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Complementary Therapies for Painful Diabetic Neuropathy: A Systematic Review

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ABSTRACT

Pharmacological treatment of neuropathic pain has various side effects, while complementary therapies have minimal risk of side effects. To explore more deeply the types of complementary therapies that can be used to treat painful diabetic neuropathy. Articles were searched using Science Direct, Pubmed, Google Scholar, and EBSCO to find articles according to inclusion and exclusion criteria. Articles that meet the criteria set by the author are then analyzed, determined by the level of evidence extracted, and then synthesized. Complementary therapies that can reduce neuropathic pain in diabetic patients are electrical stimulation, Low-Intensity Laser Therapy (LILT), Repetitive Magnetic Stimulation, Acceptance and Commitment Therapy (ACT), Aromatherapy Massage, Exercise Training, Acupuncture, and China Herbal Medicine. Among these interventions, Acupuncture and electrical stimulation were the most widely used interventions to reduce neuropathic pain in diabetic patients. Complementary therapies can reduce neuropathic pain in people with diabetes. It is hoped that future research using the RCT method with many samples can be generalized.

Keywords: *diabetic neuropathy, painful complementary therapies*

1. INTRODUCTION

Diabetes is a metabolic illness with high blood glucose levels, which makes it a chronic disease.^{1,2} With 19,5 million diabetics, Indonesia is ranked fifth in the world. It is projected that 28,4 million diabetics will exist in Indonesia by 2045.³

The challenge for nurses in response to the rise of people with diabetes gets more prominent because the problems arising from body response will also be complex.⁴ Various kinds of difficulties are connected to one. Both macrovascular problems and microvascular issues might affect diabetic patients. One of the most common microvascular complications is diabetic neuropathy.⁵ Diabetic neuropathy should be addressed as away to prevent a decline in the patient's quality of life.⁶ The study results show that neuropathy and pain can affect patients experiencing sleep disorders, symptoms of anxiety and depression, decreased appetite, and even a decrease in immunity.^{7,8}

Neuropathic pain is pain that results from a somatosensory system injury or illness.⁹ Pharmacological pain management to treat diabetic neuropathic has a risk of side effects in gastrointestinal disorders, kidney disorders, liver disorders, heart disorders, dizziness, fatigue, nausea, and insomnia¹⁰. Side effects caused by pharmacological drugs can be avoided by using complementary therapies, reducing the pain of diabetic neuropathy. Therapies that are utilized in addition to or in conjunction with traditional therapies include body-based practices, mind and energy therapies, dietary and herbal preparations, sensory therapies, and movement therapies.¹¹ Regrettably, very little study has examined various supplementary treatments for neuropathic pain relief in diabetic patients. The many supplementary treatments that can diminish neuropathic pain must therefore be thoroughly analyzed.

2. METHODS

2.1. Design

The research designs included in this systematic review are systematic reviews, meta-analyses, and RCTs. This type of research design is deemed to have been able to answer predetermined clinical questions.

2.2. Inclusion and exclusion criteria

2.2.1. Type of study

The studies that will be reviewed are all types of research that use complementary therapies to reduce pain in patients with diabetic neuropathy.

2.2.2. Type of participants/ respondent

Participants who were determined to be reviewed are adult patients who experienced painful diabetic neuropathy. Therefore, all participants who meet these criteria are included as participants in a systematic review.

2.2.3. Type of Intervention

Interventions included in the inclusion criteria are all types of complementary therapy interventions, not drug therapy, that were carried out to reduce painful diabetic neuropathy.

2.2.4. Type of Measured Outcome

The type of outcome to be measured is limited to the effect of complementary therapy on reducing painful diabetic neuropathy.

