- **Document Date**: 12 June 2023
- **Title of The Study**: The Effect of Acupressure on Fatigue, Quality of Life and Comfort in Hemodialysis Patients. Randomized Controlled Study
- **NCT Number:** 05892679
- **Document**: The Study Protocol and Statistical Analysis Plan

STUDY PROTOCOL AND STATISTICAL ANALYSIS PLAN

1. Title of the Study: The Effect of Acupressure on Fatigue, Quality of Life and Comfort in Hemodialysis Patients. Randomized Controlled Study

2. Purpose of the Study: In this study, it was aimed to determine the effect of acupressure on fatigue, quality of life and comfort in hemodialysis patients. In our research, it is aimed to reduce fatigue, increase the quality of life and comfort level in hemodialysis patients with acupressure applied.

3. Rationale for the Study: Literature was associated acupressure with fatigue (1-10), pain (11), pruritus (12), sleep problems (4,13-17), depression (7,8,18), in hemodialysis patients and chronic kidney disease patients. It has been reported acupressure to be effective in controlling many symptoms such as nausea-vomiting, muscle cramps (19) and itching (20). In the literature, it is noted that acupressure has a positive effect on the fatigue symptoms of hemodialysis patients. Studies have shown that hemodialysis patients experience high levels of fatigue, and fatigue is the most common factor in patients with CKD, significantly affecting their daily living activities and quality of life (1,2,5,20-22).

Studies on fatigue, quality of life and comfort of acupressure in hemodialysis patients are limited in the literature. However, there is no study in the literature examining the effects of acupressure on fatigue, quality of life and comfort in hemodialysis patients. High-quality, randomized controlled studies with sufficient sample size are needed to demonstrate the effect of acupressure in hemodialysis patients. There is no other randomized controlled study examining the effects of acupressure application on fatigue, quality of life and comfort in hemodialysis patients planned to be included in our study.

Therefore, in this study, it was aimed to draw attention to the importance of acupressure by revealing the effect of acupressure on comfort and quality of life in individuals who experience fatigue due to hemodialysis. It is thought that independent nursing initiatives will be supported with acupressure to be applied in the research, and it will contribute to the practices of nurses. In addition, the adoption of the results of our research by hospital administrations as an institutional policy will guide the care of nurses.

4. Research Materials and Methods:

The study is planned as a prospective, single-blind randomized controlled randomized study to determine the effect of acupressure on fatigue, quality of life and comfort in hemodialysis patients. This randomized controlled trial will be reported according to CONSORT guidelines and registered on ClinicalTrials.gov (23).

Patients who receive hemodialysis treatment in Adana City Hospital dialysis unit, volunteer to participate in the study and meet the research criteria, will be assigned to the study and control groups according to the days they come for dialysis treatment by lottery method (coin toss). Heads will be determined as the working group and heads will be determined as the control group. Randomization in the study will be done on the website of randomizer.org and patients will be included in the study and control groups with the appropriate randomization method according to the dialysis unit list (12,24).

The data obtained from the research will be evaluated using appropriate statistical methods. In the analysis of comparative data, parametric or nonparametric tests will be used by evaluating the conformity to the normal distribution. A package program will be used in the statistical analysis of the research.

4.1. Statistical analysis

Demographic and patient-reported results in the study will be summarized with descriptive statistics. Continuous, normality checks of measurements will be tested with the Shapiro Wilk test. Differences in repeated measures between groups will be tested with the Repeated Measures test (repeated measure analysis of variance). Bonferronni test will be used for pairwise comparisons. Differences between groups for each measurement will be tested with the Independent Samples t-test. Number and percentage values will be given as descriptive statistics. Pearson chi-square and Fisher Exact chi-square tests will be used for differences between categorical variables. Number and percentage values will be given as descriptive statistics. $P<0.05$ will be taken as statistical significance.

4.2. Research Design: Prospective

4.3. Design of the Research

The population of the research will be hemodialysis patients treated at Adana City Hospital between 30 May 2023 and 30 September 2023. The research sample will consist of patients who meet the research criteria and agree to participate voluntarily in the research. The sample number of the study was calculated using the G*Power 3.1.9.7 program (25). In the calculation, a sample calculation was made for repeated measures ANOVA test. In the calculation, Cohen's medium effect size (f = 0.5), 5% margin of error (α = 0.05) and 95% power (1-β = 0.95) and the correlation value between repeated measurements were taken as 0.50 for each group (study and control).) sample size was calculated as 21 patients (42 patients in total). Considering the possibility of patients leaving the groups during the research process, the number of samples for each group was increased by 30%, taking into account the possibility of data loss in order not to adversely affect the statistical power, and 30 patients (total of 60 patients) for each group (study and control) were included in the sample planned (26). Randomization in the study will be done on the website of randomizer.org and patients will be included in the study and control groups with the appropriate randomization method according to the dialysis unit list (27).

