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Comparing the Effect of Hegu Point Acupressure and Ice Massage on Pain and Physiological Responses Associated with Vincristine Administration in Children with Acute Lymphoblastic Leukemia: A Randomized Crossover Study

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Abstract

Introduction: Managing chemotherapy-related pain in children is a significant challenge for treatment teams, and complementary medicine can be used to reduce such pains. The present study aimed to compare the effect of Hegu point acupressure and ice massage on pain and physiological responses to vincristine administration in children with acute lymphoblastic leukemia (ALL).

Methods: This randomized, single-blind, crossover study was conducted from December 2021 to August 2022 on 28 children (aged 3–12 years) with ALL undergoing vincristine-based chemotherapy at the Hefdah-Shahrivar Educational and Therapeutic Center. To prevent bias, the interventions were administered by the investigator, while a blinded assessor performed all outcome assessments. The Participants were randomly assigned to two different intervention sequences. Each participant received both Hegu point acupressure and ice massage, separated by

a one-week washout period. Pain intensity, heart rate (HR), and oxygen saturation (SpO_2) were assessed using the Oucher scale and a pulse oximeter, before the intervention, 5 seconds before vincristine injection, and 15 seconds after injection. Data were analyzed using repeated measures ANOVA, multivariate analysis of variance (MANOVA) and Wilks' lambda statistical tests.

Results: There was a significant difference in pain intensity associated with vincristine administration between the two conditions of ice massage and acupressure; so that the average pain scores in the ice massage condition were lower than the acupressure condition (P = 0.016). HR increased significantly over time in both interventions, with the ice massage condition exhibiting significantly higher rates than the acupressure condition (P = ٠,٠٠٤). There were no significant differences in SpO_2 levels between the interventions (P = 0.89).

Conclusions: Ice massage at the Hegu point may serve as an effective non-pharmacological approach to alleviate pain associated with vincristine administration in children with ALL. However, further large-scale multi-center studies are warranted to confirm these findings and establish its clinical efficacy.

Keywords: Acupressure, Ice Massage, Pain, Acute Lymphoblastic Leukemia, Vincristine, Child

Introduction

Childhood cancers are the leading cause of disease burden among children worldwide, with their incidence steadily increasing in recent years.[1] In Iran, the age-standardized incidence rate (ASR) of childhood cancers is 119.56 per million individuals aged 0 to 19 years.[2] Among these cancers, acute lymphoblastic leukemia (ALL) is the most prevalent, both globally and in Iran.[3, 4] ALL accounts for 25-30% of childhood cancers and approximately 75-80% of pediatric leukemia cases.[3, 5]

Children diagnosed with cancer often experience significant treatment-related side effects, with pain being one of the most common, severe, and distressing.[6, 7] This pain can arise during diagnosis, recurrence, disease progression, and treatment, and is often induced by therapeutic interventions such as chemotherapy or by diagnostic and other painful procedures, such as venipuncture.[8-11] Research indicates that, in contrast to adults, children with cancer are at a higher risk of experiencing pain due to the frequent treatments and invasive procedures they undergo. Furthermore, over 50% of children and adolescents report that their pain remains untreated most of the time.[12, 13]

The primary treatment for childhood cancers is chemotherapy; however, it often results in pain, which is one of its most common side effects. Compared to other symptoms, pain in these patients causes greater suffering and discomfort.[13-16] More than 40% of children with acute leukemia experience pain during chemotherapy, a condition that affects approximately 75% of their lives.[17] The pain associated with chemotherapy typically results from intravenous or arterial drug infusion.[18] Vincristine, one of the most commonly used and effective drugs for treating leukemia.[3] Besides being unpleasant, the experience of pain triggers a range of physiological responses. As pain signals travel up the spinal cord to the brainstem and thalamus, they activate the autonomic nervous system as part of the body's stress response. Stimulation of the sympathetic nervous system leads to physiological reactions such as increased heart rate (HR), rapid breathing,

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sweating, erythema, decreased blood oxygen saturation, pupil dilation, restlessness, and elevated blood pressure.[19, 20]

