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Original Article

Electrical stimulation of acupuncture points for analgesia during bone marrow aspiration and biopsy: A randomized double-blind placebo-controlled trial

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Abstract

Background: Bone marrow aspiration and biopsy (BMA/BMB) is a painful procedure mostly used in diagnosing and staging of a broad spectrum of hematological diseases. In spite of local anesthesia, the prevalence and intensity of the pain and patient discomfort caused by this procedure are considerable. The effect of acupuncture and electrical stimulation of acupoints (acupuncture points) in the treatment of many medical conditions, including pain, have been approved. The study is designed to evaluate the effect of electrical stimulation of acupoints to decrease the pain during BMA/BMB in adults.

Materials and Methods: In a double-blind controlled clinical trial, 50 patients undergoing BMA/BMB were randomly allocated into two groups, to receive either true or placebo electrical stimulation of acupoints LI-4 (large intestine 4, Hegu) and LI-11 (large intestine 11, Quchi), bilaterally. Both groups received infiltrative local anesthesia. The pain level caused by BMA/BMB was measured using the Visual Analog Scale (VAS).

Results: The means of the VAS in the case and control groups were 41.84 ± 20.54 and 69.40 ± 20.06 respectively ($P < 0.001$). The systolic and diastolic blood pressure and pulse rate rose significantly in both the groups compared to the basal values. The rise was lower in the acupuncture group compared to the placebo group regarding systolic blood pressure and pulse rate ($P = 0.018$ and $P < 0.001$, respectively).

Conclusions: The results of this study show that the electrical stimulation of acupoints significantly decreases the pain caused by BMA/BMB and some of the complications of the pain.

Key Words: Acupuncture, bone marrow examination, electrical stimulation, pain

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INTRODUCTION

The bone marrow examination has a well-known role in diagnosing and staging of malignancies, evaluating platelets, white or red blood cell disorders, and defining various infectious diseases.[1] Many patients have to undergo repeated bone marrow biopsy.[2] It is a painful procedure.[1,3]

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In addition to the ethical and humanitarian reasons for minimizing pain, both physiological and pathophysiological responses to poorly controlled pain may have deleterious effects, including hypertension, tachycardia, arrhythmias, increased risk of myocardial ischemia and stroke, hyperglycemia, reduction in respiratory volume and flow rates, hypoxia, fear, demoralization, and prolonged convalescence.[4]

In many Hematology Units, the standard pain reliever for this procedure is local anesthesia (LA) alone.[2] In spite of LA, the prevalence and intensity of the pain caused by this procedure is considerable.[3] In adults, some interventions have been reported to reduce the pain and distress of BMA/BMB, including premedication with benzodiazepine alone[5,6] or in combination with the opioid hydromorphone.[1] In spite of the availability of newer drugs and techniques, the side effects of both the opioid and nonopioid analgesic techniques are still a big concern.[7] As BMA/BMB is becoming an outpatient procedure, pain management methods have to be safe, rapid acting, and free of prolonged sedation,[1] and practical to administer.

Acupuncture is a therapeutic procedure being practiced to treat different pathological symptoms and conditions in South East Asia since thousands of years.[8] In western countries also, it is the most popular part of Traditional Chinese Medicine (TCM), and has been widely used to treat many medical conditions, for example, pain.[9] In 1997, the National Institute of Health published a consensus statement concluding that acupuncture is effective or at least useful to treat 13 conditions, including dental pain and lower back pain.

Although the helpful aspects of acupuncture have been widely accepted, its mechanisms are only partially understood.[8] Now we know that by acupuncture we can activate the pain modulation system of the body and increase the release of endogenous opioids within the central nervous system, to suppress the transmission and perception of noxious stimuli.[7]

Electro acupuncture has proved to be useful to relieve pain and discomfort during colonoscopy[10] and oral surgery.[11] Hegu (LI 4) is an acupoint commonly chosen for acupuncture analgesia or anesthesia during colonoscopy,[10] first stage of labor,[12] orthodontic post-adjustment pain,[13] pain after mandibular wisdom tooth extraction, toothache,[14] headache,[15] anterior approach cervical discectomy,[16] craniotomy,[17] and appendectomy.[18] Electro acupuncture at Hegu (LI 4) induces central neural activation in the pain-modulation areas, like the periaqueduct gray matter and the median raphe nucleus.[19]