F tests - ANOVA: Repeated measures, between factors
Analysis: A priori: Compute required sample size
Input:

Effect size f	**=**	**0.5**
α err prob	**=**	**0.05**
Power (1-β err prob)	**=**	**0.95**
Number of groups	**=**	**2**
Number of measurements	**=**	**2**
Corr among rep measures	**=**	**0.5**

Output:

Noncentrality parameter λ	**=**	**14.0000000**
Critical F	**=**	**4.0847457**
Numerator df	**=**	**1.0000000**
Denominator df	**=**	**40.0000000**
Total sample size	**=**	**42**
Actual power	**=**	**0.9545279**

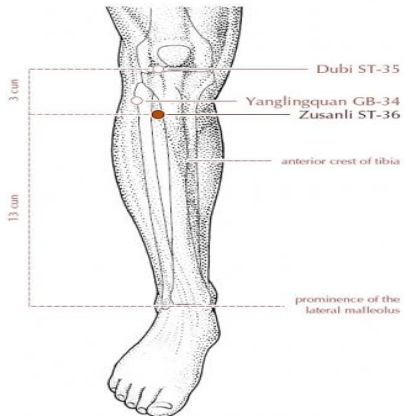
In the study, 60 hemodialysis patients were randomly assigned to the study and control groups. The study group (n=30) Acupressure is formulated according to the standards of the World Health

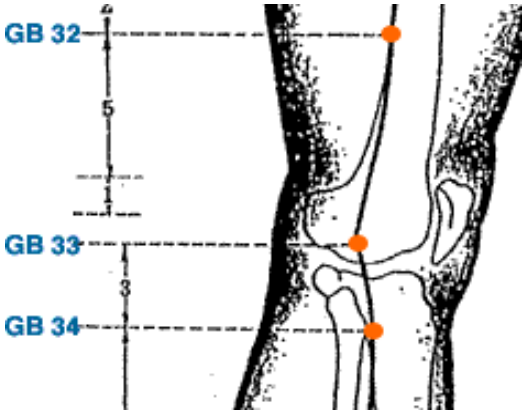
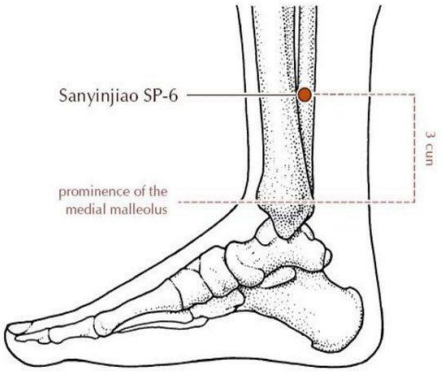
Organization and in a certain order to the points of Stomach 36 (St 36), Gall Bladder 34 point (GB 34), Spleen 6 point (SP 6) and Kidney 1 point (K 1) will be applied. Consideration will be given to the appropriate pressure intensity and duration. Since the reactions of individuals will be different from each other, the stiffness and pressure will be adjusted according to the sensitivity of the individual in order not to cause tissue damage. Pressures will be applied manually by a single practitioner. Considering the anatomical area where the point is located, the most suitable thumb, index and/or middle finger will be used for application to the relevant point. Successive compressions will be applied at a frequency that does not disturb the patient, does not cause pain, and has a calming effect.

Considering the studies done, a person will be given acupressure three times a week for four weeks. No intervention will be made to the control group (n=30). In order to avoid ethical problems both groups will be given an informative training on acupressure and fatigue, increase the quality of life and comfort level in hemodialysis patients at the end of the study. The primary outcome of the study is the effect of acupuncture on fatigue in hemodialysis patients. The secondary result of the study is the effect of acupuncture on quality of life and comfort level in hemodialysis patients.

The results will be collected before the acupressure and in the 4th week of the last intervention.

Table 1. Application Points Used in the Study (33)

Application Site Name	**Picture of Application Site**	**Description of Application Site**
Stomach 36. point (Zusanli: ST 36)		In the leg, it is one finger width lateral to the anterior crest of the tibia, and 3 cuns below the ST 35 in the depression on the lateral side of the patella.

