TKTX cream during the venipuncture procedure, while the control group (n = 44) received no cream. The outcomes of the procedure were evaluated by the children, their parents, and an observing nurse within 2–3 minutes after the procedure. *Results:* Patients receiving TKTX cream (5% lidocaine, 5% prilocaine, and 1% epinephrine) reported significantly lower mean levels of pain and fear than did the control group, as measured by the children, mothers, and nurse observers. In the control group, the average pain levels were 6.88, 6.93, and 6.98, whereas in the experimental group, they were significantly lower at 3.02, 3.02, and 2.52, respectively. Furthermore, the TKTX cream group exhibited significantly lower levels of fear than did the control group, at 2.52, 2.57, and 2.52, respectively, compared to 3.02, 3.07, and 3.97, respectively, in the control group. Additionally, TKTX-Cream has been shown to improve the success rate of procedures in children, shorten procedure times, and cause only minor changes to the dermis. *Conclusions:* This study demonstrated that TKTX-Cream is effective in reducing children's pain and fear during venipuncture procedures. (www.actabiomedica.it)

Key words: pharmacology, pain, fear, child, venipuncture

Introduction

Children frequently undergo intravenous venipuncture procedures in the emergency department. This painful procedure can cause considerable stress and anxiety for children, their parents, and the care provider (1). Therefore, pain can trigger post-traumatic stress in children, preventing them from cooperating during anaesthetic induction (1). Pain and anxiety management must be minimized to prevent long-term behavioral problems and adverse clinical outcomes (2). Therefore, pediatric nurses must actively and passionately create a safe and comfortable environment in which to perform child venipunctures.

There are a variety of ways to alleviate pain during venipuncture procedures, including pharmacological and non-pharmacological approaches. Pharmacological techniques include topical anaesthesia, such as a eutectic mixture of local anaesthetics such as EMLA cream (2.5% lignocaine and 2.5% prilocaine), 4% amethocaine cream, and nitrous oxide gas (3). The primary drawbacks of this mixture include a required application time of 60-90 minutes before venipuncture, vasoconstriction, skin blanching, and the risk of

methemoglobinemia in children younger than 1 year of age (4, 5). These preparations can be challenging to use in an emergency department, or other care setting times are limited (6).

Most topical formulations, including 5% lidocaine-prilocaine cream (EMLA; AstraZeneca, Wilmington, DE), 4% tetracaine gel (amethocaine; Smith and Nephew Healthcare, Hull, UK), 4% lidocaine cream (L.M.X.4; Ferndale Laboratories, Inc., Ferndale, MI), and iontophoresis, provide adequate skin analgesia in various clinical situations. However, adverse reactions have also been reported. Almost all patients experience skin darkening after the application of lidocaine-prilocaine cream (5%) and lidocaine iontophoresis due to vasoconstriction, making vascular access more difficult (7, 8, 9).

In a study that evaluated the effect of 8% lidocaine spray on pain in children, it was determined that the unperforated veins were not clear or deep and that after application, 30 minutes were required (10). Additionally, these sprays have risk factors that can lead to permanent skin changes and may cause local cell death if applied for more than 10 seconds due to severe local hypothermia in the area (11). Furthermore, these sprays can cause allergic reactions, burning sensations, and minor temporary skin changes(11).

The most effective local anaesthetic preparation in clinical practice is one that provides reliable pain relief with rapid onset of action. The onset time of a local anaesthetic is influenced by its physiochemical properties and the method of administration required for its penetration into the skin. On average, lidocaine-prilocaine cream (5%) requires 30 minutes, 4% tetracaine gel for 45 minutes, and 4% lidocaine cream for 60 minutes to achieve effective analgesia (8, 12). However, there are adverse reactions associated with local anaesthesia creams, such as EMLA, which are applied at the site of the procedure (13, 14, 15). Therefore, it is crucial to conduct studies on local anaesthesia creams with fewer adverse reactions that require less time before the procedure is performed on patients.

TKTX cream contains 10 g of 5% lidocaine, 5% prilocaine, and 1% epinephrine, and its effects and side effects in venipuncture procedures are scientifically unknown. According to the product's recommendation, approximately 20-25 minutes to take effect. TKTX cream is accepted by the U.S. Food and Drug Administration and is available worldwide. It has excellent tolerance and safety profile, with few side effects when used in venipuncture procedures. Although many cosmetic clinics have used TKTX cream, they have not conducted research on it to date. This study aimed to evaluate the efficacy of this cream on children's pain and fear during venipuncture procedures and to observe any side effects after 1 hour.

