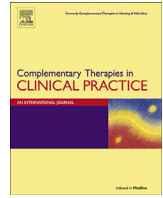




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# The effect of acupressure on pain, anxiety, and the physiological indexes of patients with cancer undergoing bone marrow biopsy



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## ABSTRACT

**Objectives:** This study aimed to determine the effect of acupressure on pain intensity, anxiety, and physiological indexes of patients with cancer undergoing bone marrow biopsy and aspiration.

**Methods:** The study was designed as a randomized, double-blinded, controlled trial.

Ninety samples was selected using the convenience sampling method, then for allocation groups random block sampling was used (30 for each group). The three groups were similar by age and gender. LI4 and HT7 (Shen Men) acupressure points were examined for the intervention. Sham pressure was used in the placebo group while no intervention was applied in the control group.

**Results:** The results showed that the lowest average anxiety score ( $1.5 \pm 0.5$ ;  $P = 0.01$ ) and the lowest average pain score ( $4.9 \pm 0.8$ ) after the intervention were related to the acupressure method ( $P = 0.001$ ).

**Conclusion:** Cost effectiveness and short-term simple education make acupressure method useful in clinical settings for different illnesses.

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## 1. Introduction

Cancer is a global problem that causes 552,200 deaths yearly [1]. In 2015, there were 17.5 million cancer cases worldwide [2]. Patients with cancer undergo painful procedures such as lumbar puncture (LP) or bone marrow biopsy and aspiration (BMBA) during their treatment process, which not only cause pain and anxiety but may also affect the quality of life, treatment duration, or further examinations [3]. Moreover, the side effects may lead to tachycardia or hypertension [4].

Numerous studies have shown that the highest level of pain in patients with cancer undergoing different kinds of intensive diagnostic or evaluation procedures was related to BMBA, lumbar puncture, and insertion of a central venous catheter (CVC) [5,6]. Moderate to unbearable pain was reported by 50%–70% of patients who had undergone BMBA [7]. Prescription of a combination of

analgesics, sublingual fentanyl, benzodiazepine, or nitrous oxide/oxygen are treatment options for reducing pain and anxiety in a patient [8].

However, pharmacotherapy is not very effective [9]. It also has different side effects such as respiratory depression, nausea, and vomiting. The patient's situation needs to be accurately monitored, which is time-consuming for the nursing staff [10]. Bao (2011) explained that local anaesthesia as a standard procedure was effective in relieving the pain due to the needle entering the body but it is not able to relieve the pain due to bone marrow aspiration [7].

Another common problem of patients with cancer before and after painful procedures is anxiety, which can influence the quality of life [7]. Anxiety increases sympathetic responses and changes some vital signs, which may lead to tachycardia and hypertension [11]. Therefore, studying non-medical methods for relieving pain, decreasing anxiety, and controlling vital signs is necessary [12]. The use of complementary and alternative medicine is now emphasized [13].

Acupuncture, acupressure, homeopathy, energy healing, and yoga are among the complementary and alternative therapies/practices used by patients with cancer [14]. Acupressure has been

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getting more attention recently [15]. Simplicity, effectiveness, and safety are the strengths of this method [16]. Appropriate points are pressed using the hand, foot, or a special device in some cases [17]. It is a method which can control pain and anxiety [13].

There are reports that the acupressure method can have rapid and average effects on relieving pain, reducing anxiety, and controlling vital signs, although more studies with accurate findings are needed to support this statement [12]. In a study by Bao and his colleagues. (2011), application of magnetic acupressure to the LI4 point relieved pain significantly in a group of patients suffering from severe pain [7].

One theory suggest that acupressure reduces anxiety by reducing 5-hydroxytryptamine and adrenocorticotrophic hormone concentrations in nerves and adjusting the concentrations of neurotransmitters [13]. Beikmoradi et al. (2015) concluded that acupressure was significantly effective in reducing patients' anxiety after the intervention [13]. Studying the use of acupressure among nurses can help improve the quality of nursing care and reduce the side-effects of the invasive methods [12]. The increasing prevalence rate of cancer and limited number of studies on acupressure led us to conduct a research and explore the effectiveness of acupressure on pain, anxiety, and physiological indexes in patients with cancer undergoing BMBA.