The enhanced effects on the pressure pain threshold by bilateral intervention compared to unilateral intervention at LI4, support the TCM assumption that bilateral needling of the same point enhances the treatment effect.[20] Application of two acupoints in a same meridian will also enhance the effect of each of the two acupoints.[21]

Considering the important role of BMA/BMB in the diagnosis and staging of a broad spectrum of diseases, its painfulness, and the need for an easy, safe, and fast-acting pain relieving technique, and with regard to the important role of acupuncture in relieving various pains, we compared the pain score in patients undergoing BMA/BMB, who received bilateral acupoint electrical stimulation (AES) in addition to infiltrative LA with the ones who did not receive AES.

MATERIALS AND METHODS

The study was a double-blind, randomized, clinical trial executed on patients undergoing BMA/BMB in the Sayed-Al-Shohada Hospital in Isfahan, in 2012 and 2013. The trial was registered in the Iranian Registry of Clinical Trials (IRCT), with registration number IRCT2012082610676N1, on September 16, 2012. The inclusion criteria were age over 18 years and not having addiction, pacemaker, history of vasovagal reaction, cardiac dysrythmias, and pregnancy. The exclusion criterion was developing a vasovagal reaction during the procedure. The calculated sample size was 25 patients in each of the two groups, and the sampling was executed by simple random sampling. None of the patients left the study.

The patients who had the inclusion criteria were informed about the study ahead were given the written consent by the hematologist, and had 24 hours to think about entering the study. Those who signed the written consent were randomly allocated into two groups of case (AES group) and control (placebo group). All patients received infiltrative LA with Lidocaine 4 mg/kg five minutes before the procedure. Skin electrodes were placed on the bilateral acupoints LI4 and LI11 in all patients, and were connected to an electro acupuncture instrument (Model G6805-2, SMIF, Shanghai, China). The location of the acupoint Hegu or LI 4 was in the middle of the angle between the first and second metacarpus;[21] and the location of the acupoint Quchi or LI 11 was at the lateral end of the elbow crease, midway between the biceps brachii tendon and the lateral epicondyle of the humerus.[22] The patients received real AES or placebo (with the electro acupuncture instrument off) on the acupoints of both sides, LI4 and LI11, from 15 minutes before starting the BMA/BMB for a duration of 25 minutes, without regard to whether the BMA/BMB procedure was finished or not. For each patient in the AES

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group the acupuncture stimulator apparatus was set to the maximum voltage and frequency that the patient could tolerate. A cloth was used to hide the patient's upper limb and the apparatus from the physician who performed BMA/BMB, so that he became blind to the patient's group. The site of the BMA/BMB was the posterior iliac crest. The procedure in the case and control groups was performed by the same physician.

At the end of the procedure, once the patients felt that they had recovered from the procedure, they were asked to complete the study questionnaire. The patients' pain levels were measured by the Visual Analog Scale (VAS). Also, before and during the BMA/BMB procedure, their blood pressure (BP), pulse rate (PR), and existence of sweating, were measured.

Finally, the collected data was analyzed by the software SPSS version 16, by student-t, paired-t, Chi-square, Fisher's exact, and Mann-Whitney U tests. A $P < 0.05$ was considered as significant.

RESULTS

In this study 50 patients were studied and randomly allocated into two groups (25 in the AES group and 25 in the placebo group). All the variables had a normal distribution, analyzed by the Kolmogorov-Smirnov test, except difference in systolic blood pressure, diastolic BP, and PR, before and during the procedure. Therefore, nonparametric tests were used for these three variables. Sex, mean age, history of the existence of BMA/BMB, systolic and diastolic BP, and PR before the procedure are presented in Table 1, and there is no significant difference between the two groups with regard to the mentioned variables.

