

Effects of catgut-embedding acupuncture technique on nitric oxide levels and blood pressure in patients with essential hypertension

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Abstract. Hypertension is common a health problem and its prevalence in Indonesia is quite high (31.7%). Catgut embedding—an acupuncture technique—is known to reduce blood pressure; however, no study has confirmed the underlying mechanism. This study examines the effect of catgut embedding on serum nitric oxide (NO) concentration and blood pressure in patients with essential hypertension. Forty hypertension patients were randomly assigned to two groups: the control group received anti-hypertensive drugs whereas the case group received anti-hypertensive drugs and catgut embedding. Results showed a statistically significant mean difference in NO concentration ($p < 0.05$) and statistically and clinically significant mean difference in systolic and diastolic blood pressure between the two groups ($p < 0.05$). The results confirm that catgut embedding can influence serum NO concentration and blood pressure in essential hypertension patients.

1. Introduction

Hypertension is one of the most prevalent health conditions worldwide, and even in Indonesia [1]. Indonesia is a developing country, where the levels of awareness, therapy compliance, and blood pressure management are lower than those in the developed countries [2]. According to basic health research data from Indonesia in 2007, 31.7% of the Indonesian population suffers from hypertension however only 0.4% of those with hypertension have drugs [3]. Such situations can result in increased morbidity and mortality [4-7]. The pathogenesis of hypertension is linked to endothelial nitric oxide synthase (eNOS), which later produces nitric oxide (NO). Nitric oxide is a strong vasodilator, which can decrease the peripheral resistance that leads to lower blood pressure [8-10]. Research has shown that a shortage of eNOS leads to hypertension [11].

Many studies on essential hypertension have shown that acupuncture is quite effective in reducing blood pressure as well as increasing the level of nitric oxide (NO) [12-18]. For example, Kim *et al* studied the effect of acupuncture stimulation at ST36 (zusanli) in hamsters with renal hypertension, which was induced via the two-kidney one-clip (2K1C) procedure. They found a significant difference in NO levels ($p < 0.05$) between the 2K1C group that received acupuncture (417.9 ± 20.9 nM) and the 2K1C group that did not (309.0 ± 21.7 nM) [17].



Acupuncture has various techniques, and one of them uses catgut. The superiority of this technique is that it involves minimal puncture points, requires fewer visits, and provides a longer stimulative effect, which is associated with therapeutic benefits. These advantages can reduce therapy-related non-compliance among hypertension patients, and the embedding of catgut can reduce drug dosage, as well as the combination of anti-hypertensive drugs prescribed [19]. Li *et al* have published the only study that examines the use of catgut embedding for the management of hypertension; however, their study does not examine the NO level [16]. To examine how the catgut embedding technique of acupuncture induces a decrease in blood pressure among hypertensive patients, this study focuses on the level of NO serum.

2. Materials and Methods

This single-blind random-controlled clinical trial has been approved by the ethics committee of the Medical Faculty Universitas of Indonesia and Cipto Mangunkusumo General Hospital. The participants of this study agreed to participate voluntarily and signed the informed consent form, which assured confidentiality. The study was conducted from July to December 2013 at the Internal Medicine Clinic of the Renal Hypertension Division at RSCM Hospital, Jakarta. The patients were randomly divided into two groups: case and control. The case group received anti-hypertensive drugs and catgut embedding. The control group received only anti-hypertensive drugs. The inclusion criteria were as follows: age between 18 and 60 years, first degree essential hypertension based on JNC 7 criteria (systolic pressure between 140-159 mmHg or diastolic pressure between 90-99 mmHg), ongoing anti-hypertensive therapy (angiotensin converting enzyme (ACE) inhibitor, angiotensin receptor blocker (ARB), calcium channel blocker, diuretic, and β -adrenergic blocker), informed consent, willingness to follow the study until complete. The following patients were excluded: those who were given nitric therapy (isosorbide dinitrate isosorbide mononitrate, nitroglycerin), those in whom catgut embedding was contraindicated (because of pregnancy, medical emergency, malignancy, blood clotting problem, consumption of anticoagulant, animal protein allergy, diabetes (one time glucose level > 200 mg/dl)), and those who had a scar or infection at the location of catgut embedding. This study required a medicine wash out period: the participants were asked to stop taking anti-hypertensive drugs for 1 week before the study began.