Management of pain is a critical aspect of nursing care and one of the primary responsibilities of nurses caring for children.[21] Developing effective methods to control and reduce pain, particularly in children undergoing chemotherapy, presents a significant challenge for treatment teams.[16, 20] In children with cancer, pain management is typically achieved through pharmacological interventions; however, side effects of these drugs (e.g., gastrointestinal or respiratory issues) can limit their effectiveness.[22] Therefore, comprehensive pain management requires the application of a combination of pharmacological and non-pharmacological approaches,[8] a point also emphasized by the American Academy of Pediatrics (AAP). In this regard, there has been a growing focus in recent years on non-pharmacological methods as effective, complementary strategies for pain management.[23-25] Nurses can often apply these approaches without a physician's order, enhancing their professional autonomy. Additionally, incorporating these treatments into nursing practice expands the scope of comprehensive care that can be provided.[16, 26]

Acupressure is a widely used physical intervention within complementary medicine; compared to acupuncture, it is considered a safer, non-invasive method and is particularly appealing for children.[8, 27, 28] In this approach, applying pressure to acupuncture points can stimulate the body's regulatory processes and help alleviate pain.[29, 30] According to research, this process may occur through mechanisms such as the release of endorphins, encephalins, and serotonin.[28] The acupoint 'Hegu' is an acupuncture site connected to the large intestine energy channel and is regarded as one of the most important points for pain relief. The energy flow in this area is closer to the surface of the skin, making it easily accessible and more responsive to stimulation. Various methods, including acupuncture, transcutaneous electrical nerve stimulation (TENS), ice massage, and acupressure, can be used to stimulate this point.[31-33]

Ice massage is another non-pharmacological method capable of producing pain-relieving effects, similar to those achieved through TENS or acupuncture; these effects are typically explained by the "gate control theory" of pain.[32, 34] According to this theory, impulses generated by ice massage may slow the transmission of pain signals to the brain by modulating the neural gates and help improve the pain perception threshold.[28, 35, 36] Ice massage at the "Hegu" point offers advantages such as relative simplicity, cost-effectiveness, ease of application and instruction, and a minimal risk of side effects. However, further research is needed to provide additional evidence-based support for its use in pain relief. [32]

Various studies have investigated the effects of acupressure and ice massage on pain and physiological indicators associated with venipuncture, vaccination, and tonsillectomy in children.[11, 33-38] However, evidence comparing these two interventions on pain induced by chemotherapy administration in children with cancer remains limited. Additionally, previous studies have primarily focused on the effects of reflexology, massage therapy, and other interventions in this population. Some studies have reported varying results regarding the effects of acupressure and ice massage, with some indicating that acupressure is more effective, while others suggest the opposite.[31, 39] Given that painful procedures and repeated chemotherapy

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injections are the primary sources of pain in children with cancer, and nurses play a crucial role in preventing and managing this pain, non-pharmacological, non-invasive, evidence-based approaches should be considered to alleviate pain associated with medical procedures in children. Moreover, considering the importance of pain management in nursing and the uncertainty surrounding the effectiveness of complementary medicine posing a challenge for its integration into care practices there is a clear need for further studies and robust research to identify new pain management treatments that offer maximum efficacy with minimal side effects. Therefore, the current study aimed to compare the effect of Hegu point ice massage and acupressure on pain and physiological responses associated with vincristine administration in children with acute lymphoblastic leukemia.

Methods and Materials

Study design and setting

This study was conducted as a two-period randomized crossover trial between December 20۲1 and August 20۲2 in the pediatric oncology Department of 17-Shahrivar Educational and Therapeutic Center in Rasht, Iran. To minimize the effects of potential bias, a single-blind design was employed, in which the outcome assessor was blinded to the allocation of the subjects. The two periods were separated by a one-week washout period to prevent carryover effects.

Participants and eligibility criteria

The study population included children aged 3 to 12 years who had been diagnosed with ALL for over one month and were undergoing chemotherapy. The inclusion criteria were as follows: receiving Vincristine-based chemotherapy, not undergoing chemotherapy through a Port-a-Cath, not having any genetic or mental disorder, having a healthy area for massage, not having received Hegu point acupressure or ice massage prior to the study, not having taken analgesics within 8 hours before chemotherapy, and requiring no more than three venipuncture attempts for the administration of vincristine. Children who had allergic reactions to the chemotherapy drug or missed their scheduled appointment were excluded from the study.