In this study, the following hypotheses were evaluated according to the scope of the research:

H1: The TKTX group showed lower levels of pain than did the control group during venipuncture.
H2: The TKTX group showed lower levels of fear than did the control group during venipuncture.
H3: The TKTX group demonstrated decreased attempts and durations of the venipuncture procedure.
H4: The TKTX group showed no adverse effects.

Methods and materials

Design

A prospective randomized controlled trial (RCT) was conducted on pediatric patients requiring venipuncture procedures using a double-blind design. The study was performed at the Heevi Pediatric Teaching Hospital in Kurdistan Region/Iraq between July 2022 and October 2023. This study was registered with the Clinical Trials Registry on July 10, 2023, with the number NCT05957718.

Patients and setting

This study was conducted at the Emergency Department of Heevi Pediatric Teaching Hospital, which is located in Duhok Province, a regional public hospital. A clinical nurse performed the venipuncture procedure in the treatment room. The children included in this study were aged between 6 and 12 years, capable of verbally expressing themselves, without visual, auditory, or developmental problems, experiencing no pain

before IV treatment, without chronic diseases, having their first hospitalization, locating an IV catheter, and experiencing no problems with the IV catheter.

Estimate sample size of the study

The sample size was determined based on an effect estimation from the results of two previous TICK-B studies (16, 17). There was a standard deviation of 2.0 for the control group and 1.5 for the experimental group. To achieve a power of 80 and a Type I error size of 0.05, 40 individuals were recruited for each group. The study group needed approximately 44 participants to achieve a 20% loss rate. To ensure the effectiveness of the new pharmacological intervention and to better estimate the effects of TKTX'-C, the sample size was increased. In this study, Cohen's d was 0.81, but the effect size could not be determined due to the small size of the effect.

Measurement tools

The Child and Family Information Form, Wong-Baker FACES (WB-FACES) Pain Rating Scale, and Children's Fear Scale (CFS) were used to collect the data. The tools described are as follows. The general characteristics of the patients, including age, gender, hospitalization days, and number of attempts, were recorded using a predesigned questionnaire as a child and family information form. In addition, the Wong–Baker FACES scale (WB-FACES) was used to assess the intensity of children's pain levels based on self-reports. The scale ranged from 0 to 10 and included six different illustrated faces, demonstrating different emotions from smiling (0, very happy, no pain) to crying (10, which hurts way worse) (18). Additionally, the scale was used to measure the children's fear levels during venipuncture procedures based on their facial expressions. Scores ranged from 0 to 4 and included five facial expressions, each of which was given a score. The face picture with no reaction indicated that the child was not afraid (0 points), whereas the face picture of the child who was scared (4 points) indicated that the child was very afraid (19). Finally, to examine the tolerability and safety of the study drugs, their frequency of adverse events (AEs) (e.g., erythema, blanching, edema, burn, or itching) and their effects on the skin after they were removed from the body were assessed. Five categorical scales were used (none, mild, moderate, severe, and extreme). Additionally, the number of attempts and duration of the venipuncture procedures were assessed.

Study procedure and groups

In the intervention group, tattoo creams such as KTX-Cream are currently available in cosmetic clinics. Two pharmacologists were consulted about the uses and side effects of TKTX and provided insight into its mechanism of action. They advised that this cream's formulation was effective and safe, with few side effects. Despite the FDA's acceptance of this cream, they suggested conducting a pilot study of approximately 10–20 children to determine its safety and side effects. A pilot study was conducted with 20 patients from our hospital before the current study was initiated three months later. The patients were administered TKTX cream 20-25 minutes before the procedure. Based on the pharmacologists' advice and the pilot practice study, this cream was applied. The TKTX cream was provided before the procedure, and the children were allowed to proceed until the venipuncture procedure was completed.

The intervention was conducted by the first author, a pediatric nurse with a master's degree who has worked in pediatrics for more than fifteen years and is currently pursuing a Ph.D. in Pediatrics. The children, the mother, and a nurse observer assessed the outcome. The researcher trained the nurse observer to measure fear and pain. As a pediatric nurse, the observer had eight years of experience. In the pediatric wards, the pediatrician was responsible for making clinical decisions regarding venipuncture procedures. The clinical nurses who performed the venipuncture procedure had a minimum of ten to twelve years of experience. Therefore, we did not provide any additional education to the nurses regarding venipuncture. In the control group, the participants received routine venipuncture care without the use of any pharmacological or non-pharmacological agents; as a placebo treatment, this group of children was given Vaseline® as a placebo group. The venipuncture procedure was performed by a nurse in the presence of the child's parents.