All subjects with essential hypertension who met the inclusion criteria were examined for the NO serum level and initial blood pressure. The examination was repeated on the fourth week after treatment. Blood pressure was measured with patient in seated position (after a 3-5 minute break), with patient standing, and with the arm was positioned at the same level as the heart. The examination was performed, with a 1-2 minute break in between. Another examination was performed if the second examination was significantly different from the first [1,20].

Catgut embedding was performed at BL18 (ganshu), BL20 (pishu), and BL23 (senshu), two times with an interval of two weeks. Sterile chromic catgut 3.0 sutures of 1 cm were placed in a petri dish containing 70% alcohol. The sutures were threaded into a 21 G needle using an anatomical pinset. The patient was asked to lie on his/her stomach, and the catgut was embedded by pushing the 21G needle (with the sterile catgut) at a 45-degree angle toward the body's medial 1.5 cm deep into the acupuncture points: BL18 (ganshu), BL20 (pishu), and BL23 (shenshu). Once the needle was thrust, the catgut was pushed by another acupuncture needle (0.30x50 mm). After the catgut was embedded, the acupuncture needle was pulled followed by the 21G needle. Pressure was exerted on the puncture point until bleeding ceased. The puncture point was covered with plaster. Catgut was embedded in one point at a time. On the initial visit, catgut was embedded on the left side of the back, and two weeks later, it was embedded on the right side.

Measuring the NO level involved enzymatic conversion of nitrate into nitric by the reductase nitrate enzyme, followed by the addition of Griess reagent, which changed nitric into a colored azo compound, which was measured with a spectrophotometer (wavelength 540 nm) as nitrate and nitric concentrations. Serum samples were used for NO level measurement. The measurement was performed at Laboratorium Riset dan Esoterik Prodia. A special reagent kit used was nitrate/nitrite

colorimetric (Cayman Chemical, US, Cat: 780001, Lot: 0446454, Expiry date: 9 November 2013). The standard level of NO serum was 2.5–35 μM . SPSS version 11.5 was used for data analysis. Independent sample t-test was done for analyzing the differences between the groups, with Mann-Whitney test used as an alternative for non-normally distributed data. Differences with two-sided p-values >0.05 were considered statistically significant [21].

3. Results and Discussion

3.1 Results

Forty hypertension patients who met the inclusion criteria were randomly divided into two groups: case and control. Each group consisted of 20 patients. Most of the patients were female. On average, the patients were non-smokers, had completed high school, and the type of medicine was almost equally distributed in both groups. Age, BMI, number of drugs, initial systolic blood pressure, initial diastolic blood pressure, and initial NO serum level of the two groups were not significantly different ($p > 0.05$).

Table 1. Patient characteristics: gender, education, smoking status, and type of hypertensive drug

Variable	Case	Control
Number of Participants	20	20
Gender		
Male	9/20	4/20
Female	11/20	16/20
Education		
Junior High School	0/20	1/20
High School	9/20	9/20
Diploma	5/20	5/20
Undergraduate School	6/20	4/20
Graduate School	0/20	1/20
Subjects who smoke	2/20	1/20
Type of consumed medicine		
ACE Inhibitor	6/20	5/20
B Blocker	1/20	1/20
Calcium Antagonist	6/20	7/20
Angiotensin Receptor Blocker	7/20	8/20
Diuretic	3/20	1/20

Table 2. Patient characteristics: age, body mass index (BMI), type of drug, systolic blood pressure, diastolic blood pressure, and NO serum level

Variable	Case		Control		p-value
	Mean (SD)	Median (min-max)	Mean (SD)	Median (min-max)	
Age (years)	50.8 (7.8)	-	52.7 (5.93)	-	0.391*
Body Mass Index (BMI)	27.42 (3.81)	26.24 (21.63-35.85)	27.48 (2.88)	26.79 (23.02-32.02)	0.892**
Types of Drugs	1.2 (0.4)	1 (1-2)	1.1 (0.1)	1 (1-2)	0.637**
Systolic Blood Pressure (mmHg)	151.2 (6.2)	-	148 (7.32)	-	0.139*
Diastolic Blood Pressure (mmHg)	90.0 (6.4)	-	88.7 (6.4)	-	0.527*
NO Level (μM)	9.27 (4.84)	7.6 (3.5-19.3)	9.68 (4.59)	9.4 (2.5-18.1)	0.850**