Recruitment and randomization

The sampling process began with obtaining approval from the ethics committee with code **IR.GUMS.RES.1400.356** and registering the study in the Iranian Registry of Clinical Trials (IRCT). The first author provided an explanation of the research objectives, intervention methods, and ethical considerations to both the children and their parents. Written informed consent was obtained from the parents before enrollment. Initially, 42 patients were selected by the first author using a convenience sampling method and subsequently evaluated. Following the application of inclusion and exclusion criteria, 9 children were excluded from the study prior to randomization: 4 due to age, 2 due to the presence of a Port-a-Cath, one due to a lack of consent, and 2 for other reasons. Given the limited access to the target population, the sample size was determined based on availability; this was acknowledged as a study limitation. A total of 33 children were enrolled and randomly assigned to two sequences by the fourth author (a statistics professor) using the Random Allocation Software version 1.0: sequence A (acupressure-ice massage) and sequence B (ice massage-acupressure). This randomization process was structured into ۱۳ blocks of 4. The list

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of random sequences was kept in a sealed, opaque envelope in the nursing administration office and remained unopened until the study commenced. Once the study began, the first author opened the envelope and assigned participants to one of the sequences as they presented. During the study period, five participants did not receive the assigned intervention and were subsequently removed from the analysis. Specifically, in sequence A, two participants discontinued the intervention due to skin sensitivity in the massage area and an allergic reaction to the vincristine. In sequence B, three participants were removed from the study: two were lost to follow-up due to missed appointments, and one discontinued the intervention due to the development of an infection, which precluded the administration of vincristine. Consequently, data analysis was performed following the study protocol on the 28 participants who fully completed the crossover study protocol (Figure 1).

