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Effect of Electroacupuncture on Sensory Peripheral Nerve Function in Diabetic Peripheral Neuropathy: A Randomized Controlled Trial Protocol.

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Abstract

Background: Diabetes, a chronic metabolic disorder, affects millions globally, with Type 2 diabetes being the most prevalent. Diabetic Peripheral Neuropathy (DPN) is a common complication, characterized by symptoms such as pain, tingling, and numbness due to peripheral nerve damage. The global burden of diabetes has been rising, particularly in low- and middle-income countries. In India, the number of diabetes cases is projected to reach over 134 million by 2045. Traditional treatments for DPN often have limited efficacy and adverse long-term effects, highlighting the need for alternative therapies.

Objective: This study aims to investigate the efficacy of electroacupuncture in improving sensory nerve functions in patients with DPN. Specific acupuncture points will be targeted to assess their impact on vibration perception, hot and cold perception, touch sensitivity, and skin temperature.

Methods: A randomized controlled trial will be conducted with 80 participants divided equally into an interventional group and a control group. The interventional group will receive electroacupuncture at specific points (ST44, ST36, ST43, K2, K3, BL60, SP9, and GB41) three times a week for 8 weeks. The control group will continue their usual routine and receive the treatment post-study. Primary outcomes will be measured using the NEURO TOUCH instrument to assess sensory thresholds and skin temperature. Secondary outcomes will include pain assessment using the Visual Analog Scale (VAS). Data will be analyzed using SPSS version 16.

Results: The study will evaluate the degree of sensory improvement in peripheral nerves and the effectiveness of electroacupuncture in reducing neuropathic pain. This research seeks to bridge the gap in understanding the mechanisms and efficacy of electroacupuncture in DPN treatment.

Conclusion: This study will provide significant insights into the potential benefits of electroacupuncture for DPN, offering an alternative approach to improve the management of this debilitating condition. The findings could inform future clinical practices and guidelines for DPN treatment.

INTRODUCTION

Diabetes is a chronic metabolic disease that affects millions of people globally. Type 2 diabetes is the most common form, and type 1 diabetes is persistent and requires insulin. Symptoms include frequent urination, thirst, hunger, weight loss, vision changes, and fatigue. Healthy habits such as regular exercise and healthy eating can prevent type 2 diabetes and its complications. The bulk of the approximately 422 million individuals with diabetes globally reside in low- and middle-income nations, and diabetes is directly responsible for 1.5 million fatalities annually. Over the past several decades, there has been a consistent rise in both the incidence and prevalence of diabetes. (1) Over the past three decades, the worldwide burden of diabetes has gradually increased, with India bearing a substantial share of this burden. In India, 77 million people were estimated to have diabetes in 2019, and by 2045, that number is projected to reach over 134 million. (2) Diabetes can damage the peripheral nervous system, causing distal symmetric polyneuropathy (DSP) with symmetrical sensory problems like pain, tingling, and

numbness. The prevalence of Diabetic Peripheral Neuropathy is 33.33% in southern India, with risk factors including hypertensive diabetes and diabetes with dyslipidemia. (3) The treatment of diabetic peripheral neuropathy is frequently insufficient, and it is yet unknown how to precisely improve glycemic control in type-2 diabetes. Exploring the mechanisms of action and efficacy of various treatments is essential. For the management of DPN, important worldwide clinical guidelines suggest a number of symptomatic therapies. Tricyclic antidepressants, serotonin-norepinephrine reuptake inhibitors, and anticonvulsants that block calcium channels are among the first-line treatments. Opioids and topical medications like lidocaine and capsaicin are examples of other treatments. (4) Pharmacological management of Diabetic Peripheral neuropathy is bearing more deteriorate effects after long-term use of pharmacological remedies. So, the implementation of non-pharmacological interventions like acupuncture and its different modalities is much needed for the hour. Acupuncture is the most popular traditional Chinese medicine accepted worldwide for the treatment of various illnesses. According to traditional Chinese medicine, Diabetic Peripheral Neuropathy is considered a type of “Bi Syndrome”. It occurs when pathogenic factors block the meridian, leading to blood stasis and meridian starvation. (5) Acupuncture and moxibustion can treat diabetic peripheral neuropathy by clearing the meridians and stimulating qi flow. Acupuncture has been researched more, moxibustion may be a safer and less invasive option for diabetic peripheral neuropathy patients with poor wound healing. (5) There are some recent studies showing the effect of acupuncture, acupuncture, and tuina on the treatment of diabetic neuropathy. Acupuncture and Tuina are useful in treating DPN, according to clinical reports. (6) Although electroacupuncture have been studied as a potential treatment for diabetic peripheral neuropathy, there is still a lack of research on the effects of particular point combinations on neuropathic abnormalities or the degree of improvement in sensory function in the lower extremities. This research will center on specific points [(ST44 (Neiting), ST36 (Zusanli), ST43 (Xiangu), K2 (Rangu), K3 (Taixi), BL60 (Kunlun), SP9 (Yinlingquan), and GB 41 (Zulinqi)] to examine various sensory components (Vibration Perception Threshold, Cold & Hot Perception Threshold, Touch Perception and Skin temperature). This study aims to bridge this critical gap in knowledge by conducting a comprehensive investigation of the effect of electroacupuncture on Sensory Peripheral Nerve Functions in Diabetic Peripheral Neuropathy. The study will contribute significant insight into the potential benefits of this novel intervention, thereby offering a better option for improved management and alleviation of diabetic peripheral neuropathy-associated symptoms.