2.3. Systematic review search strategy

This systematic review was carried out by searching published research articles, and we used the keywords complementary medicine OR complementary therapies, NOT drug therapy AND painful diabetic neuropathy AND diabetic neuropathy for finding the articles. The population in this study are diabetic neuropathic patients who received nonpharmacological therapy, and the results are reduced levels of diabetic neuropathic pain. Searches are done by using the EBSCO search engine, which includes Medline, CINAHL, Science Direct, Google Scholar, and Pubmed, with keywords for each variable that has been selected. After carefully reading the articles that satisfied the author's inclusion criteria to be included in the literature for this systematic review, articles were discovered from each of those searches. The search period included the period from January 5, 2017, through June 30, 2022, and it may be accessed in full text in PDF format with

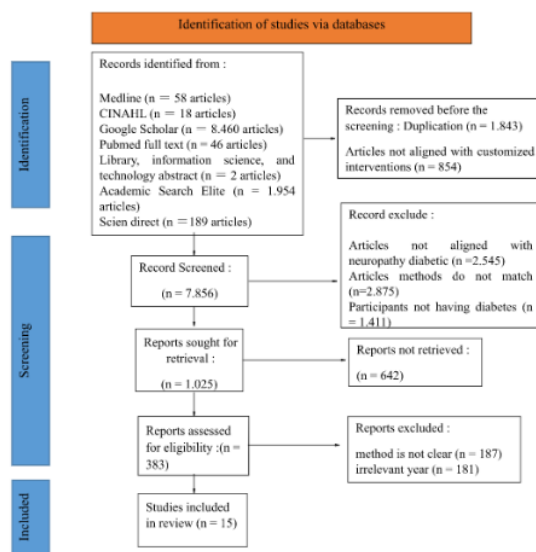
RCTs. A comprehensive review will include all published studies that employ complementary therapies that can lessen the discomfort associated with diabetic neuropathy.

The level of evidence up to data extraction and synthesis will be assessed and used to construct the methodology for rating the quality of study articles that meet the defined criteria. The expectation from these many studies is to conclude that later becomes the basis for nursing practice in hospitals, society, or the community.

2.4. Extraction data method

Research data is extracted by reading a research's results and then taking the essence of the research. The essence of the research that has been taken is the title of the study, the name of the researcher, the research method, the number of samples by looking at the characteristic sample and the number of interventions and control groups, the instrument that has been used, and the final results completed with the significance value. All parts are organized in a table to make the extraction. We use PRISMA flow diagram to make searching easier.

Figure 1. PRISMA Flow Cart



3. RESULT

To get the research articles it needs, the author runs a search with keywords. The number of articles obtained and met the inclusion and exclusion criteria is 15, of which 9 were systematic review articles and 6 RCT articles. For example, research on the management of neuropathic pain may be performed with electrical stimulation¹², acupuncture therapy¹³⁻¹⁵, massage therapy

and aromatherapy^{16,17}, herbal therapy¹⁸, ACT psychotherapy¹⁹, and Exercises Training^{20,21}. Those articles are then analyzed. The following are the lists of extracted articles in tabular form: (the extraction table can be seen at the end of this article).

Table 1: The level of evidence and quality of the articles

No	Author & years	Method	Level of evidence	Summary
1	Emmanuel <i>et al.</i> (2019)	Systematic review	2	Good
2	Andreas, L, <i>et al.</i> (2020)	Systematic review	2	Good
3	Abdullah, Amir, <i>et al.</i> (2020)	Systematic review	2	Good
4	Barnetti, Andrea, <i>et al.</i> (2021)	Systematic review	2	Good
5	Anju M, <i>et al.</i> (2019)	Systematic review	2	Good
6	Davaodi, <i>et al.</i> (2020)	Randomized clinical trial	1	Good
7	Dietzel J, <i>et al.</i> (2021)	Randomized clinical trial	1	Good
8	Wang Li-Qin, <i>et al.</i> (2020)	Systematic review	2	Good
9	Dimitrova Alexandra, <i>et al.</i> (2017)	Systematic review and Meta-Analysis	2	Good
10	Nash Jane, <i>et al.</i> (2019)	Systematic review	2	Good
11	Longsheng Ren, <i>et al.</i> (2022)	Systematic review	2	Good
12	Yong Shi, <i>et al.</i> (2021)	Randomized clinical trial	1	Good
13	Zehra Gok Metin, <i>et al.</i> (2017)	Randomized clinical trial	1	Good
14	MiMi Thet Mon Win, <i>et al.</i> (2019)	Randomized clinical trial	1	Good
15	Emily R. Cox <i>et al.</i> (2020)	Randomized clinical trial	1	Good