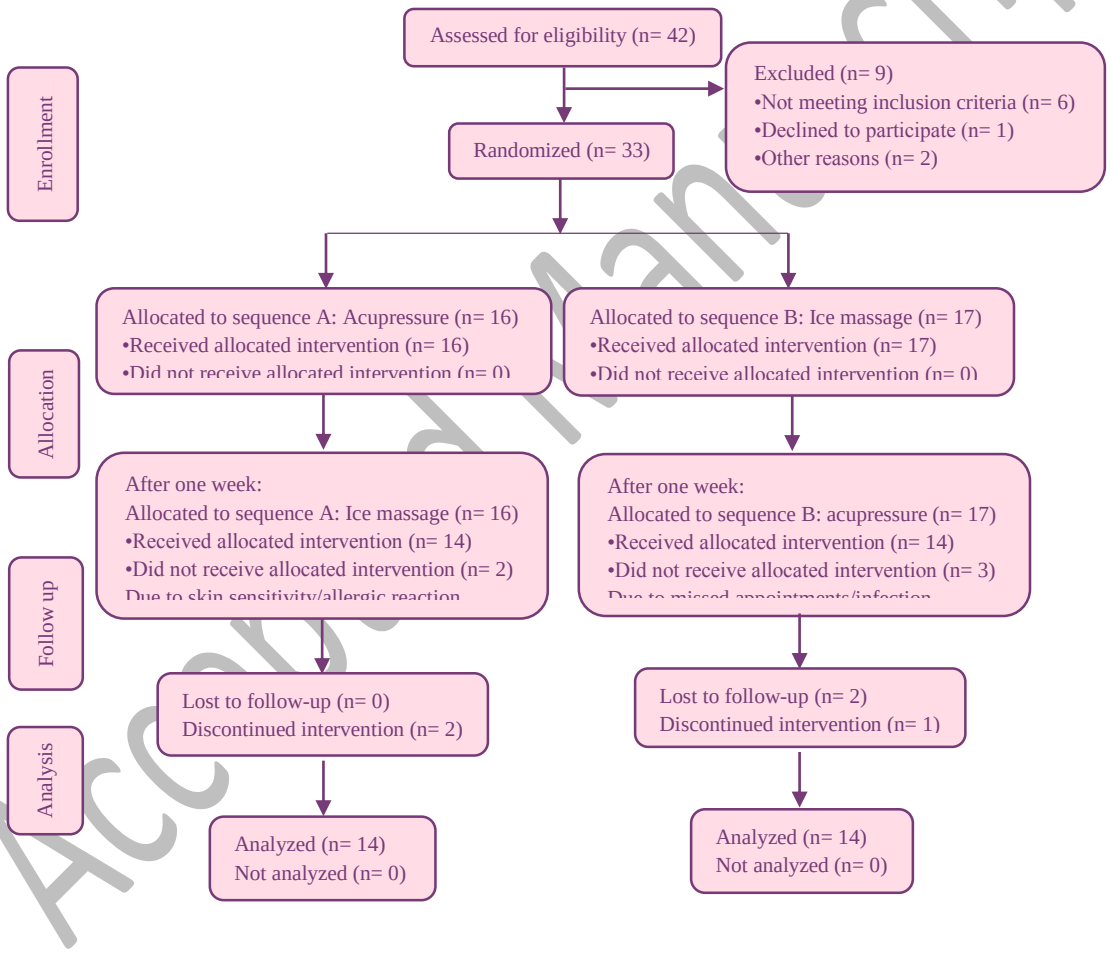

Figure 1. Study flowchart

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Data collection instruments

In this study, data were collected using a questionnaire on demographic characteristics and disease-related factors, the Oucher self-report pain intensity scale, and an Abadis pulse oximeter (manufactured in Iran). The questionnaire comprised three sections: (1) the child's profile, including sex, age, weight, and birth order; (2) family-related information, such as parents' education and occupation, monthly income, place of residence, and number of children; and (3) disease-related factors, including disease duration, history of other illnesses, number of hospitalizations, and chemotherapy drug dosage. The Oucher Scale is a widely used and highly valid self-report pain intensity tool for children, commonly employed by pediatric healthcare professionals worldwide. It comprises two scales: a 0-10 numerical scale for older children and a six-picture photographic scale for younger children. In this study, the numerical scale was used for children aged 7 years and older who could count and understand numbers. Each child selected a number representing their pain score, with 0 indicating no pain, 1–3 mild pain, 3–6 moderate pain, 6–9 severe pain, and 10 the worst pain imaginable. The photographic scale was used for children under 7 years who could not yet count or understand numbers. The selected facial expressions were converted into numerical values, where the first image (bottom) represented 0 (no pain), the second image 1 (mild pain), the third 2 (moderate pain), the fourth 3 (slightly more pain), the fifth 4 (severe pain), and the sixth (top) 5 (worst pain imaginable). Its content and construct validity, and reliability have been established and documented through statistical tests.[40] To ensure comparability across different age groups, the scores from the different formats of the Oucher tool were standardized prior to statistical analysis, in accordance with the official guidelines and original reference materials.[40, 41] The Oucher Scale has been validated for use across various ethnic groups and populations.[42] Additionally, it has been utilized in numerous studies, with its validity and reliability confirmed in multiple references.[20, 29, 43-46] The Abadis pulse oximeter was used to measure HR and SpO_2. To evaluate the reliability of the device, inter-rater reliability assessment was performed. In this approach, HR and SpO_2 were measured in 20 children across two sessions spaced 20 minutes apart first by the principal investigator, and subsequently by an experienced nurse. The results from both measurement sessions were then compared. The agreement between the two raters was assessed using the Intraclass Correlation Coefficient (ICC). The results indicated excellent inter-rater reliability for both parameters: the ICC value was 0.96 ($P < 0.001$) for HR and 0.88 for SpO_2. These findings confirm the high reliability of the device for clinical use in research.

Intervention procedures

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Sequence A (acupressure-ice massage) received acupressure in the first phase of the study, followed by a one-week washout period, after which ice massage was administered in the second phase. Sequence B (ice massage-acupressure) received ice massage in the first phase, followed by a one-week washout, then acupressure in the second phase. Both interventions were performed by the first author, who under the supervision of an anesthesiologist specializing in pain medicine completed an intensive one-month training course. This course comprised four theoretical and four practical in-person sessions, based on established resources and protocols for acupressure and ice massage, and concluded with the instructor certifying the author's competence. Each intervention was performed approximately 5 minutes before the Vincristine injection. To begin the intervention, children were positioned comfortably lying on their backs. To locate the Hegu point, the child's thumb was placed in an adduction position. The Hegu point is a muscular prominence on the back of the hand, at the midpoint of the bisector of the angle between the first and second metacarpal bones, between the thumb and index finger (Figure 2).



Figure 2. The Hegu point location

Venipuncture and the Vincristine injection were performed on one hand, while interventions and measurements were conducted on the opposite hand. For the ice massage, a 2 cm diameter piece of ice wrapped in a plastic glove and cotton cloth was massaged on the Hegu point of the non-venipuncture hand for a maximum of 1 minute, in a clockwise motion with moderate pressure (3 to 4 kg).[29] The procedure was repeated 5 times with 10-second breaks, totaling 5 minutes. The acupressure intervention followed the same procedure but used the thumb instead of ice. Afterward, the nurse administered the Vincristine injection intravenously over about one minute. The nurse responsible for venipuncture and drug injection, venipuncture needle size (22- and 24-gauge Angiocath), and the location and conditions of the venipuncture and drug injection (outpatient room) were consistent for all participants throughout the study. Additionally, the pulse oximeter probe was placed on the hand that did not undergo venipuncture or injection.