The level of pain caused by BMA/BMB, which was measured by VAS in millimeters, was significantly less in the AES group ($P < 0.001$) [Table 2].

There was no significant difference between the two groups with regard to the duration of the procedure and frequency of non-successful BMA/BMB before the successful one [Table 2].

All of the patients answered positively to the question, "If you need BMA/BMB again in the future without any study, will you want to undergo the used acupuncture method to decrease the pain caused by it?", except one patient from the placebo group, who perceived the pain caused by BMA/BMB more than the previous times he had undertaken this procedure. All the patients described the acupuncture method as 'easy', except one patient, who was a 65-year-old woman from the AES group, who described it as, 'a bit hard'. There were no significant differences between the two groups with regard to the two latter variables. Regarding the patients' sweating, it is categorised as the patients

Table 1: Demographic and baseline characteristics compared between AES and placebo groups

Variables	AES group *n*=25	Placebo group *n*=25	*P* value
Sex*			0.571
Male	11 (44)	13 (52)	
Female	14 (56)	12 (48)	
Age**	40.36±15.48	38.00±14.88	0.585
Diagnosis*			
Cytopenia	9 (36)	3 (12)	
Leukemia	6 (24)	12 (48)	
Lymphoma	5 (20)	4 (16)	
Multiple myeloma	5 (20)	6 (24)	
History of BMA/BMB*			0.345
Positive	5 (20)	9 (36)	
Negative	20 (80)	16 (64)	
Systolic BP before procedure (mmHg)**	118.4±10.48	119.60±9.45	0.673
Diastolic BP before procedure (mmHg)**	73.20±8.88	75.80±9.31	0.318
PR before procedure (/min)**	82.88±11.46	85.44±9.79	0.400

*: Frequency (%) **: Mean±Standard Deviation BMA/BMB: Bone marrow aspiration and biopsy, BP: Blood pressure, PR: Pulse rate, AES: Acupoint electrical stimulation

Table 2: The studied parameters compared between AES and placebo groups

Variables	AES group	Placebo group	*P* value
Visual Analog Scale (mm)*	41.84±20.54	69.40±20.06	<0.001
Duration of procedure (min)*	10.56±2.02	11.04±1.94	0.397
Systolic BP during procedure (mmHg)*	122.60±8.91	128.60±9.41	0.025
Diastolic BP during procedure (mmHg)*	77.40±9.58	81.20±8.57	0.146
PR during procedure(/min)*	86.16±11.74	95.20±10.77	0.007
Difference of systolic BP before and during procedure (mmHg)**	4.20±9.43 (20.76)	9.00±6.45 (30.24)	0.018
Difference of diastolic BP before and during procedure (mmHg)**	4.20±6.72 (24.56)	5.40±5.38 (26.44)	0.634
Difference of PR before and during procedure (/min)**	3.28±6.99 (17.70)	9.76±6.33 (33.30)	<0.001
Sweating before and during procedure***			1.000
Before: − , during: +	2 (8)	2 (8)	
Others	23 (92)	23 (92)	
Frequency of non-successful BMA/BMB before the successful one*	0.12±0.33	0.28±0.73	0.329
Patient's positive will to undertake AES next time too***	25 (100)	24 (96)	1.000
Patient's feeling of AES itself***			1.000
Easy	24 (96)	25 (100)	
A bit hard	1 (4)	0 (0)	

*: Mean±Standard Deviation **: Non-parametric, Man Whitney U test, Mean±Standard Deviation (Mean Rank) ***: Frequency (%), BMA/BMB: Bone marrow aspiration and biopsy, BP: Blood pressure, PR: Pulse rate, AES: Acupoint electrical stimulation

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who had not had sweating before the procedure and had sweating during the procedure (the only meaningful condition, as a pain complication), and other conditions. There was no significant difference with regard to sweating between the two groups.