## 2. Trial design

This research was a randomized double-blinded clinical trial in which the patients were not aware about the grouping orders. The acupressure and BMBA operators were blinded to baseline pain and anxiety scores. The questionnaires were seen only by an independent data collector. The proposal is registered in the Iranian Registry of Clinical Trials with the registration number of "IRCT 2016080229159N1".

## 3. Participants

The participants included cancer patients who were undergoing BMBA and who were referred to oncology wards or oncology doctors' offices in the western regions of Mazandaran province,. The sample was selected using the convenience sampling method, then for allocation groups random block sampling was used. The three groups were similar by age and gender.

## 4. Sample size

Estimates of variability for the three key outcomes (pain, anxiety, and physiological indexes) were obtained from a pilot study and power calculation ( $\alpha = 0.05$ ;  $(1 - \beta) = 0.90$ ; effect size = 0.84). Therefore, 30 participants were required for each group.

## 5. Inclusion criteria

The inclusion criteria were as follows: a pathology test result confirming the cancer, being fully aware, 18–65 years of age, no intake of anxiolytic and analgesic medications 12 h before the BMBA, no surface limitation like wounds or angiocath at the point of acupressure, platelet levels greater than 100000 mg/dl, new to the whole procedure, no visual impairment, and no previous knowledge about acupressure.

## 6. Interventions

The intervention was performed by a researcher who was a certified acupressure practitioner. Different points have been used in previous studies [18–20] including EX-HN3 (Extral), HT7 (Shen

Men), and LI4 [12].

The researcher selected the LI4 or Hegu point located at the middle of the bisector of the angle between the first and second metacarpal (Fig. 1) and the HT7 point on the lateral wrist located radial towards the tendon of the flexor carpi ulnaris (Fig. 2) by reviewing different studies [21,22] and by soliciting advice from an expert. The LI4 point is located where the energy flow is closer to the skin and thus, is incited by chilling out, pressure or a needle much easier.

The pressure points were pressed for 2 min [23] symmetrically immediately after the start and the end of the biopsy. Fingers were pressed gently on the point and pressure was increased gradually until there was a sensation of soreness. All the patients were placed in the same position and 5 mg of lidocaine was injected locally. The same doctor performed the BMBA for all patients.

For the placebo group, a point at 1.5 cm distance from the main points (LI4 and HT7) was selected. These points are called ineffective or sham pressure points. No intervention was performed in the control group; only routine procedures like blood pressure measurement, pulse, and breathing controls were performed.

Ninety patients participated in this study. Thirty patients were randomized to receive acupressure at LI4, and 30 to receive acupressure at HT7. Another 30 patients were randomized to the sham acupressure group. The remaining 30 patients were randomized to the control group (Fig. 3).

Three patients were excluded from analysis because they did not meet the eligibility criteria for this study. They had platelet counts less than 100,000 mg/dl and an obstacle on the pressure points. One of the patients experienced severe bleeding and severe dyspnoea during the bone marrow aspiration, which caused his exit from the probing process. None of the patients withdrew during the intervention.

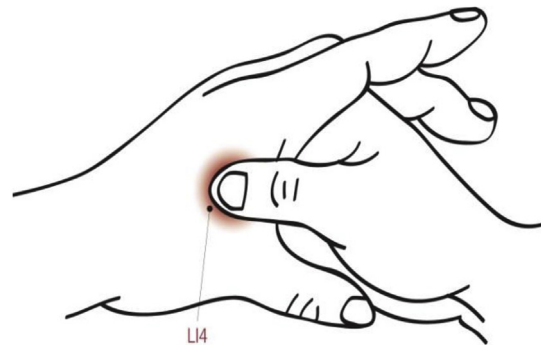


Fig. 1. The LI 4 point is located between the first and second metacarpal bones.<sup>11</sup>