Outcome assessment

Pain intensity, HR, and SpO2 were measured at three time points: before the intervention, 5 seconds prior to the vincristine injection, and 15 seconds after the vincristine injection. All assessments were conducted by a blinded research assistant. The outcome assessor adhered to

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standardized guidelines for the data collection instruments used to record pain levels and physiological parameters.

Statistical analysis

The collected data was entered into IBM SPSS Statistics for Windows, version 21.0. Descriptive statistics, including mean, standard deviation, median, maximum, and minimum values, were used to summarize the data. The repeated measures Analysis of Variance (ANOVA) was employed to evaluate the effects of the interventions, incorporating intervention and time as within-subject factors, and phase (period) and sequence to assess potential period effects. Multivariate Analysis of Variance (MANOVA) and Wilks' lambda were also used to compare the overall effects on the correlated dependent variables (pain, HR, and SpO2). Effect sizes were reported using Partial Eta Squared. All tests were evaluated at a 95% confidence interval, and a P-value< 0.05 was considered statistically significant. To examine the assumptions for repeated-measures ANOVA and MANOVA, the normality of distributions and the homogeneity of variances (using Levene's test) were assessed. The assumption of homogeneity of variances was met for all variables; however, the assumption of normality was not satisfied for some variables. Nevertheless, ANOVA and MANOVA tests remain robust to violations of the normality assumption. Furthermore, Mauchly's test of sphericity was conducted to evaluate the assumption for repeated measures. Since the test was not significant ($p > 0.05$), the assumption of sphericity was met, and no further corrections were required.

Ethical considerations

The present study was approved by the Ethics Committee of Guilan University of Medical Sciences (Ethics ID: IR.GUMS.RES.1400.356) on November 26, 2021, and registered in the Iranian Registry of Clinical Trials (IRCT20110122005663N2) on December 9, 2021. Written informed consent was obtained from the parents, and verbal assent was secured from the children (age-appropriate) prior to their inclusion in the study. Furthermore, participants were assured that their information would remain confidential and that they could withdraw from the study at any time without any impact on their ongoing treatment. Adverse effects (such as skin redness, burning, or intolerable localized pain at the intervention site) were monitored before and after each session; the occurrence of any such effect resulted in the cessation of the intervention, the participant's withdrawal from the study, referral to a physician (if necessary), and documentation and reporting to the ethics committee.

Results

Out of 42 pediatric patients assessed for eligibility, 33 were successfully randomized into the crossover sequences (sequence A and sequence B). During the study course, 5 participants Did not reach the final analysis: 3 due to discontinuation of the intervention (2 in sequence A due to skin sensitivity and vincristine-related allergic reactions, and 1 in sequence B due to an intervening infection), and 2 in sequence B who were lost to follow-up owing to missed appointment schedules. Consequently, a total of 28 participants fully completed the trial protocol and were included in the final statistical analysis (Figure 1).

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In this study, 75% of the participants were male and others were female. The mean (SD) age of the participants was 7.07(2.65) years. Other demographic characteristics are presented in Table 1.

Table 1. Participants' demographics characteristics (n= 28)

Variables	**N (%)**
Gender	
Female	7 (25.0)
Male	21 (75.0)
Age	
Mean (SD)	7.07 (2.65)
Weight	
Mean (SD)	25.04 (10.34)
Birth order	
Mean (SD)	1.46 (0.69)
Father's education*	
Illiterate	0 (0.0)
Under diploma	9 (33.33)
Diploma	9 (33.33)
University	9 (33.33)
Mother's education	
Illiterate	0 (0.0)
Under diploma	7 (25.0)
Diploma	11 (39.29)
University	10 (35.71)
Father's occupation	
Unemployed	2 (7.14)
Freelance	22 (78.57)
Employee	4 (14.29)
Mother's occupation	
Housewife	25 (89.29)
Employee	3 (10.71)
Place of residence	
City	20 (71.43)
Village	8 (28.57)
Number of children in the family	
۱	12 (42.86)
۲	12 (42.86)
۳	2 (7.14)
> 3	2 (7.14)
Disease duration	
Mean (SD)	13.64 (11.70)
Number of hospitalizations*	
Mean (SD)	23.70 (15.58)
Vincristine dosage	
Mean (SD)	1.38 (0.38)
History of other illnesses	

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Yes	6 (21.43)
No	22 (78.57)

*Note: Data were complete (n=28) for all variables except for father's education and Number of hospitalizations, each with one missing observation (n=27). Percentages are calculated based on valid responses (n=27).