Regarding BP and PR, as indicated in Table 1, there was no significant difference between the two groups in systolic and diastolic BP and PR before the procedure. As shown in Table 3, these three variables were compared before and after the procedure in each of the AES and placebo groups by the paired *t*-test, and all of them were significantly different. As indicated in Table 2, the systolic BP and PR after the procedure were significantly different between the two groups ($P = 0.025$ and $P = 0.007$, respectively), but the diastolic BP after the procedure was not significantly different between the two groups. The differences of systolic and diastolic BP and PR during and before the procedure (during minus before) are also presented in Table 2. They were significantly different between the two groups with regard to systolic BP ($P = 0.018$) and PR ($P < 0.001$), but not significantly different with regard to diastolic BP.

The line graphs for the increase in systolic and diastolic BP and PR during the procedure compared to those before the procedure, in each of the two groups, are illustrated in Figures 1-3, respectively.

DISCUSSION

Considering the important role of BMA/BMB in the diagnosis and staging of a broad spectrum of diseases, its painfulness, and the need for an easy, safe, and fast-acting pain relieving technique, and with regard to the important role of acupuncture in relieving various pains, we evaluated the effect of the electrical stimulation of acupoints on decreasing the pain caused by BMA/BMB in adults. Whereas pain itself may have deleterious effects,[4] BP, PR, and sweating were also compared before and during the procedure in the two groups. As indicated in the results, pain caused by BMA/BMB was decreased significantly by this method. The systolic and diastolic blood pressure and pulse rate rose significantly in both the groups when compared with the basal values. The rise was lower in acupuncture group compared to the placebo group with regard to the systolic blood pressure and pulse rate. However, this method did not have a significant effect on the rise of diastolic BP, duration of the procedure, sweating or frequency of non-successful BMA/BMB before the successful one.

Table 3: BP and PR before and during procedure in each group (paired *t* test)

Variables	Before procedure	During procedure	*P* value
Systolic BP in the AES group (mmHg)*	118.40±10.48	122.60±8.91	0.036
Systolic BP in the placebo group (mmHg)*	119.60±9.45	128.60±9.41	<0.001
Diastolic BP in the AES group (mmHg)*	73.20±8.88	77.40±9.58	0.005
Diastolic BP in the placebo group (mmHg)*	75.80±9.31	81.20±8.57	<0.001
PR in the AES group (/min)*	82.88±11.46	86.16±11.74	0.028
PR in the placebo group (/min)*	85.44±9.79	95.20±10.77	<0.001

*: Mean±Standard deviation, P: Blood pressure, PR: Pulse rate, AES: Acupoint electrical stimulation

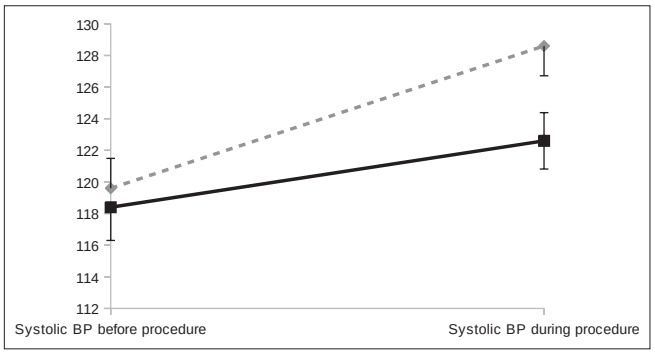

Figure 1: Comparing the rise of systolic BP in the two groups AES Groups, Placebo Group

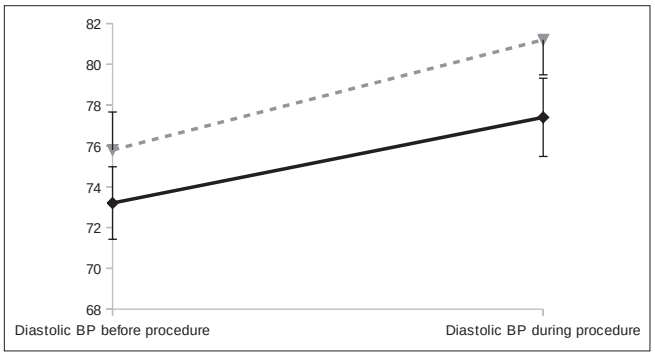

Figure 2: Comparing the rise of diastolic BP in the two groups AES Groups, Placebo Group