Randomization process

Patients who underwent venipuncture procedures in a public pediatric hospital were required to fill out a predesigned registration form. Additionally, written informed consent was obtained from all parents, as well as verbal assent from the children, before participation in this study. To avoid bias, closed envelopes were used for simple randomization; each envelope had either "TKTX (TCG)" or "Placebo (PG)" written inside. The nurses were blinded to the group assignments, as the envelopes for the children were sealed and opaque. Additionally, the observer nurses who measured pain and fear were unaware of the group assignment.

To further avoid bias, the observer nurse was not shown the TKTX cream during the patients' assignment or intervention. In addition, we coordinated with the head nurse of the emergency department to prevent any other nurses from entering the room. All 88 invited patients agreed to participate and were randomly assigned to either the TKTX or placebo group. We used the allocation concealment method and selected one child from each room in the emergency unit. There were four to six children in each room in the emergency department. Children were unaware that they were comparing their levels of pain and fear with those of a different group. We requested that nurses and mothers not inform their children about the intervention, so the children were unaware of the main objectives of the intervention (see Figure 1). In total, 44 children were randomly assigned to the TKTX group, while 44 patients were assigned to the placebo group.

Data collection procedures

A clinical performance nurse with more than five years of experience in pediatric patient care conducted the venipuncture procedure. There were no conflicts of interest. Pediatricians made clinical decisions regarding venipuncture. The observer nurse has extensive experience in providing care for pediatric patients. With more than 15 years of experience, she has been collecting demographic information from patients using self-report forms. This included age, gender, hospitalizations, and attempts. Researchers read the parents and children a standardized description of the pain and fear tools prior to randomization, and both acknowledged understanding the instructions. The observer nurse, patient, and parent assessed pain and fear before and after the procedure using the 0–4 CFS scale for fear and the 0–10 WB-FACES scale for pain. The second nurse then performed the venipuncture procedure for all the children. After the procedure, the children were asked to assess their levels of fear and pain. The 88 children were randomly divided into two groups of 44 using opaque sealed envelopes. Following group assignments, the children and their parents went to the venipuncture room.

Venipuncture procedures were conducted between 8:30 a.m. and 2:00 p.m. The parents remained in the venipuncture room with their children. TKTX-Cream was administered to the children in the intervention groups 20 minutes prior to the insertion of the needle. Following the procedure, the pain levels of the children were assessed using the same method as their level of fear.

Statistical analyses

All the statistical analyses were conducted using the Statistical Package for the Social Sciences version 28.0 (SPSS Inc., Chicago, IL, USA). Descriptive data were analysed using means, standard deviations, frequencies, and percentages. To determine whether the data were normally distributed, a histogram chart was used. Chi-square tests and t tests were employed to analyse all parametric data and baseline characteristics. Independent t tests were utilized to compare the outcomes (pain and fear) between the two groups. Statistical analyses were conducted on both sides with a significance level of $P = 0.05$.

Ethical statement

The paper was part of a Ph.D. On June 1, 2021, it was approved by the Scientific Research Department of the General Directorate of Health in Duhok with registration number 0106202I-5-2, granting publication rights and receiving administrative approval from Heevi Hospital. Written informed consent was obtained from the parents of all patients before they were