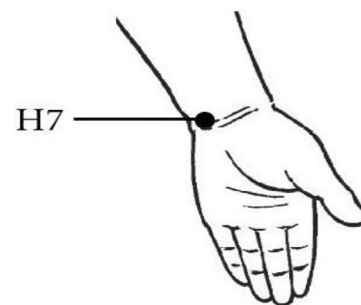


Fig. 2. The Shen Men is located on the transverse crease of the wrist in the articular region between the pisiform bone ulna in the depression on the radial side of the tendon of the flexor carpi ulnaris muscle.

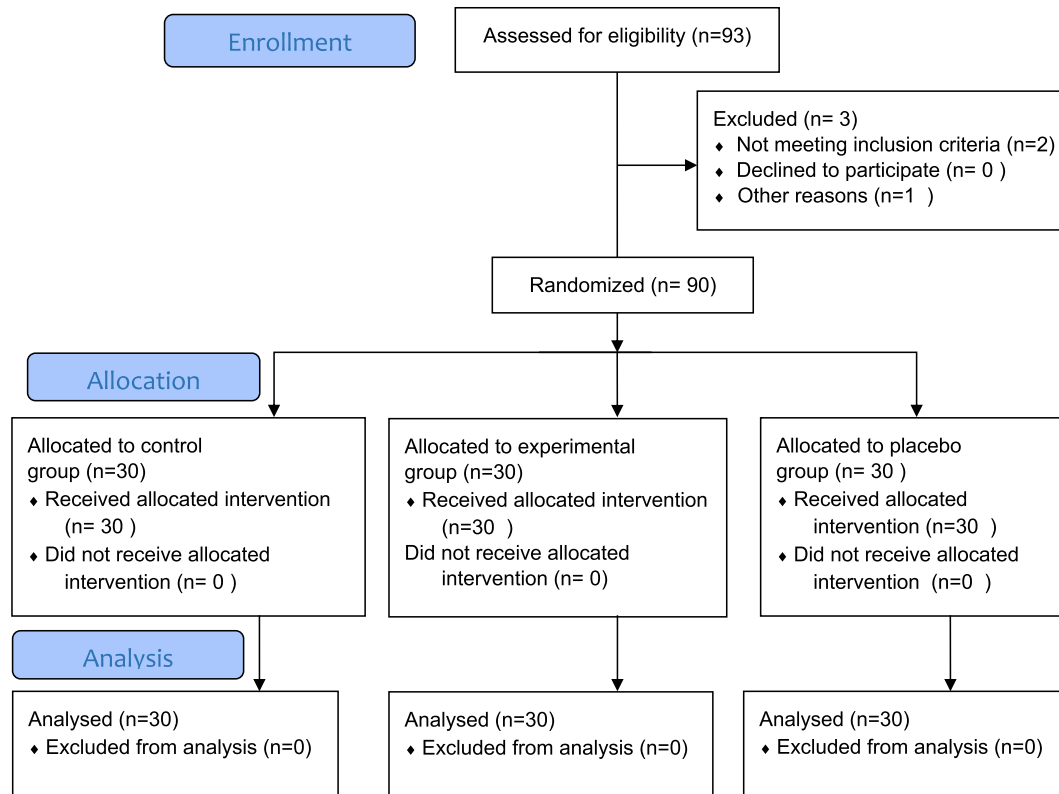


Fig. 3. Consort diagram.

## 7. Outcome measurements

### 7.1. Demographic characteristics questionnaire

This questionnaire was filled out by the researcher before the start of the procedure. It includes data on age, sex, marital status, education level, and body mass index (BMI).

### 7.2. Spielberger anxiety questionnaire

State-Trait Anxiety Inventory (STAI): The STAI has 20 questions with a 1–4 scoring system. The total score is between 20 and 80 [24]. The reliability and validity of this questionnaire has been examined in different studies [25,26]. This is a psychometric tool that has been used since 1994 in Iran. Cronbach's alpha of state anxiety is reported to be 0.93 [24,27]. The anxiety questionnaire was filled out 10 min before and after the procedure for each group in this study.