AIM AND OBJECTIVES

Aim:

- To assess the degree of sensory improvement in peripheral nerves of Diabetic Peripheral Neuropathy patients.

Objectives:

Primary Objective:

- To study the impact of electroacupuncture at particular acupuncture points on the vibration threshold, hot and cold perception, touch sensitivity, and skin temperature in patients with diabetic patients.

Secondary Objectives:

- To evaluate how patients with diabetic peripheral neuropathy respond to electroacupuncture at particular acupuncture points for neuropathic pain.

Participating Units:

1. International Institute of Yoga and Naturopathy Medical Sciences, Chengalpattu (Outpatient Department):

- This unit serves as the primary site for patient recruitment, intervention administration, and data collection. Located in Chengalpattu, it offers outpatient services specializing in yoga, naturopathy, acupuncture, and energy medicine.

- The Outpatient Department (OPD) of the International Institute of Yoga and Naturopathy Medical Sciences is responsible for identifying eligible participants, explaining the study protocol, obtaining informed consent, and conducting acupuncture interventions.

- Additionally, this unit will manage the follow-up visits, monitor participants' progress, and oversee data collection procedures throughout the study period.

- The OPD ensures adherence to the study protocol, ethical standards, and safety measures outlined by the Institutional Ethics Committee (IEC) and regulatory authorities.

Laboratories:

- Although the study primarily focuses on clinical interventions and outcome assessments rather than laboratory analyses, certain biochemical parameters such as fasting plasma glucose levels may be measured to confirm eligibility criteria or as secondary outcome measures.

- Laboratory facilities within the International Institute of Yoga and Naturopathy Medical Sciences or affiliated institutions may be utilized for any necessary laboratory analyses.

- The laboratories ensure accurate and timely processing of biological samples, adhering to standardized protocols and quality assurance measures.

Data Management Center:

- The Data Management Center is responsible for overseeing data collection, storage, and analysis throughout the study.

- It may be located within the International Institute of Yoga and Naturopathy Medical Sciences or in a separate facility equipped with appropriate infrastructure and personnel.

- The Data Management Center ensures the confidentiality, integrity, and security of all study-related data, adhering to Good Clinical Practice (GCP) guidelines and regulatory requirements.

- Data management activities include data entry, cleaning, coding, validation, and statistical analysis.

Coordinating Center:

- The Coordinating Center serves as the central administrative hub responsible for coordinating various aspects of the study, including protocol development, regulatory submissions, participant recruitment, training of study personnel, and monitoring study progress.

- It may be housed within the International Institute of Yoga and Naturopathy Medical Sciences or operate as a separate entity closely collaborating with the study team.

- The Coordinating Center facilitates communication among investigators, study personnel, regulatory authorities, and other stakeholders involved in the research.

- It plays a pivotal role in ensuring the smooth implementation of the study protocol, addressing any issues or concerns, and maintaining overall study integrity and compliance.

MATERIALS AND METHODS

Study design:

The study will employ a randomized control study design, as it is a widely recognized method for testing the effectiveness of interventions. This design involves randomly assigning participants to either a treatment group or a control group, to compare the outcomes of the two groups. By utilizing this rigorous approach, we can ensure that the results of the study are accurate and reliable, and can be used to inform future research and practice in the field.