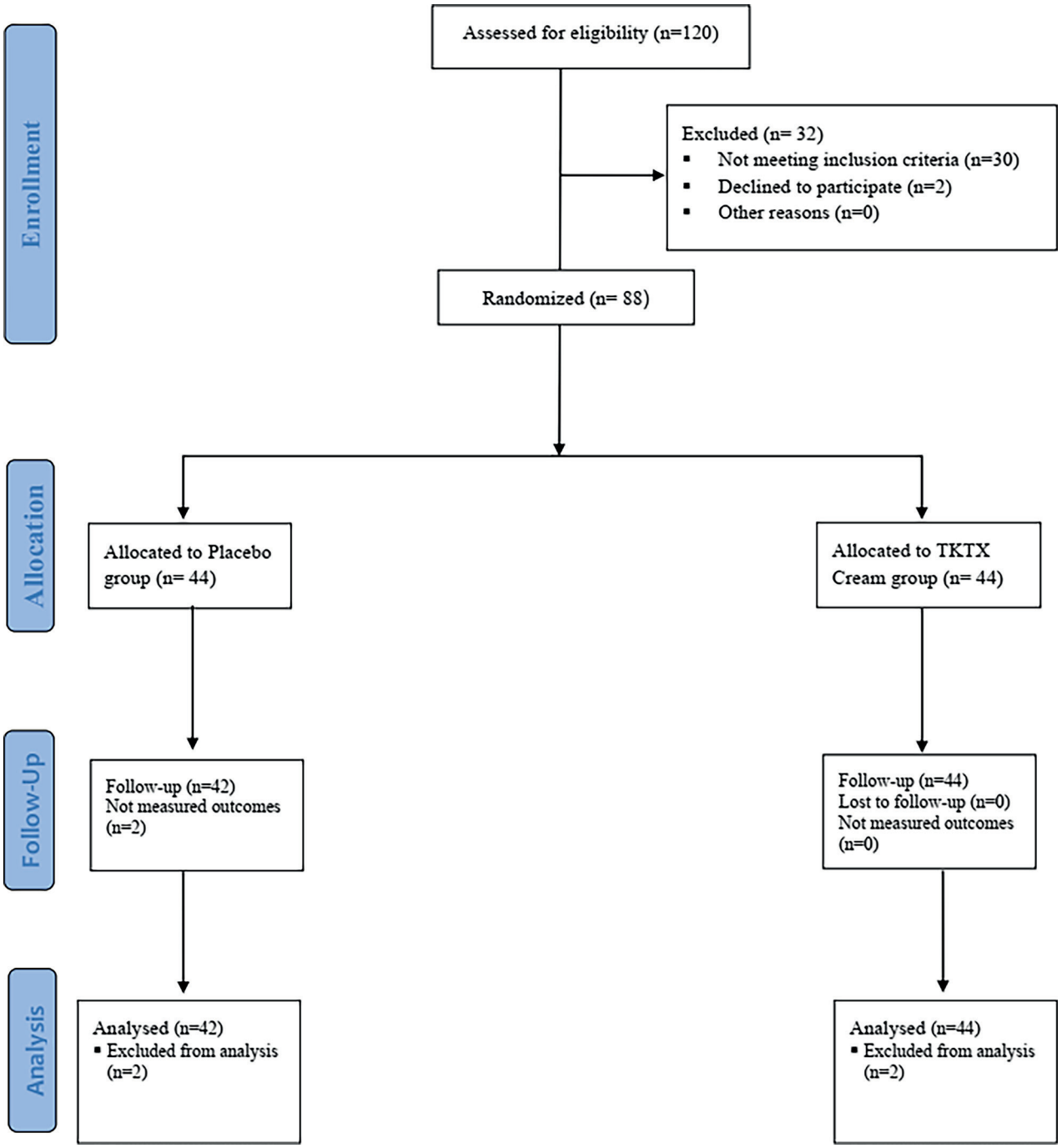

Figure 1. Flow chart showing the recruitment of patients for the study.

included in the study, in accordance with the Declaration of Helsinki. No harmful interventions were performed in this study. The study was registered with Clinical Trials.gov on 10.07.2023 under the number NCT05957718.

Results

The study involved approximately 120 children who were assessed for eligibility, 88 of whom were enrolled and randomly assigned to the groups. The other

Table 1. A comparison of baseline characteristics and preprocedural fear scores among the study groups.

Child's Characteristics	Study groups		*P* (two-sided)
	TKTX-C group (n=44)	Control group (n=42)	
No. and Frequencies			
Gender: Male Female	 22 (50%) 22 (50%)	 20 (47.6%) 22 (52.4%)	0.833†
Site: Dorsum of hand Other	 42 (95.5%) 2 (4.5%)	 36 (85.7%) 6 (14.3%)	0.120†
Clinical: Fever Gastrointestinal Respiratory	 10 (22.7%) 17 (38.65%) 17 (38.65%)	 9 (21.4%) 17 (40.5%) 16 (38.1%)	0.982†
Mean and Standard Deviation			
Age	8.61 (1.63)	8.88 (1.25)	0.398§
Hospitalization days	3.59 (0.84)	3.74 (1.03)	0.472§
Previous pain	7.00 (1.71)	6.86 (1.71)	0.700§
Pre-cannulation Fear	3.20 (0.594)	3.19 (0.594)	0.913§

Notes: †: Chi-square test; §= *t test*.

32 participants were not included because they did not meet the inclusion criteria, because their parents refused to participate, or because they were scheduled for discharge. Homogeneity tests of the general characteristics of the patients in the study group revealed no significant differences in age, gender, hospitalization duration, clinical diagnosis, or site of venipuncture (Table 1).

The study revealed that patients in the intervention group had significantly less pain (as measured by the children) after the procedure (3.02 versus 6.88, respectively, P=0.000) than patients in the placebo group. In addition, parents and an observer nurse reported significantly lower mean pain values in the intervention group than in the placebo group. The same pattern was observed for fear after the procedure (2.52 vs. 3.02; P=0.007) (Table 2).