Table 2: Extraction table of the included studies

No	Title Author (years)	Objectives	Methods	Results	Significant to the topic under review
1	Effectiveness of electrical stimulation and low intensity laser therapy on diabetic neuropathy: A systematic review Emmanuel <i>et al.</i> (2019)	This study is a systematic assessment of the available data to assess the efficacy of low-intensity laser therapy and electrical stimulation (LILT)	Systematic review	This study is a systematic assessment of the available data to assess the efficacy of low-intensity laser therapy and electrical stimulation (LILT)	Transcutaneous electrical nerve stimulation (TENS), pulsed-dose electrical stimulation, and frequency-modulated electromagnetic neural stimulation are all effective treatments for diabetic neuropathy.
2	Nonpharmacological Management of Painful Peripheral Neuropathies: A Systematic Review Andreas, L <i>et</i>	This systematic review's objective was to assess the most recent data collected from RCTs that evaluate non-	Systematic review	Adjuvant repeated transcranial magnetic stimulation of the motor cortex is helpful in lowering overall level of pain, while adjuvant	Pain intensity can be decreased by repeatedly stimulating the motor cortex using transcranial magnetic stimulation.

	<i>al.(2020)</i>	pharmacological therapies for the treatment of PNP.		static magnetic field therapy is efficient in significantly lowering workout pain.	
3	Repetitive Magnetic Stimulation for the Management of Peripheral Neuropathic Pain: A Systematic Review Abdullah, Amir, <i>et al.</i> (2020)	Pain intensity can be decreased by repeatedly stimulating the motor cortex using transcranial magnetic stimulation.	Systematic review	Pain alleviation with repetitive magnetic stimulation (RMS) is evidently experienced immediately and, in the majority of trials, is sustained for a few weeks.	RMS (repetitive magnetic stimulation) provides instant pain alleviation.
4	Neuropathic Pain and Rehabilitation: A Systematic Review of International Guidelines Barnetti, Andrea <i>et al.</i> (2021)	used therapy modalities and make rehabilitation suggestions for the treatment of neuropathic pain	Systematic review	To treat neuropathic pain, both pharmaceutical and nonpharmacologic treatments should be used.	This review emphasizes the value of rehabilitation while also pointing out the paucity of research on various forms of rehabilitation.
5	Low-level laser therapy for patients with painful diabetic peripheral neuropathy - A systematic review Anju M, <i>et al.</i> (2019)	centered on locating data demonstrating LLLT's value in the treatment of uncomfortable diabetic neuropathy.	Systematic review	The QoL questionnaire, the nerve conduction velocity test, and the fluctuation in pain score were considered as the concluding measures.	According to the data, LLLT is effective at reducing diabetic neuropathic pain.
6	Effectiveness of Acceptance and Commitment Therapy (ACT) on depression and sleep quality in painful diabetic neuropathy: a randomized clinical trial Davaodi, <i>et al.</i> (2020)	In patients with painful diabetic neuropathy, evaluate the impact of acceptance and commitment therapy on depression and sleep disturbance.	Randomized clinical trial	According to the study's findings, the ACT group's total sleep quality significantly improved.	As a supplemental therapy, ACT can help persons with neuropathic pain with their psychiatric symptoms and issues. Consequently, medical care and psychological services must be provided in outpatient and inpatient units.
7	Acupuncture in diabetic peripheral Neuropathy protocol for the randomized, multicenter ACUDPN trial Dietzel J, <i>et al.</i> (2021)	to find out if acupuncture works well for treating DPN symptoms.	This study Randomized clinical trial	the conclusions of this acupuncture trial for the treatment of DPN can be regarded as successful	Acupuncture is thought to be successful in treating DPN in terms of neuropathic conditions
8	Effectiveness of warm needling acupuncture (WNA) for pain relief in patients with diabetic peripheral neuropathy Wang Li-Qin, <i>et al.</i> (2020)	Examine WNA's ability to reduce pain in DPN and its safety.	Systematic Review	the data confirming WNA's effectiveness and safety in treating pain in DPN patients.	The goal of this study is to determine how well and safely WNA treats pain in DPN.
9	Acupuncture for the Treatment of Peripheral Neuropathy: A Systematic Review	to evaluate acupuncture's effectiveness in treating neuropathy caused by different	Systematic Review and Meta-Analysis	The majority of RCTs revealed acupuncture control to be beneficial for the management of diabetic neuropathy.	A thorough investigation including a sham-acupuncture control is needed to thoroughly characterize