Gall Bladder 34. point (GB 34 or Yangligquan)		It is located on the lateral side of the leg, in the lower anterior depression of the head of the fibula.
Spleen 6. point (Sanyinjiao: SP 6)		It is located on the medial leg, 3 cuns above the medial malleolus, at the posterior border of the tibia.
Kidney 1. Point **(K 1)**		It is located between the 2nd and 3rd metatarsal bones on the sole of the foot (in the front of 1/3 when we divide the sole of the foot into 3 parts).

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5. Research Flow Process

The Flow Chart of this research will be completed in three stages and four steps as indicated in Figure 1.

First Stage (Preparatory Stage): An internationally approved acupressure certificate was obtained by the researcher in July 2022 (the certificate is in Annex I). The place where the acupressure application will be made will be arranged in accordance with the acupressure application. Necessary materials will be purchased for acupressure application (bed cover, pillow, etc.)

Second Stage (Implementation Stage): This stage will consist of four steps.

In the first step: In the first step of the application, patients who receive hemodialysis treatment in Adana City Hospital dialysis unit and meet the research criteria and are willing to participate in the research will be given brief information about the research and their verbal consent will be obtained. The fatigue experience VAS scores of the patients who accepted to participate in the study on a voluntary basis will be calculated. Those with a VAS value of fatigue severity ≥ 4.0 between 0 and 10 points will constitute the sample of the study.

In the second step: Sample selection will be completed in accordance with the inclusion, exclusion and exclusion criteria of the study, and then randomization will be performed. The patients will be informed about the purpose of the research and the research process, and the patients will be asked to fill in the "Piper Fatigue Scale", "Kidney Disease and Quality of Life Form" and "Hemodialysis Comfort Scale" as a pre-test with an informed consent form.

Third step: Patients in the study group will be given a total of 12 sessions of acupressure application bilaterally to Stomach 36 (St36), Gall Bladder 34 (GB34), Spleen 6 (SP6) and Kidney 1 (K1) acupuncture points for 4 weeks and 3 days a week for 20 minutes. No intervention will be made to the control group other than routine maintenance during the four-week period.

Fourth step: After the 4-week acupressure process is over, after the last acupressure session, the patients in the study group will have the "Piper Fatigue Scale", "Kidney Disease and Quality of Life Form" and "Hemodialysis Comfort Scale" filled face-to-face as a post-test. At the end of 4 weeks, the control group will have to fill in the “Piper Fatigue Scale”, “Kidney Disease and Quality of Life Form” and “Hemodialysis Comfort Scale” as a post-test before hemodialysis.

Third Stage (Reporting Stage): At this stage Statistical analysis of the data obtained from the patients will be made and a research report will be written.

Figure 1. Flow Chart of the Research

STAGE 1. PREPARATION STAGE	Arrangement of Adana City Hospital dialysis unit in accordance with acupressure application in order to perform acupressure application.		
STAGE 2 IMPLEMENTATION PHASE	**1. Step**	Contacting patients receiving hemodialysis treatment in Adana City Hospital dialysis unit, Determining compliance with the criteria, Measuring fatigue experience VAS scores, Recruiting patients willing to participate in the study	
	2. Step	Determining the sample according to the criteria Performing the randomization (Study Group; n=30 - Control Group; n=30) Getting Informed Consent and pre-test data collection forms ("Patient Description Form", "Piper Fatigue Scale", "Kidney Disease and Quality of Life Form" and "Hemodialysis Comfort Scale")	
	3. Step	Making acupressure group (n=30) apply acupressure for 20 minutes three times a week for four weeks.	No intervention in the control group (n=30)
	4. Step	Having the study group (n=30) fill out the post-test data collection forms ("Piper Fatigue Scale", "Kidney Disease and Quality of Life Form" and "Hemodialysis Comfort Scale") after the last acupressure session, after the 4-week acupressure process is over.	The control group to be fill out the post-test data collection forms ("Piper Fatigue Scale", "Kidney Disease and Quality of Life Form" and "Hemodialysis Comfort Scale") at the end of the interview at the end of 4 weeks.
STAGE 3 REPORTING PHASE	ANALYSIS OF DATA AND WRITTEN RESEARCH REPORT		

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5. Data Collection Tools of the Research

"Data Collection Form" will be used in the data collection phase of the research.

5.1. Data Collection Form

In the study, data will be collected with a data collection form consisting of four parts: "Patient Description Form", "Piper Fatigue Scale", "Kidney Disease and Quality of Life Form (KDQOLTM-36)" and "Hemodialysis Comfort Scale".

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ANNEX I

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