The information presented in Table ۲ regarding pain intensity indicates that the effect of time on pain intensity was significant in both Phase 1 (P= 0.007) and Phase 2 (P= 0.006). The effect of ice massage on pain intensity was not significant in Phase 1; however, in Phase 2, it showed a borderline effect (P= 0.05). Regarding HR, there was a significant difference between the two sequences 5 seconds before (P= 0.015) and 15 seconds after the injection (P= 0.009) in Phase 1. Overall, the effect of time on HR was significant in both Phase 1 (P= 0.002) and Phase 2 (P= 0.001). Additionally, the effect of ice massage intervention on HR in phase 1 was significant (P= 0.017), with higher values recorded following the intervention. Specifically, at T2, the HR for the ice massage condition (Sequence B) was 124.79±15.75 compared to 108.57±17.01 for the acupressure condition (Sequence A). Furthermore, at T3, the HR under the ice massage condition (sequence B) was 126.14±13.18, whereas under the acupressure condition (sequence A), it was 110.07±16.73. However, the interaction between time and intervention was not significant (P= 0.17). As for oxygen saturation (SpO_2), no significant difference between the two sequences in terms of time was found in either Phase 1 and Phase 2 (P> 0.05) (Table 2).

Table ۲. A comparison of pain scores, HR, and SpO_2 in the two study sequences (n= 28) across different phases and measurement times

sequence /Time	**Pain**		**HR**		**SpO_2**	
	Mean (SD[a])	**Mean (SD)**	**Mean (SD)**		**Mean (SD)**	
	Phase 1	**Phase 2**	**Phase 1**	**Phase 2**	**Phase 1**	**Phase 2**
A (n= 14)						
T1[b]	0 (0)	0 (0)	105.50 (18.25)	103.43 (17.35)	98.57 (0.85)	98.64 (0.63)
T2[c]	0.21 (0.43)	0.57 (0.94)	108.57 (17.01)	115.29 (19.95)	98.64 (1.15)	99.00 (0.55)
T3[d]	0.29 (0.47)	0/29 (0/61)	110.07 (16.73)	112.14 (17.59)	98.64 (1.22)	98.79 (0.70)
B (n = 14)						
T1	0 (0)	0 (0)	113.64 (13.41)	112.00 (14.75)	98.71 (0.73)	98.36 (1.28)
T2	1.07 (1.59)	2.50 (3.59)	124.79 (15.75)	125.50 (18.15)	99.07 (1.14)	98.29 (1.68)
T3	0.43 (0.85)	0.93 (1.44)	126.14 (13.18)	125.00 (18.15)	99.14 (0.86)	98.50 (1.56)
P_{T1}	--	--	۰.19	۰.17	۰.64	۰.46
P_{T2}	۰.07	۰.07	۰.015	۰.17	۰.33	۰.14
P_{T3}	۰.59	۰.14	۰.009	۰.07	۰.22	۰.54
P_{Time}	۰.007	۰.006	۰.002	۰.001	۰.27	۰.45
$P_{intervention}$	۰.13	۰.05	۰.017	۰.10	۰.29	۰.31
$P_{interaction}$	۰.06	۰.08	۰.17	۰.60	۰.51	۰.17

[a]SD: standard deviation, [b]T1: Before the intervention, [c]T2: 5 seconds before the Vincristine injection, [d]T3: 15 seconds after the Vincristine injection, Statistical test: Repeated Measures ANOVA (RM ANOVA)

The information presented in Table ۳ regarding pain intensity indicates a significant difference between the ice massage and acupressure conditions 5 seconds before the injection (P= 0.017).