	and Meta-Analysis Dimitrova Alexandra, Murhison Charles, Okan Barry (2017)	etiologies.			acupuncture's effects and suggested applications for some peripheral neuropathies.
10	Acupuncture for the treatment of lower limb diabetic peripheral neuropathy: a Systematic Review Nash Jane, Armour Mike & Penkala Stefania (2019)	to assess the data supporting the use of acupuncture for the treatment of diabetes- related peripheral neuropathy (DPN) symptoms	Systematic review	Studies involving DPN individuals who received acupuncture treatment and reported on the condition's results before and after were looked up in five electronic databases.	The use of acupuncture varied significantly, and the included research' quality was generally subpar.
11	The efficacy and safety of massage adjuvant therapy in the treatment of diabetic peripheral neuropathy Longsheng Ren, <i>et al.</i> (2022)	This investigation will look at the efficiency and security of massage therapy used in DPN.	Systematic review Eight	Adjuvant massage therapy's effectiveness in DPN. This investigation will offer proof of the efficacy and security of massage adjuvant therapy in DPN.	However, there isn't enough scientific proof to recommend massage therapy for DPN.
12	Efficacy and safety of Acupuncture combined Chinese herbal medicine for diabetic peripheral Neuropathy Yong Shi, <i>et al.</i> (2021)	A thorough and systematic investigation of the efficiency and security of acupuncture along with Chinese herbal medicine for pain treatment in DPN will be conducted.	Randomized controlled trials	In order to treat DPN, this study will offer a thorough and high- quality assessment of the safety of acupuncture and Chinese herbal therapy.	The outcomes will encourage broader use of acupuncture and Chinese herbal therapy as supplementary DPN treatments, and they will provide solid evidence to back up the clinical decision to use these therapies.
13	Aromatherapy for Massage for Neuropathic Pain and Quality of Life In Diabetic Patients Zehra Gok Metin, <i>et al.</i> (2017)	Examine how aromatherapy massage affects patients with painful diabetic neuropathy's quality of life (QoL) and neuropathic pain severity.	Randomized controlled clinical	In the fourth week of the trial, neuropathic pain scores decreased in the intervention group compared to the control group. QoL scores significantly increased in the intervention group.	For patients with painful neuropathy, an aromatherapy massage is a quick and efficient intervention that can be used to control neuropathic pain and enhance quality of life.
14	Hand and foot exercises for diabetic peripheral neuropathy: A randomized controlled trial MiMi Thet Mon Win, <i>et al.</i> (2019)	To determine how easy hand, finger, and foot exercises performed during 8 weeks will affect individuals with diabetic peripheral neuropathy.	Randomized controlled trial	The exercise group had more decreased pain on the VAS than the control group in terms of pain outcomes, although there were no significant differences between or among groups.	These activities can help people in Myanmar who have DPN avoid functional challenges and other DPN consequences.
15	Effect of Different Exercise Training Intensities on Musculoskeletal and Neuropathic Pain in Inactive Individuals with Type 2 Diabetes: Preliminary Randomized Controlled Trial Emily R. Cox <i>et al.</i> (2020)	This exploratory investigation looked at whether exercise of various intensities affected the self- reported musculoskeletal pain or diabetic neuropathy symptoms in type 2 diabetics who were inactive.	Randomised Controlled Trial	There were no group differences in sensory function. Both exercise regimens had comparable incidence of adverse effects, although only one of them was serious.	According to preliminary research, inactive people with T2D may be prescribed high-intensity mixed aerobic and resistance exercise for 8 weeks to safely reduce musculoskeletal discomfort but not neuropathic symptoms.