Table 3 shows that the duration of the venipuncture procedure decreased in the intervention group compared to the control group. Furthermore, according to the number of attempts to perform the procedure, children in the intervention group made only one attempt, while children in the control group made more than one attempt. Adverse events related to venipuncture occurred more frequently in the control group than in the intervention group.

As shown in Table 4, there was no statistically significant difference in pain or fear in the control group (6.86 vs 6.88, P = 0.550; 3.19 vs 3.02; P = 0.320), whereas there was a statistically significant difference in pain or fear in the intervention group (7.00 vs 3.02, P = 0.000; 3.20 vs 2.52, P = 0.000).

According to Table 5, neither the level of pain the children experienced before the procedure nor their other medical conditions impacted their level of pain after the procedure.

Discussion

On the basis of this discussion, this study reported that TKTX-Cream reduced the pain level of children, according to the children, their parents, and the nurse who observed them after the procedure. Furthermore, it was observed to be weak in reducing children's fear after undergoing the procedure. For the first time, TKTX cream was used as a local cream for painful procedures in school-aged children. Pain is

Table 2. Comparison of pain and fear between the TKTX-C and placebo groups.

Outcome measurements	Study groups mean (SD)		*P*	(Mean diff 95% CI)	Effect size (Cohen's d)
	TKTX-Cream Mean (Standard Deviation)	Placebo Mean (Standard Deviation)			
After procedure					
Pain					
Child reported	3.02 (1.532)	6.88 (1.685)	0.000†	(3.168-4.548)	2.398
Mother-reported	3.02 (1.502)	6.93 (1.659)	0.000†	(3.228-4.584)	2.472
Observer-reported	3.00 (1.540)	6.98 (1.689)	0.000†	(3.284-4.669)	2.463
Fear					
Child reported	2.52 (.952)	3.02 (.715)	0.007†	(0.139-0.864)	0.593
Mother-reported	2.57 (.998)	3.07 (.745)	0.010†	(0.124-0.882)	0.570
Observer-reported	2.52 (.952)	2.98 (.680)	0.013†	(0.040-0.776)	0.476

Note: †: t test was performed for analysis.

Table 3. The safety and tolerability of the cannulation procedures among the groups.

Outcome Measurements	Study groups mean (SD)		*P*
	TKTX-Cream Mean (SD)	Placebo Mean (SD)	
Duration procedure, min	4.40 (0.87)	7.71 (0.77)	0.000†
Attempts to perform cannulation First Attempt Second Attempt	 42 (95.5%) 2 (4.5%)	 28 (66.7%) 14 (33.3%)	0.000§
Side effects None	 37 (84.1%)	 5 (11.9%)	0.000§
Erythema	3 (6.8%)	16 (38.1%)	
Edema	2 (4.5%)	12 (28.6%)	
Blanching	0 (0.0%)	2 (4.8%)	
Burns or itching	2 (4.5%)	7 (16.7%)	

Notes: † =*t* test was performed for analysis; §= chi-square test.

Table 4. Pain and fear over time among the study groups.

Groups	Study groups mean (SD)		*P*	(Mean diff 95% CI)	Effect size (Cohen's d)
	Pain before the procedure by children	Pain after the procedure by children			
Placebo Mean (SD)	6.86 (1.71)	6.88 (1.68)	0.555†	-0.31-0.17	NA
TKTX-Cream Mean (SD)	7.00 (1.71)	3.02 (1.50)	0.000†	3.23-4.63	1.84
Fear					
Groups	**Fear before the procedure by the children**	**Fear after the procedure by the children**			
Placebo Mean (SD)	3.19 (0.59)	3.02 (0.71)	0.323†	-0.17-0.50	N/A
TKTX-Cream Mean (SD)	3.20 (0.59)	2.52 (0.95)	0.000†	0.30-1.06	0.54

Note: †= Paired samples t test was performed for analysis.

Table 5. Role of fear, pain before the procedure, hospitalization day, and general postoperative pain characteristics in the intervention group.

	Dependent variable: post-procedure pain			
	Standardized Coefficients			
Controlling Factors	**Beta**	**t**	***P***	**95.0% Confidence Interval for B**
Pain before procedure	-.099	-0.601	0.550	-0.387-0.210
Fear before procedure	.053	0.329	0.740	-0.713-0.989
Age	-.062	-0.354	0.720	-.391-0.275
Gender	.211	1.313	0.190	-.348-1.628
Hospitalization days	-.296	-1.827	0.070	-1.135-0.059
Clinical diagnosis	-.161	-.928	0.35	-1.011-0.376

Note: Linear regression was performed for the statistical analyses.

often experienced during procedures that are routinely performed in hospitals, such as phlebotomies and peripheral intravenous catheterization. This can cause tension, anxiety, and fear in children (16, 17).