Study Population General Description:

The study population will consist of individuals aged 40 to 60 years visiting the outpatient department of the International Institute of Yoga and Naturopathy Medical Sciences in Chengalpattu, India. Participants will be diagnosed with Diabetic Peripheral Neuropathy (DPN) and have had diabetes for more than 5 years, with an HbA1C level greater than 7%. They will exhibit symptoms and/or signs of peripheral nerve damage, such as altered sensitivity to pain, vibration, or pressure, after ruling out other potential causes.

The inclusion criteria ensure that participants are willing to provide written informed consent, capable of understanding research procedures, and willing to adhere to them for the study's duration. Exclusion

criteria include DPN caused by factors other than diabetes, cardiovascular disorders, psychoneurotic conditions, known hypersensitivity to acupuncture, and open wounds or burns in specific acupuncture points of intervention.

The study population aims to represent individuals with DPN seeking treatment in a clinical setting, providing a diverse sample for the evaluation of electroacupuncture as a therapeutic intervention.

Sample Size Determination and Power Analyses:

The sample size for this study was determined based on achieving 90% power to detect a statistically significant difference in sensory improvement between the interventional and control groups. Given the complexity of the analysis and the need to ensure adequate power, a sample size of 40 participants per group was calculated.

The power analysis was conducted using standard statistical methods, taking into account the expected effect size based on previous literature, the chosen significance level (typically $\alpha = 0.05$), and the desired power level (typically 80% or higher).

For this study, a power analysis was performed using software such as G*Power or PASS, considering the primary outcome measures of vibration perception threshold, hot and cold perception, touch sensitivity, and skin temperature. The effect size was estimated based on previous studies examining similar interventions, allowing for a conservative estimation to ensure adequate power.

The resulting sample size of 40 participants per group provides sufficient statistical power to detect meaningful differences in sensory improvement between the intervention and control groups, while also considering potential dropouts and variability within the study population.

Overall, the sample size determination and power analysis were conducted rigorously to ensure that the study would yield reliable and statistically significant results, contributing valuable insights into the efficacy of electroacupuncture for diabetic peripheral neuropathy.

Study Outcomes/Endpoints:

Primary Outcomes:

1. Vibration Perception Threshold:

- Assessed using NEURO TOUCH, a validated neurothesiometer.

- Measurement of the threshold for vibration perception in the lower extremities before and after the intervention period.

2. Hot and Cold Perception Threshold:

- Evaluated using NEURO TOUCH to determine sensitivity to thermal stimuli.

- Measurement of the thresholds for detecting hot and cold sensations in the lower extremities before and after the intervention.

3. Touch Sensitivity:

- Assessed through NEURO TOUCH to evaluate the degree of sensitivity to touch stimuli.

- Measurement of touch sensitivity in the lower extremities before and after the intervention.

4. Skin Temperature:

- Measured using NEURO TOUCH to assess changes in skin temperature in the lower extremities.

- Evaluation conducted before and after the intervention period.

Secondary Outcomes:

1. Pain Assessment:

- Pain levels will be measured using the Visual Analog Scale (VAS).

- Participants will rate their pain on a scale from 0 (no pain) to 10 (worst possible pain) before and after the intervention, as well as at the end of the 8-week study period.

Assessment Timeline:

- **Baseline**: All primary and secondary outcomes will be measured before the start of the intervention.

-**Midpoint (4 weeks):** Interim assessment of primary outcomes to monitor progress.

-**Post-intervention (8 weeks):** Final assessment of all primary and secondary outcomes to evaluate the effect of the intervention.

Data Collection and Analysis:

- Data Collection: Outcomes will be measured by trained personnel using standardized procedures and instruments. Data will be recorded in a structured format to ensure consistency and accuracy.

-Data Analysis: Statistical analyses will be conducted using SPSS version 16. Descriptive statistics will summarize the baseline characteristics of the study population. Inferential statistics, including t-tests or ANOVA for continuous variables and chi-square tests for categorical variables, will be used to compare outcomes between the intervention and control groups. A p-value of <0.05 will be considered statistically significant.

Significance of Study Outcomes:

The primary outcomes will provide objective measures of sensory nerve function improvements in patients with diabetic peripheral neuropathy following electroacupuncture treatment. The secondary outcome will offer subjective insights into the pain relief experienced by the participants. Together, these outcomes will help determine the efficacy of electroacupuncture as a viable treatment option for managing sensory abnormalities and pain associated with diabetic peripheral neuropathy.

Study Procedures

1. Participant Recruitment:

-**Location:** Outpatient department of the International Institute of Yoga and Naturopathy Medical Sciences in Chengalpattu, India.

-**Recruitment Method**: Participants will be identified through routine clinical visits. Information sessions and flyers may also be used to inform potential participants about the study.