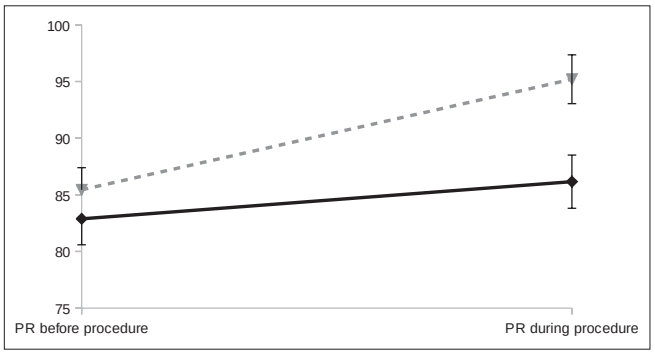

Figure 3: Comparing the rise of PR in two groups AES Groups, Placebo Group

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All the patients, except one, recognized this method as easy.

In the study of Ni and colleagues, the level of pain during colonoscopy was significantly lower in the group who got electro acupuncture compared to the control group. The time to reach the cecum was also significantly shorter, and patient satisfaction was significantly higher in the electro acupuncture group.[10] However, in our study no significant effect on the duration of the BMA/BMB procedure was detected.

Chao *et al*. showed that the electrical stimulation of some acupoints including LI4 could reduce the level of pain during the first stage of labor. In their study, unlike our study, willingness of using the same analgesic method for a future childbirth was also significantly higher in the acupuncture group.[12]

In the study of Wang and colleagues, the patients undergoing craniotomy were allocated to three groups. Group A received enflurane only. Group B received enflurane and transcutaneous acupoint electrical stimulation, and group C received enflurane, transcutaneous acupoint electrical stimulation, and scalp infiltration with procain. The anesthetic effect was the best in group C. A better anesthetic effect, more stable hemodynamics during the operation, faster recovery after the operation, and less enflurane side effects were seen in group B than in group A.[17]

In patients undergoing appendectomy also, Sun *et al*. showed that there were less respiratory depression, hypotension, cardiac arrhythmia, and less amount of liquid infusion needed during operation in the acupuncture anesthesia group than in the epidural anesthesia group. In addition, in the acupuncture anesthesia group, the intestinal gas excreted earlier and the analgesics and antibiotics administered were less, and the rate of the wound infection was reduced after operation.[18]

In all of the mentioned studies, Hegu or LI4 was one of the used acupoints.[10,12,17,18]

To decrease the pain caused by BMA/BMB in adults, other than local anesthesia, some methods like the use of benzodiazepine or opioid proved to be effective. For example, in the study of Milligan and colleagues, the group with premedication of lorazepam had less pain recall 24 hours after BMA/BMB than the placebo group. However, there was no significant difference between the two groups in the level of pain, when asked 15 minutes after the procedure.[5] Mainwaring *et al*. indicated that intravenous midazolam in addition to local anesthesia could reduce the pain caused by BMA/BMB, but drowsiness and some psychomotor impairment were the notable sedation-related side-effects in approximately 20% of the patients.[6] Also, in the study of Dunlop and colleagues, a combination of oral lorazepam and hydromorphone reduced the pain during BMA/BMB.[1] In spite of the availability of newer drugs and techniques, the side effects of both opioid and nonopioid analgesic techniques are still a cause of concern.[7]

As BMA/BMB is becoming an outpatient procedure, pain management methods have to be safe, rapid acting, free of prolonged sedation, and practical to administer.

In conclusion, the results of the current study indicate that electrical stimulation of acupoints, besides being easy, cheap, and safe, does have a significant ability to decrease the pain caused by BMA/BMB and also to reduce some complications of its pain. Hence, we hope that this method will be practiced to lower the pain in many patients.

Although a significant decrease in pain was indicated in this study, future studies entering only patients with a first experience of BMA/BMB will indicate results with less bias. Also future studies comparing the effect of benzodiazepines and opioids with the electrical stimulation of acupoints method is recommended.

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