*Unpaired t-Test, **Mann-Whitney Test, SD – Standard Deviation

The mean reduction in systolic blood pressure was 26.2 mmHg in the case group and 12.9 in the control group, showing a statistically significant difference of 13.3 mmHg between the groups (95% CI: 5.63 – 20.97 mmHg). Similarly, a significant difference was observed in the mean diastolic blood pressure reduction of 6.5 mmHg between the groups (The mean decrease in systolic blood pressure in the case group was 26.2 mmHg whereas that in the control group was 12.9 mmHg. That is, the mean systolic blood pressure in the case group was 13.3 mmHg lower than the control group ($p = 0.001$, 95% IK: 5.63 until 20.97 mmHg). The mean decrease in diastolic blood pressure in the case group was 11.4 mmHg whereas that in the control group was 4.9 mmHg. That is, the mean diastolic blood pressure in the case group was 6.5 mmHg lower than that in the control group ($p = 0.011$) 1.64-1.26 mmHg. The median value of increase in NO level in the case group was 1.35 μM , while median value of decrease in NO level in the control group was 1.25 μM . The median value of in NO level in the case group was 2.6 μM higher than that of the control group. The mean NO level in the case group was 4.2 μM higher than that of the control group ($p = 0.045$).

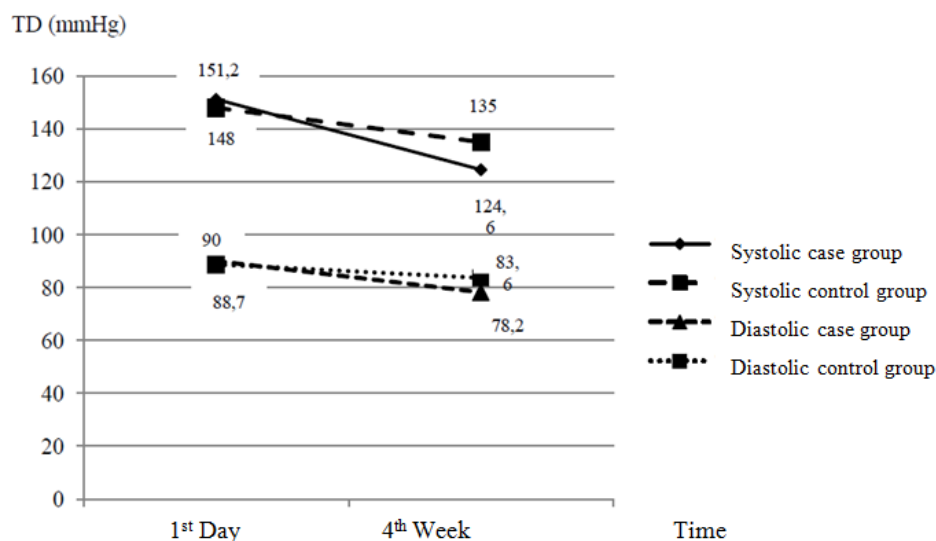


Figure 1. Systolic blood pressure and diastolic blood pressure in case and control groups