-**Screening**: Participants will undergo an initial screening to ensure they meet the inclusion and exclusion criteria.

Inclusion criteria:

Participants will only be accepted for enrolment if they satisfy all of the prerequisites listed below.

- Aged 40 to 60 years.
- After ruling out other potential causes, Diabetic peripheral neuropathy is defined as the existence of symptoms and/or indications of peripheral nerve damage in diabetics.

b. peripheral neuropathy is described as having either (a) altered sensitivity to pain or (b) altered sensitivity to vibration in addition to altered sensitivity to pressure. (10)

- Patients diagnosed with diabetes for more than 5 years.
- HbA1C more than 7%
- Patients who are willing to written informed consent.
- Patients who are able to understand research procedures and desire to adhere to them for the duration of the study.

Exclusion criteria:

Participants who fit any of the above descriptions will not be accepted.

- Diabetic peripheral neuropathy brought on by illnesses other than diabetes, such as alcoholism, chemotherapy, and Vitamin B12 deficiency.

- Cardiovascular disorder (e.g., arrhythmia) or using pacemakers, or artificial implants.
- Psychoneurotic causes: epilepsy, depression, panic disorder.
- Known hypersensitivity reaction after acupuncture treatment or inability to cooperate with acupuncture procedure.
- Open wound, Scald or burn in Specific Points of intervention.

Withdrawal criteria:

All subjects are free to withdraw from participation in the study at any time, for any reason, specified or unspecified, and without prejudice to further treatment.

2. Informed Consent:

-Process: Detailed information about the study, including its purpose, procedures, potential risks, and benefits, will be provided. Participants will have the opportunity to ask questions.

-Consent: Written informed consent will be obtained from all participants prior to their inclusion in the study.

3. Baseline Assessment:

- Data Collection: Baseline demographic and clinical data will be collected, including age, gender, duration of diabetes, HbA1C levels, and current medications.

-Primary and Secondary Outcomes: Initial measurements of vibration perception threshold, hot and cold perception threshold, touch sensitivity, skin temperature, and pain levels using NEURO TOUCH and VAS.

4. Randomization:

-Method: Participants will be randomly assigned to either the intervention group (electroacupuncture) or the control group using computerized randomization and basic random methods.

-Allocation Concealment: The SNOSE (Sequentially Numbered Opaque Sealed Envelope) method will be used to conceal group allocation from participants and researchers.

5. Intervention:

- Electroacupuncture Group:

- Procedure: Sterile needles will be inserted bilaterally at specific acupuncture points (ST44, ST36, ST43, K2, K3, BL60, SP9, GB41).

-Electrical Stimulation: Hwato Electronic Acupuncture instrument with an adjustable pulse frequency of 1-100 Hz will be used for electrical stimulation.

-Session Duration: 20 minutes per session, three sessions per week for 8 weeks.

-Point Combinations: ST44, GB41, UB60, and ST36 during the first four weeks; ST43, K2, K3, and SP9 during the second four weeks.

-Control Group:

-Procedure: Participants will continue their usual routine and will not receive the electroacupuncture intervention during the study period. They will receive the treatment after the study is completed.

6. Midpoint Assessment (4 weeks):

-Data Collection: Interim measurement of primary outcomes (vibration perception threshold, hot and cold perception threshold, touch sensitivity, and skin temperature).

7. Post-Intervention Assessment (8 weeks):

-Data Collection: Final measurements of primary and secondary outcomes using NEURO TOUCH and VAS.

-Comparison: Data will be compared to baseline and midpoint assessments to evaluate changes.

8. Data Management:

-Storage: All data will be securely stored in a password-protected database. Hard copies will be stored in a locked cabinet.

-Confidentiality: Participant confidentiality will be maintained throughout the study. Data will be anonymized before analysis.

9. Data Analysis:

-Statistical Methods: SPSS version 16 will be used for data analysis. Descriptive statistics will summarize baseline characteristics. Inferential statistics (t-tests or ANOVA) will compare outcomes between the groups. Chi-square tests will be used for categorical data.

-Significance Level: A p-value of <0.05 will be considered statistically significant.

10. Ethical Considerations:

-Approval: Ethical approval will be obtained from the Institutional Ethical Committee (IEC) of the International Institute of Yoga and Naturopathy Medical Sciences.

-Participant Rights: Participants can withdraw from the study at any time without prejudice to further treatment.

11. Dissemination of Results:

- Publication: Results will be published in peer-reviewed journals.