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Additionally, the pain intensity was lower in the ice massage condition compared to the acupressure condition. Overall, the combined results from both phases indicate that the effect of ice massage on pain intensity was significantly greater than that of acupressure (P= 0.016), particularly at T3 (ice massage: 0.36±0.73, acupressure: 0.61±1.10). The effect size of ice massage on pain relief, measured using partial Eta squared, was 0.103. Furthermore, there was a statistically significant difference in HR between the two interventions, with significant differences observed 5 seconds before (P= 0.007) and 15 seconds after the injection (P= 0.002).

Table ۳. A comparison of pain scores, HR, and SpO_2 between the two intervention conditions (n= 28) in relation to time and combination of the two phases

Intervention conditions/Time	**Pain**	**HR**	**SpO_2**
	Mean (SD[a])	**Mean (SD)**	**Mean (SD)**
Ice massage (n = 28)			
T1[b]	0 (0)	108.54 (16.08)	98.68 (0.67)
T2[c]	0.82 (1.31)	120.04 (18.29)	99.04 (0.88)
T3[d]	0.36 (0.73)	119.14 (16.84)	98.96 (0.79)
Acupressure (n = 28)			
T1	0 (0)	108.75 (16.62)	98.46 (1.07)
T2	1.36 (2.77)	117.04 (19.29)	98.46 (1.43)
T3	0.61 (1.10)	117.54 (18.74)	98.57 (1.37)
P_{T1}	--	0.05	0.77
P_{T2}	0.017	0.007	0.66
P_{T3}	0.12	0.002	0.73
P_{Time}	0.001	0.001	0.12
$P_{intervention}$	0.016	0.004	0.89
$P_{interaction}$	0.016	0.14	0.46
Partial Eta Squared	0.10	0.14	0.001
Observed Power	0.69	0.83	0.05

[a]SD: standard deviation, [b]T1: Before the intervention, [c]T2: 5 seconds before the Vincristine injection, [d]T3: 15 seconds after the Vincristine injection, Statistical test: Repeated Measures ANOVA (RM ANOVA)

Furthermore, the effect of time on the intervention was significant in both conditions (P= 0.001). Overall, a significant effect of the intervention on HR was observed (P= 0.004, partial Eta squared= 0.14), with higher HR values recorded following ice massage, particularly during the post-intervention phase (ice massage: 119.14±16.84, acupressure: 117.54±18.74). The changes in SpO_2 between assessments and during measurements remained constant in both interventions, and the effect of the interventions on SpO_2 percentage was not significant (P= 0.89, ice massage: 98.96±0.79, acupressure: 98.57±1.37) (Table 2).

In general, according to the results of MANOVA and Wilks' lambda, the effect of ice massage on the three variables pain, HR, and SpO_2 was significant compared to acupressure (P< 0.01, Partial Eta Squared= 0.05), suggesting that ice massage had a stronger effect on pain intensity.

Discussion

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Nurses play a crucial role in caring for children with cancer and alleviating their pain. This study found that ice massage at the Hegu point is more effective than acupressure in reducing pain associated with vincristine injection, with a significant difference between the two conditions. Some studies also showed that both Hegu point ice massage and acupressure help alleviate venipuncture pain in children with thalassemia, with ice massage being more effective.[36, 39] Additionally, other research indicated that ice massage at the Hegu point effectively reduces the pain from painful procedures in children.[34, 35] These findings may be explained through the gate control theory of pain, which suggests that the impulses generated by ice massage stimulate A-delta fibers, which has been proposed to lead to the closure of neural gates and potentially contribute to preventing the transmission of pain signals to the spinal cord.[28, 36] Ice massage might also slow the conduction of peripheral nerve fibers, could reduce the release of inflammatory mediators and pain receptors, and potentially induce relative skin anesthesia.[35] Furthermore, studies have also suggested that ice massage at the Hegu point can block sensory fibers and reduce skin sensations by numbing the nerve endings.[36] In fact, as skin temperature decreases, pain tolerance and pain threshold increase.[47] In contrast, other studies reported similar pain relief in both acupressure and ice massage groups, with minimal differences between the two interventions.[31] Another study found that pain intensity is significantly lower in the acupressure group compared to the Hegu point cold therapy group, with 46% of participants in the cold therapy group experiencing severe pain.[48]