### 7.3. Visual analog scale (VAS)

This tool is a pain severity ruler divided into 10 states categorizing pain into 5 levels: no pain (0), mild pain (1–3), moderate pain (3–6), strong pain (7–9), and maximum possible intense pain (9–10) [28]. VAS is applied to many cases and its standard is approvable [29]. In this study to determine the reliability of VAS, the Cronbach  $\alpha$  coefficient was used to check its internal consistency. In this regard, 10 patients from the research population who

had the profile of the patients with cancer under the study filled out the questionnaires, and by using the results, the Cronbach  $\alpha$  coefficient for VAS ( $r = 0.81$ ) was calculated. The severity of pain was measured right after the procedure for each group in this study.

### 7.4. Measurement of physiological indexes

A digital barometer (Omron M6) was used to calibrate the blood pressure data measured. Pulse and respiratory rates were measured using an analog clock. The physiological indexes were measured 10 min before and after the procedure for each group in this study.

## 8. Statistical analysis

All data were analysed using the Statistical Package for the Social Sciences (version 18.0). Descriptive statistics such as mean and standard error of the mean were calculated and reported. Kolmogorov–Smirnov test was used to test the normality of data. As a normal distribution was obtained for the data, parametric tests were used in the statistical analysis, the Analysis of Variance (ANOVA) and LSD testes for repeated measures. The p-value of the outcomes is less than 0.50.

## 9. Ethical considerations

The study was approved by the Research Committee of the Babol University of Medical Sciences.

- The participant was informed about the aims and methods of the study.
- Written consent for participation was obtained from all participants.

<sup>1</sup> Dabiri, F. and A. Shahi (2014). "The Effect of LI4 Acupressure on Labor Pain Intensity and Duration of Labor: A Randomized Controlled Trial." *Oman Med J* 29(6): 425–429.

- Confidentiality was observed.
- The proposal was registered in the Iranian Registry of Clinical Trials ([www.irct.ir/](http://www.irct.ir/); Registration number: IRCT 201608022 9159N1).

## 10. Findings

The average duration of the procedure was very similar in patients in the placebo group, the LI4 and HT7 groups, and control group (1 vs. 1.1 min,  $P = 0.51$ ). No serious side effects or discomfort related to acupuncture were reported by patients in any of the groups.

The results show that the participant's age average was  $56.67 \pm 10.9$  years. The average BMI was  $25.2 \pm 5.1$ . None of the participants had a university degree but 40% of them had a high school diploma. Most of the patients (95.6%) were married. The three groups had no square difference in demographic characteristics including age ( $P = 0.61$ ), sex ( $P = 0.11$ ), weight ( $P = 0.42$ ), height ( $P = 0.81$ ), and BMI ( $P = 0.51$ ). Bone marrow aspiration was performed for all the patients during the biopsy.

The ANOVA was used to test the null hypothesis. The results show that the least anxiety average score was related to the acupuncture ( $1.5 \pm 0.5$ ) after the intervention. The acupuncture successfully resulted in less anxiety in the intervention group ( $F = 4.189$ ,  $df = 2$ ,  $P = 0.01$ ). Before the intervention, the anxiety average score had no statistical difference between the groups ( $P = 0.415$ ) (Table 1). A post hoc test was used to determine the square difference between each pair of average scores. The results of least square difference (LSD) test show that there is a statistical square difference between the anxiety average of acupuncture and placebo ( $P = 0.02$ ) and control group ( $P = 0.008$ ).