A novel aspect of this study is that it examines the effects of TKTX cream on a group of school-age children experiencing pain during venipuncture procedures. To our knowledge, this was the first study to evaluate the effectiveness of TKTX-C in reducing the pain experienced by children following painful procedures, such as venipuncture.

Painful procedures cause considerable stress and anxiety in children, their parents, and healthcare providers (1). To minimize the pain and fear associated with these situations, a variety of methods for the relief of pain through intravenous venipuncture are available, such as pharmacological methods, such as local anaesthesia (EMLA cream) (3). According to the literature, TKTX-C reduces pain by numbing the needle area in school-age children after venipuncture.

Various types of topical anaesthetics are available in different formulations and vehicles, allowing compounds to exist in liquid form and at higher concentrations while still being safe (20). TKTX-C thus has a higher concentration than other locally applied creams reported in the literature.

Vaporizing sprays such as Pain Ease may be an alternative to anaesthetic creams. It is important to note that their main advantage is their immediate effectiveness in reducing pain during IV venipuncture without increasing the procedure's difficulty, although their duration of action is limited (3). When applied, they may cause mild discomfort (a cold sensation) (14), which limits their usefulness in younger children who are unable to comprehend the feeling. TKTX cream has shown effectiveness as a spray for reducing and analysing successful procedures, with longer durations of action than these sprays and with a low frequency of discomfort to the patient.

There were no specific age restrictions imposed on the use of this new preparation cream; however, it is important to exercise caution when applying lidocaine to younger children (21). Adverse outcomes in topical lidocaine exposure: a pediatric case series From the United States National Poison Data System (21).

A number of studies have been conducted to determine the length of time that creams are applied during venipuncture procedures among children; most of them require 30-60 minutes; however, some require only one minute, such as sprays, which are known to have serious side effects on children's skin (10, 13, 14). In contrast, TKTX-Cream required only 20-25 minutes and had few adverse effects on children's skin compared to the spray previously discussed.

Based on the results of the present study, the average duration of the venipuncture procedure decreased compared to that in the placebo group. According to previous literature, local anaesthesia was used to achieve this result, which may be part of the reason for this effect.

The success rate of procedures and the number of attempts previously reported provide evidence to

support the claim that the use of topical local anaesthesia interferes with the success of venipuncture procedures (22). Additionally, the results have important implications for the management of procedural pain in school-age children. Consistent with our results, there was a reduction in the number of attempts made to perform venipuncture among the children who received TKTX-C.

This new preparation provides prompt and effective analgesia, increasing the likelihood of successful venipuncture on the first attempt and reducing the overall procedure time. Therefore, children, parents, and healthcare workers experience less fear during venipuncture procedures and future procedures. This not only saves time but also allows healthcare workers to spend more time addressing other patient concerns. The results of this study indicate that TKTX-C improves procedure success rates; however, it is unknown whether other anaesthetic preparations have similar effects. Future studies must address how different agents compare.

In terms of assessing the safety and tolerance of local anaesthetic creams, various side effects have been reported (23). One of the most commonly used topical anaesthetics is a combination of 2.5% lidocaine and 2.5% prilocaine (EMLA®). Several factors affect systemic absorption, such as application duration, anatomic location, and treatment area. Analgesia was found to decrease 3 mm after 60 minutes and 5 mm after 120 minutes following application. Several reactions have been reported due to the use of this drug, including erythema, pallor, and edema. Although these side effects usually disappear within a few days, they can make venous venipuncture difficult, as they are likely to cause local reactions (23). The inclusion of epinephrine in local anaesthetics has been established as a safe practice for achieving vasoconstriction in the hands, feet, or other regions. TKTX-Cream was administered topically to the skin approximately 20-25 minutes prior to venipuncture in school-age children, with a subsequent evaluation of the skin's reaction conducted 90 minutes post-procedure.

In light of the results of this study, it may not be possible to generalize the findings to younger patients in other settings, such as outpatient clinics, as only one hospital was involved. To increase the generalizability and validity of the findings generated from this study, future studies should consider recruiting participants from multiple sites with larger and more diverse sample sizes. We used only subjective measures to evaluate venous venipuncture pain; therefore, to evaluate pain objectively, it is recommended that heart rate and blood pressure be measured before and after venipuncture. Additionally, emotional factors can easily influence these parameters, resulting in poor accuracy when estimating venipuncture pain.