4. DISCUSSION

4.1 Electrical stimulation

Electrical stimulation is a therapy that delivers electricity to certain parts of the skin to activate the nerves under the skin, which are usually used to reduce pain symptoms such as diabetic neuropathy¹². Transcutaneous electrical nerve stimulation, which conducts electricity and results in paresthesias or inhibits nerve fibers to have an analgesic effect (TENS)²². Transcutaneous Electrical Nerve Stimulation (TENS), frequency-modulated electromagnetic neural stimulation (FREMS), and percutaneous Electrical Nerve Stimulation are the electrical stimulation treatments that have been identified (PENS).

In a double-blind RCT trial using frequency-modulated electromagnetic neural stimulation (FREMS) as monotherapy, Liampas et al. and Bosi et al. found that a patient with polyneuropathic pain diabetes witnessed a significant improvement in pain intensity that can be resisted for at least four months (2020). In addition, there is a significant rise in the quality of life, an analgesic effect, and the speed of motor nerve transmission.²²

A systematic review study by Bernetti et al. (2021) on international guidelines for neuropathy from 6 articles found that TENS can be used to reduce diabetic neuropathic pain either early or late and can be combined with psychotherapy and physiotherapist for neuropathic pain diabetic²³.

4.2 Low-Intensity Laser Therapy (LILT)

Low-power waves are employed in Low-Intensity Laser Therapy (LILT) with wavelengths ranging from 632 to 1064 nm with a power output of 1 to 1000 mW. Helium-Neon lasers (Heene) operating at 632.8 nm, Aluminum Gallium Arsenide (Al, Ga), diode lasers operating at 780–830 nm (infrared light), and Helium-Neon diode lasers are all examples of LILT. This approach is affordable, efficient, and combines well with other approaches.^{24,25} In a systematic review on the usage of LILT in diabetic neuropathy patients that Anju conducted at A. (2019), it significantly influences the alleviation of diabetic neuropathy pain. In five of the six articles discussed, the use of LILT for reducing diabetic neuropathy pain was shown to be successful.²⁶

Electrical stimulation and Low-Intensity Laser Therapy (LILT) can be used together. Emanual et al (2019) which was conducted to assess the efficacy of electrical stimulation paired with LILT, demonstrated its efficacy in the management of diabetic neuropathy pain.¹²

4.3 (RMS) Repetitive Magnetic Stimulation

Transcranial magnetic stimulation is founded on the concept of electromagnetic induction of electric fields in the brain. The length of administration varies greatly. TMS uses frequencies that range from low frequencies (1 Hz) to high frequencies (RTM, 5–20 Hz) to induce inhibitory effects that last for a long time on the motor cortex. This TMS treatment is a well-tolerated, risk-free procedure.^{22,27} The discomfort associated with diabetic neuropathy may be lessened by repetitive transcranial magnetic stimulation (rTMS). A neuropathic patient who had three weeks of rTMS therapy at a frequency of 20 Hz in the lower motor cortex was demonstrated to experience less pain in a systematic review by Aamir et al. (2019).²⁷

4.4 Acceptance and Commitment Therapy (ACT)

Pain management strategies using biopsychosocial treatment, such as Acceptance and Commitment Therapy (ACT). ACT is a psychological intervention technique that tries to promote increased receptivity to the experience of pain, alter behavior toward pain, and speed up the process of behavior modification. The ACT has six stages: acceptance, cognitive diffusion, action based on values, recognizing the situation as it is, developing skills, and recognizing one's own potential.^{28–30} In dealing with neuropathy pain, ACT can be used, as in a study by Davoudi et al. (2020), where ACT is used as an intervention for patients with neuropathic pain who experience sleep disorders and depression. The findings of this study demonstrate that ACT can help people with diabetic neuropathy discomfort who are experiencing psychological issues. As a result, outpatients require psychotherapy¹⁹.