ANOVA statistical test results show that the least pain average score was related to the acupuncture group ( $4.9 \pm 0.8$ ). The F-test also had square results ( $F = 17.824$ ,  $df = 2$ ,  $P = 0.001$ ) (Table 1). The results of LSD test show that there is a statistical square difference between acupuncture and placebo ( $P = 0.04$ ) and control group ( $P = 0.001$ ). The difference between the placebo and control groups ( $P = 0.001$ ) is evident but the difference between the pain average scores of acupuncture and control groups ( $1.3 \pm 0.2$ ) is greater than that of the placebo and control groups ( $0.8 \pm 0.2$ ), which means that the effect of acupuncture on decreasing pain is greater than sham pressure.

The results of this study show that the systolic ( $F = 16.154$ ,  $df = 2$ ,  $P = 0.93$ ) and diastolic ( $F = 14.118$ ,  $df = 2$ ,  $P = 0.66$ ) blood pressure average scores had no square difference with each other after the intervention while the same results for respiratory rate ( $F = 17.554$ ,  $df = 2$ ,  $P = 0.05$ ) and pulse ( $F = 14.639$ ,  $df = 2$ ,  $p = 0.02$ ) had square differences in all groups (Table 2). LSD test results also show square differences between the respiratory rate average in acupuncture and placebo groups ( $P = 0.04$ ) and the control group ( $P = 0.03$ ). The difference is also evident between the acupuncture

and the placebo group ( $P = 0.05$ ) while it is not been seen between the acupuncture and the control group ( $P = 0.5$ ). There is square difference between the placebo and the control group ( $P = 0.01$ ) in average pulse rate, which means that the effect of pressing sham pressure points on decreasing the pulse rate was greater than the acupuncture ones.

## 11. Discussion

The results of this study show that acupuncture was effective in decreasing anxiety level in patients with cancer after BMBA. The results of other studies also showed a decrease in anxiety scores of the intervention group compared with the sham pressure groups [11,18–20,30]. Other studies have explored the role of acupuncture on the release of neurotransmitters like serotonin which affects the patient's sense of calm [31,32].

The results of this study show that acupuncture is effective in decreasing the pain caused by BMBA. This finding is in agreement with the results of previous studies [20,30]. Decrease in pain has also been seen in the placebo group which is statistically square. Possible reasons for this might be the hypnosis of the intervention, the safety felt by the patient due to the presence of the researcher, or the Hawthorne effect. In the study conducted by Bao et al. (2011), no significant difference in median pain scores was observed in patients treated at the LI4 site vs. the sham site (3.0 vs. 3.0,  $P = 0.8$ , Mann-Whitney test) [7].

Our results show no square differences between the average scores of systolic and diastolic blood pressures after intervention in each group. This might be related to the short duration of acupuncture (2 min) and the sympathetic system's response to anxiety.

The square difference between the average score of respiratory rate and pulse rate in three groups after the intervention is observed. Decreased pulse and respiratory rates are statically reasonable but clinically meaningless since both of the numbers are in the normal range and might have decreased due to the patient's steady situation and feeling calm while being observed during the intervention. Padmanabhan et al. (2005) stated that subjective parameters including heartbeat, blood pressure, respiratory rate, catecholamine and cortisol levels, and skin's temperature have weak relationship to mental changes and acute anxiety felt by patients before surgery [33].

Barker (2006) believes that the cardiovascular system is highly reactive to the psychological and behavioural states. Heartbeat and blood pressure are two dependent variables to the anxiety levels in behavioural studies [11].

The results of a study by Bassampour et al. (2008) show statically square differences ( $P < 0.001$ ) in vital signs of the intervention group before and right after the intervention. Such a difference is also observed in the vital signs of the placebo group (pulse rate ( $P = 0.016$ ) and respiratory rate ( $p = 0.007$ )). The square difference is reported by comparing the anxiety of the two groups ( $P < 0.001$ )