-Presentation: Findings will be presented at relevant conferences and seminars to inform practitioners and researchers about the efficacy of electroacupuncture in treating diabetic peripheral neuropathy.

Abbreviations

1. ST- STOMACH
2. GB – GALL BLADDER
3. K – KIDNEY
4. SP – SPLEEN
5. DPN – Diabetes Peripheral Neuropathy
6. MDCN – Medial Dorsal Cutaneous Nerve
7. IDCN – Intermediate Dorsal Cutaneous Nerve
8. LDCN – Lateral Dorsal Cutaneous Nerve

Declarations

Ethics Approval and Consent to Participate

Ethics approval for this study was obtained from the Ethics Committee of the International Institute of Yoga and Naturopathy Medical Sciences, Chengalpattu, Tamil Nadu. All participants provided written informed consent before their involvement in the study.

Consent for Publication

All participants provided consent for the publication of anonymized data and study findings.

Availability of Data and Materials

The datasets generated and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Competing Interests: The authors declare that they have no competing interests.

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Authors' Contributions:

Syam Kumar C P: Methodology, Investigation, Writing - Original Draft

Gokulakrishnan: Supervision, Conceptualization.

Prabu Narasimman: Supervision, Co-guidance.

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Figures

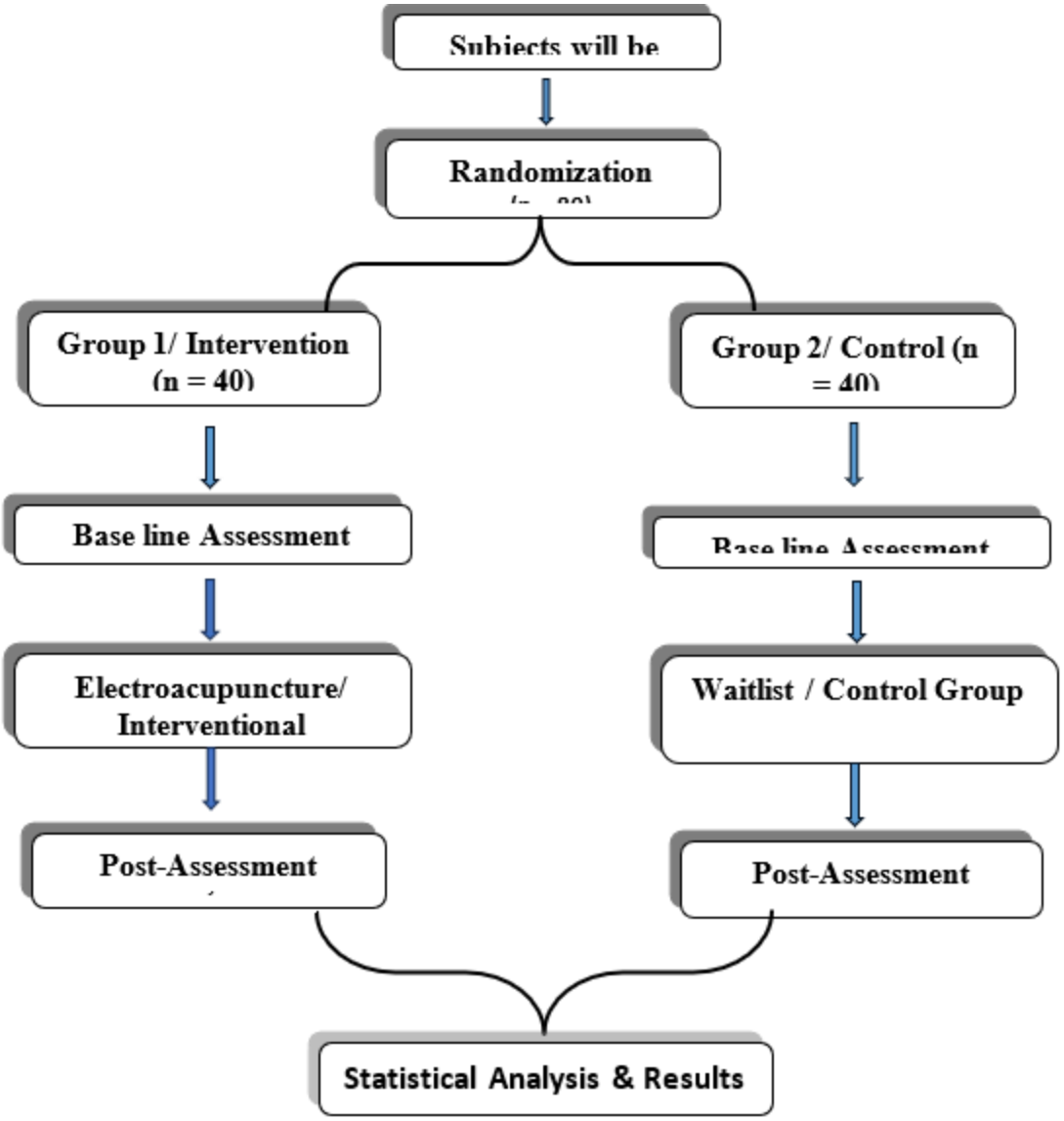


Figure 1

Trial profile

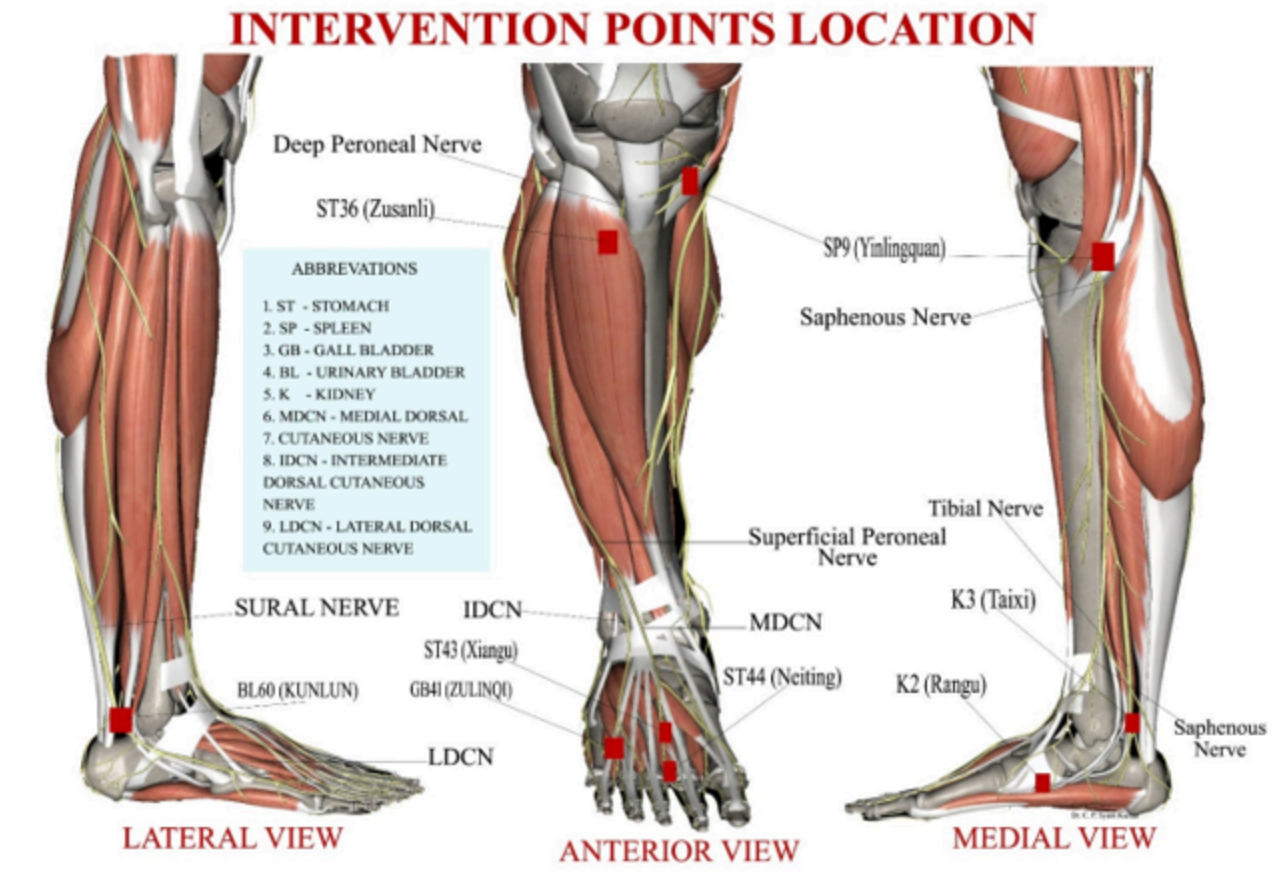


Figure 2

INTERVENTION POINTS AND ITS LOCATION