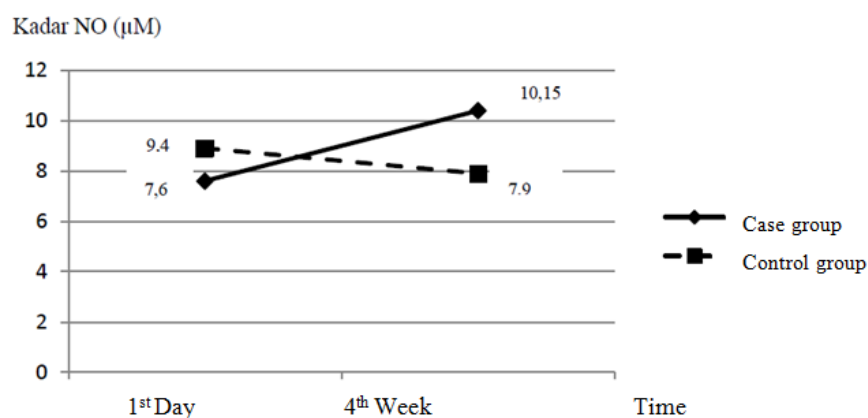


Figure 2. Median of NO serum level on case group and control group

3.2 Discussion

Patients with hypertension are known to benefit from efforts to reduce blood pressure. The diagnosis of hypertension has been arrived at by consensus. According to the European Society of Hypertension (ESH) 2013, hypertension results when the systolic blood pressure is ≥ 140 mmHg and the diastolic blood pressure is ≥ 90 mmHg [22]. A healthy lifestyle is known to prevent hypertension and plays an important role in the therapy for hypertension. Lifestyle changes recommended for lowering blood pressure include limiting the salt and alcohol intake, increasing the consumption of vegetables, fruits and low fat meal, reduction in body weight, regular physical exercise, and cessation of smoking [22]. The anti-hypertensive drugs recommended by ESH 2013 include diuretics (thiazide, chlortalidone and indapamide), β -blockers, calcium antagonists, ACE inhibitors, ARB, renin inhibitor, α receptor inhibitor, and drugs that work centrally. The prescription of drugs is based on the clinical condition [22]. Patients with hypertension generally need long-term therapy—sometimes life-long—so the side effect of drugs cannot be avoided. Additionally, patient compliance for consuming anti-hypertensive drugs is low.

The catgut embedding technique of acupuncture is relatively safe to perform, it involves a minimal number of points, and it has a longer stimulative effect that provides therapeutic benefits. As a result, the frequency of doctor visits for patients goes down from twice a week to once every two weeks. The side effects of catgut embedding include slight pain at the embedding site, hematoma at the embedding site, and stiffness that disappears after a couple of days [19]. In this study, catgut embedding was performed at three acupuncture points—BL18 (ganshu), BL20 (pishu), and BL23 (shenshu)—on the left side at the initial session and on the right side in the second week. Four patients reported myalgia at the puncture points, which healed in two to three days. There was also a report of a nodule at the left BL23 site (shenshu) after the initial catgut embedding. Although an analgesic and corticosteroid were prescribed, the patient did not take the drugs. The nodule disappeared after 4 days, and no complaint was received from patient in the second session of catgut embedding. Li *et al.* had used the same three points for catgut embedding in their study. After four weeks, they found a decrease in both systolic and diastolic blood pressure [16]. Kim *et al.* showed, with the help of histologic images, that the puncture points BL18 (ganshu) and BL23 (shenshu) were located close to many nerve fibers [23]. Puncture stimulation at both these points increases the level of β endorphin in the spinal fluid (Skarda *et al.*) [24]. Cheng *et al.* showed that puncturing at BL20 (pishu) increased the β endorphin level in nucleus tractus solitarius. β endorphin inhibits rVLM activity, resulting in the suppression of the sympathetic nervous system, which reduces blood pressure [25]. The study by Paterno *et al.* showed that BL23 (shenshu) can increase the NO serum level and that NO acts as a vasodilator [26].

In terms of the mean difference in the systolic blood pressure of the case group, the results of this study (26.2 (9.66) mmHg) showed a greater difference than that by Li *et al.* (17.47 (12.65)) mmHg. Similarly, the mean difference in diastolic blood pressure of the case group in this study was 11.4 (3.98) mmHg, whereas in the study by Li *et al.*, the mean difference was 10.94 (14.10) mmHg [16]. Both studies show that acupuncture via the catgut embedding technique can reduce blood pressure in patients with essential hypertension. A reduction of 10 mmHg in systolic blood pressure and of 5 mmHg in diastolic blood pressure is considered clinically significant [27]. In this study, the difference in systolic blood pressure between the case and control groups was 13.3 mmHg and that in diastolic blood pressure between the case and control groups was 6.5 mmHg. Thus, these results are significant, both clinically and statistically. The median difference in the NO level in the case group was 1.35 μ M, with minimum value of -10 μ M and maximum value 32.2 μ M. In the control group, the median difference was -1.25 μ M, with a minimum value of -9.7 μ M and maximum value of 9 μ M. A significant difference between was observed between the two groups ($p = 0.045$). The results of this study on catgut embedding support those of Kim *et al.*, Hwang *et al.* and Severcan *et al.* [16,17,28] which focus on other techniques of acupuncture.

4. Conclusion

Acupuncture therapy with the catgut embedding technique produces clinically significant differences in the level of NO, systolic blood pressure, and diastolic blood pressure. It can be utilized as

supplemental therapy to reduce the dosage as well as the combination of anti-hypertensive drugs prescribed to patients. Additionally, it can improve the condition of the blood vessels by increasing the level of NO. The embedding of catgut is expected to reduce cardiovascular risks, although more long-term studies with a larger sample size are needed to confirm this.

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