**Table 1**  
Comparison of the pain and anxiety average scores before and after the intervention.

Variable	Group	Pre-intervention	Post-intervention	F	P Value
		(n = 30) mean $\pm$ SD	(n = 30) mean $\pm$ SD		
Pain score	Experimental	7.9 $\pm$ 1.31	4.9 $\pm$ 0.84	17.824	0.000
	Placebo	7.6 $\pm$ 1.35	5.3 $\pm$ 0.99		
	Control	7.5 $\pm$ 1.61	6.2 $\pm$ 0.77		
Anxiety score	Experimental	2.1 $\pm$ 0.54	1.5 $\pm$ 0.50	4.189	0.018
	Placebo	1.9 $\pm$ 0.54	1.8 $\pm$ 0.48		
	Control	2 $\pm$ 0.64	1.8 $\pm$ 0.57		

**Table 2**  
Comparison of the physiological indexes average scores before and after the intervention.

Physiological indexes	Group	Pre-intervention	Post-intervention	F	P Value
		(n = 30) mean ± SD	(n = 30) mean ± SD		
Respiratory/min	Experimental	18.13 ± 2.34	18.60 ± 2.41	3.032	0.053
	Placebo	17.93 ± 1.92	17.66 ± 1.18		
	control	17.53 ± 1.35	17.60 ± 1.42		
Pulse/min	Experimental	80.16 ± 5.48	81.03 ± 4.95	3.772	0.027
	Placebo	80.33 ± 5.35	79 ± 3		
	control	80 ± 3.48	81.73 ± 3.81		
Systolic Blood pressure (mmHg)	Experimental	124.66 ± 17.36	123.66 ± 14.73	0.070	0.932
	Placebo	126.66 ± 18.63	124 ± 13.54		
	control	122.33 ± 13.56	125 ± 14.79		
Diastolic Blood pressure (mmHg)	Experimental	68.33 ± 21.50	75 ± 15.25	0.408	0.666
	Placebo	75.03 ± 15.55	77.66 ± 9.35		
	control	75.33 ± 8.60	76.33 ± 8.50		

where the respiratory rate p was equal to 0.013 and systolic blood pressure p was equal to 0.008 [4].

Valiee (2012) has reported a greater decrease in systolic blood pressure in the acupressure group compared to the sham control group [19]. The results of other studies show a similar decrease in pulse rate [11,25]. Hosseinabadi (2015) reported significant differences in pain scores ( $P = 0.004$ ) between the 3 groups (acupressure, placebo, and control) after the intervention only. No significant differences between the 3 groups were found after the intervention with regard to pulse rate, systolic blood pressure, or diastolic blood pressure ( $P > 0.05$ ) [34].

Implications for Practice:

- Our results show that application of acupressure in patients undergoing BMBA prevents pain, anxiety, and an increase in some of the physiological indexes.
- Acupressure would be a suitable intervention in clinical settings where the patient experiences high levels of pain and anxiety.
- Acupressure is cost-effective and doesn't require professional and long-term education for patients and nurses.
- Teaching acupressure to patients can be effective in reducing pain and anxiety in patients with cancer.

### 11.1. Limitations

This study is limited by its relatively small sample size and the overall number of patients experiencing severe pain. Numerous factors could influence the pain and anxiety scores. Controlling for these factors was impossible for the researcher because of personal differences and cultural, mental, and psychological factors. The study was carried out at a single treatment centre, and an operator experienced in BMBA and an experienced acupressure practitioner were involved in the procedures. It is unknown if the same results would be obtained if these persons were inexperienced. Thus, more studies are needed to verify the results of this study.

Local anesthesia by infiltration with sodium channel blockers, such as lidocaine is the most basic and widely used means of providing analgesia, however, pain relief is limited and does not affect the severe pain associated with bone puncture and marrow aspiration. Buffered local anesthetic solutions are associated with reduced pain and discomfort during infiltration but may or may not provide better analgesia during the actual biopsy.

The author also agrees that because of limited number of studies, effects of acupressure on pain, anxiety, and the physiological indexes of patients with cancer unclear. Further studies, systematic reviews and meta-analysis are required to comment on effects of acupressure on pain, anxiety, and the physiological

indexes of patients with cancer undergoing bone marrow biopsy.

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### Conflict of interest statement

None declared.

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