Conclusion

In conclusion, TKTX-C improves the success rate of procedures, reduces pain, shortens procedure times, and is associated with minor changes to the dermis when used for cutaneous analgesia in children. These results indicate that the use of TKTX-C for superficial anaesthesia is an effective and safe treatment method. This effect, in combination with the ease of administration, long duration, and rapid onset of action of the drug (epinephrine), makes TKTX-C an ideal drug for routine use. Based on the findings of this study, TKTX-C is recommended as the new standard of care for cutaneous analgesia in children. Practice implications: Nurses can use tattoo cream (TKTX-Cream) to decrease children's pain and fear during venipuncture procedures in less than 20 minutes.

Acknowledgements: The authors would like to extend their gratitude to the pediatric nurses at Heevi Pediatric Teaching Hospital. We would like to express our deepest gratitude to the nurses for their kind cooperation and interest in the financial statement. In addition, we would like to thank all the families and children who participated in this study. We thank Mr. Deldar Morad Abdullah, an assistant professor at Duhok University, for support in the data analysis and the review of the manuscript.

Funding: The authors have no funding to disclose.

Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki and was approved by the Scientific Research Department of the General Directorate of Health in Duhok (Resolution No. NCT05957718 of 7 July 2023). Furthermore, the manager of Heeve Pediatric Teaching Hospital provided consent for this study.

Conflict of Interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article.

Relationship with TKTX Cream Company: The authors confirm that I have no direct relationship with the TKTX cream company. As the lead researcher on this study, we have not received any funding, sponsorship, or other support from the company, nor do we have any ownership, advisory, or affiliation with them. The decision to use TKTX cream was based solely on its scientific merit and potential benefits for the pediatric participants, without any personal or professional ties to the company. I maintain complete objectivity and independence in conducting this research, with no conflicts of interest that could influence the integrity or findings of the study.

Author Contributions: S.S.: conceptualization, methodology, validation, formal analysis, investigation, data curation, writing-original draft, writing-review and editing, project administration; N.Y.: conceptualization, methodology, formal analysis, investigation, resources, writing-review and editing; S.N.: conceptualization, methodology, formal analysis, investigation, resources, writing-review and editing; K.E.: conceptualization, methodology, validation, formal analysis, investigation, writing-original draft, writing-review and editing supervision.