This study also showed that HR increased following both interventions, with the increase being greater after ice massage than after acupressure. In line with this finding, Koç Özkan and Balcı[37] in 2020 showed that acupressure did not lead to a significant decrease in HR associated with venipuncture in children.[37] Attia and Hassan[49] in 2017 also found that changes in HR before and after cold therapy are not significant; in other words, cold therapy did not lead to a reduction in HR.[49] The observed changes in HR may have been influenced by factors other than the interventions, such as underlying comorbidities or procedure-related stress. In this context, anemia, a common consequence of ALL resulting from a reduction in red blood cells, may have played a role; symptoms such as an elevated HR, tachypnea, and shortness of breath are frequently associated with anemia in children with ALL.[15, 50] Exposure to cold may also affect cardiovascular responses through peripheral vasoconstriction, which can potentially increase HR.[48, 51] However, the presence of anemia, baseline HR, and cold-induced vasoconstriction were not specifically assessed or analyzed in the current study; therefore, these factors cannot be confirmed as explanations for the observed changes in HR. Furthermore, fluctuations in physiological indicators may not always be directly linked to pain, as they can be influenced by various other physical and psychological factors, including hyperthermia, physical activity, medications, the nature of the illness, body position, and stress.[19, 49, 51] Future research should account for relevant clinical and physiological factors when evaluating HR responses to non-pharmacological pain interventions in children with cancer. In contrast, some previous studies found that acupressure reduces HR in children after tonsillectomy.[38] Another study also showed that cold therapy decreased HR following intramuscular injection.[52] The differences in findings may be attributed to the fact that

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in the study by Yaghobi and Pouy[38], acupressure was performed three times, each session lasting 12 minutes, targeting three pressure points (including the Hegu point and two others) on a sample of 144 children.[38]

This study also showed that neither acupressure nor ice massage result in significant changes in SpO_2 percentages. SpO_2 levels in both interventions remained within the normal range before and after the intervention. However, in the ice massage condition, SpO_2 levels were slightly higher compared to the acupressure condition, though this difference was not statistically significant. In line with this finding, two studies reported that both acupressure and ice massage have almost no effect on SpO_2 in children, with SpO_2 levels remaining constant.[37, 53] It is challenging to identify physiological changes, particularly in SpO_2, associated with painful procedures within a short time frame. This is because SpO_2 requires a longer period to be influenced by various factors, such as interventions, and as a result, it may not have been affected in our study. However, other studies reported that acupressure and cold therapy improve SpO_2 levels in children.[38, 49] The authors believes that the difference in the results of some studies, such as the one by Attia and Hassan[49], can be attributed to the fact that in their study, cold therapy was applied to the arterial-venipuncture area of 40 children undergoing hemodialysis. This intervention was performed in four sessions, each lasting about 10 minutes.[49]

This study has several limitations. First, the use of convenience sampling, participant attrition following randomization, and a small sample size may limit the generalizability of our findings to the broader population of children. Furthermore, although a crossover design is efficient, it is susceptible to potential carryover and sequence effects, which could influence the study results. The lack of complete blinding for participants and intervention providers may also introduce potential bias. Regarding pain assessment, although the Oucher scale was employed as an age-appropriate tool, the subjective nature of pain—combined with the likelihood of lower baseline pain scores in this group—may affect the sensitivity and interpretation of the scale's results.

Conclusion

The study results indicated that in children with acute lymphoblastic leukemia, pain scores associated with vincristine administration were significantly lower following ice massage at the Hegu acupoint compared to acupressure at the same site. No statistically significant difference in oxygen saturation was observed between the interventions; however, heart rate findings suggested a notable intervention effect, which warrants cautious interpretation. Ice massage at the Hegu point may serve as a potential non-pharmacological approach for managing procedure-related pain in this population. Further studies with larger sample sizes are required to confirm these findings and to evaluate their clinical relevance and safety.

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Conflict of Interest

The authors declare no conflicts of interest.

Data Accessibility

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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Research Highlights

What is the current knowledge?

- Diagnostic and therapeutic procedures are the most common sources of pain in children with cancer.
- Non-pharmacological pain management approaches are crucial in reducing the use of painkillers and their side effects in children with cancer.
- Various studies have investigated the effects of reflexology, massage therapy, distraction therapy, and cryotherapy on pain in children with cancer.

What is new here?

- This study compared the effect of Hegu point ice massage and acupressure on pain associated with vincristine administration in children with acute lymphoblastic leukemia.
- Pain scores were significantly lower following Hegu point ice massage than following Hegu point acupressure.
- No statistically significant difference in oxygen saturation was observed between the interventions, whereas a significant intervention effect on heart rate was reported.

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