References

1. Kulkarni MM, Patil AT, Sinha S. A comparative study of 10% lidocaine spray versus eutectic mixture of 2.5% lidocaine and 2.5% prilocaine (EMLA) to attenuate pain of peripheral venous cannulation in children: A prospective randomized control trial at a tertiary care centre. Indian J Anaesth 2023 February 16; 67(2):167-72. doi: 10.4103/ija.ija_705_22.
2. Cunningham NR, Nelson S, Jagpal A, et al. Development of the Aim to Decrease Anxiety and Pain Treatment (ADAPT) for pediatric functional abdominal pain disorders. JPGN. 2018 January 4; 66(1):16-20. doi:10.1097/MPG.0000000000001714.
3. Trottier ED, Doré-Bergeron M-J, Chauvin-Kimoff L, Baerg K, Ali S. Managing pain and distress in children undergoing brief diagnostic and therapeutic procedures. Paediatr Child Health. 2019 December 09; 24(8):509-21. doi: 10.1093/pch/pxz026.
4. Naik VM, Mantha SSP, Rayani BK. Vascular access in children. Indian J Anaesth. 2019 September; 63(9):737-45. doi: 10.4103/ija.IJA_489_19.
5. Egekvist H, Bjerring P. Effect of EMLA Creamon Skin Thickness and Subcutaneous Venous Diameter. A Randomized, Placebo-controlled Studyin Children. Acta Derm Venereol. 2000 December; 80(11):340-3. doi: 10.1080/000155500459268.
6. Zempsky WT, Cravero JP, Committee on Pediatric Emergency Medicine, Anesthesiology Therefore, Medicine P. Relief of pain and anxiety in pediatric patients in emergency medical systems. Pediatrics. 2004 November 01; 114(5):1348-56. doi: 10.1542/peds.2004-1752.
7. Zempsky WT, Anand K, Sullivan KM, Fraser D, Cucina K. Lidocaine iontophoresis for topical anaesthesia before intravenous line placement in children. J Pediatr. 1998 June; 132(6):1061-3. doi: 10.1016/s0022-3476(98)70413-5.
8. Eichenfield LF, Funk A, Fallon-Friedlander S, Cunningham BB. A clinical study to evaluate the efficacy of ELA-Max (4% liposomal lidocaine) as compared with eutectic mixture of local anaesthetics cream for pain reduction of venipuncture in children. Pediatrics. 2002 June 01; 109(6):1093-9. doi: 10.1542/peds.109.6.1093.
9. Kleiber C, Sorenson M, Whiteside K, Gronstal BA, Tannous R. Topical anaesthetics for intravenous insertion in children: a randomized equivalency study. Pediatrics. 2002 October 01; 110(4):758-61. doi: 10.1542/peds.110.4.758.
10. Kanai A, Suzuki A, Okamoto H. Comparison of cutaneous anaesthetic effect of 8% lidocaine spray with lidocaine patch using current perception threshold test. Pain Med. 2010 January 22; 11(3):472-5. doi: 10.1111/j.1526-4637.2009.00790.x.
11. Farion KJ, Splinter KL, Newhook K, Gaboury I, Splinter WM. The effect of vapocoolant spray on pain due to intravenous cannulation in children: a randomized controlled trial. Cmaj. 2008 July 01; 179(1):31-6. doi: 10.1503/cmaj.070874.
12. Doyle E, Freeman J, Im N, Morton N. An evaluation of a new self□adhesive patch preparation of amethocaine for topical anaesthesia prior to venous cannulation in children. Anaesth Rep. 1993 December; 48(12):1050-2. doi: 10.1111/j.1365-2044.1993.tb07523.x.
13. Greveling K, Prens E, Ten Bosch N, van Doorn M. Comparison of lidocaine/tetracaine cream and lidocaine/prilocaine cream for local anaesthesia during laser treatment of acne keloidalis nuchae and tattoo removal: results of two randomized controlled trials. Br J Dermatol. 2017 January 01; 176(1):81-6. doi: 10.1111/bjd.14848.
14. Griffith RJ, Jordan V, Herd D, Reed PW, Dalziel SR. Vapocoolants (cold spray) for pain treatment during intravenous cannulation. Cochrane Database Syst Rev. 2016 April 26; (4):1-34. doi: 10.1002/14651858.CD009484.pub2.
15. Dave NM. Premedication and induction of anaesthesia in paediatric patients. Indian J Anaesth. 2019 September; 63(9):713-20. doi: 10.4103/ija.IJA_491_19.
16. Suleman SK, Atrushi A, Enskär K. Effectiveness of art-based distraction on reducing pediatric patients' pain and anxiety during venipuncture: A randomized controlled trial. Complement Ther Clin Pract. 2022 August 1; 48:101597. doi:10.1016/j.ctcp.2022.101597.
17. Suleman SK, Atrushi A, Enskär K. Effectiveness of art-based distraction in reducing pain and anxiety of hospitalized children during cannulation procedure: A randomized controlled trial. Belitung Nurs J 2022 June 28; 8(3):213-21. doi: 10.33546/bnj.2054

18. Mayer DM, Torma L, Byock I, Norris K. Speaking the language of pain. Am J Nurs 2001 February; 101(2):44-50. doi: 10.1097/00000446-200102000-00047.
19. McMurtry CM, Noel M, Chambers CT, McGrath PJ. Children's Fear During Procedural Pain: Preliminary Investigation of the Children's Fear Scale. Health Psychol. 2011 Augst 01; 30(6):780-8. DOI: 10.1037/a0024817.
20. Kundu S, Achar S. Principles of office anaesthesia: part II. Topical anaesthesia. J Anaesthesiol Clin Pharmacol. 2002 July 01; 66(1):99-102. PMID: 12126037.
21. Eisenberg J, Tedford NJ, Weaver N, Becker S, Moss MJ. Adverse Outcomes in Topical Lidocaine Exposure: A Pediatric Case Series From the United States National Poison Data System. Clin Pediatr (Phila). 2023 March 12; 62(11):1390-7. doi: 10.1177/00099228231159646.
22. Taddio A, Soin HK, Schuh S, Koren G, Scolnik D. Liposomal lidocaine to improve procedural success rates and reduce procedural pain among children: a randomized controlled trial. Cmaj. 2005 Jun 21; 172(13):1691-5. doi: 10.1503/cmaj.045316.
23. Sobanko JF, Miller CJ, Alster TS. Topical anaesthetics for dermatologic procedures: a review. Dermatol Surg. 2012 May; 38(5):709-21. doi: 10.1111/j.1524-4725.2011.02271.x.

Correspondence:
Received: 4 October 2023
Accepted: 4 April 2024
Sherzad Khudeida Suleman
Department of Women's and Children's Health, University of Uppsala, Uppsala, 751 85 Sweden
Phone: 0049762616780
E-mail: sherzad.khudeida@kbh.uu.se; sherzadkhudeida@uod.ac