4.5 Acupuncture and Chine Herbal Medicine

Acupuncture is a Chinese medical practice It leverages the life energy of the body's flow, known as De Qi energy. De Qi energy is believed to recover the body when a needle enters the skin, with or without needle manipulation on specific points of the body, which can stimulate the sense of pain, numbness, and tingly^{31,32}. In a study using the RCT method, Dietzel et al. (2021) examined the impact of acupuncture on diabetic neuropathy pain and concluded that it may be both beneficial and safe for those with the condition.¹³

Acupuncture with warm needles or Warm Needle Acupuncture (WNA) is an acupuncture technique combined with moxibustion. This method is better because it increases blood flow and reduces pain, compared to acupuncture or moxibustion techniques³³. A study of a systematic review done by Nash, Jane et al.. (2019) explains that acupuncture therapy was seen only to improve symptoms. However, the applications are still varied, and the quality of study is still low, so

further studies on the effectiveness of Acupuncture are needed with a better method. This is similar to the results of a systematic review study by Dimitrova et al. (2017)^{14,15}. Acupuncture can be related to the gate control theory, where pain input is inhibited by other painful stimuli (needling). In addition, a study proved that Acupuncture stimulates the formation of antipain hormones that may reduce pain. Furthermore, Acupuncture is also closely related to psychosocial beliefs, expectations, and environment therapeutic.³²

Acupuncture therapy combined with Chinese herbs, which was researched by Shi et al. (2021), the use of drugs has not been standardized, so in practice, clinicians choose drugs based on their experience.

4.6 Hydrotherapy

Hydrotherapy is one of the aquatic exercises such as pool therapy and balneotherapy. Hydrotherapy is usually done in patients with neurological disorders and musculoskeletal disorders. Hot water and buoyancy of water block nociceptors that work on thermal receptors and mechanoreceptors and positively affect the spine. Warm water also improves blood circulation and provides a relaxing effect³⁴.

4.7 Aromatherapy massage

Essential oils are used in aromatherapy, a complementary therapy technique. Aromatherapy has been shown to help older patients with pain, anxiety, depression, and sleep difficulties [35]. For instance, lavender aromatherapy and massage were used on patients with osteoarthritis pain and were successful in reducing the frequency of everyday activities.³⁵ Metin et al. (2017) conducted an RCT study with 46 participants over the course of four weeks to examine the effects of aromatherapy massage on neuropathic pain and quality of life for diabetic neuropathy. Participants were divided into 21 intervention group participants and 25 control group participants. This study's statistical findings demonstrated that massage aromatherapy reduces pain in 4 weeks (p 0,000) and enhances quality of life (p 0,049)¹⁶.

4.8 Exercises Training

Exercise Training is physical exercise (Physical Activity) according to WHO (2020), is all physical activity of body movement that uses muscles and requires energy, where this activity can reduce depression and anxiety and can be used in the prevention and management of heart disease, cancer, and diabetes. A study conducted by Cox et al. (2020) about the differences in the intensity of physical exercise in patients with musculoskeletal and neuropathic pain in a patient with type 2 diabetes was carried out for eight weeks. The number of respondents

was 32 people and divided into three groups, the CON Group, the C-MICT group, and the C-HIIT group. From the eight-week research results, we obtained the effect on the intensity of musculoskeletal pain and neuropathic pain C-HIIT intervention, a significant effect on reducing pain compared to the CON and C-MICT. Meanwhile, the effects on the sensory function of all interventions had no significant effects.²⁰

For 16 weeks, two groups of individuals with neuropathic pain participated in a study (Win et al. 2018) on exercise training with hand and foot exercises. The findings show that there was a significant improvement in motor and specific activities in the intervention group, but there was no significant difference in the severity of pain during the exercise period between the two groups. However, the intervention group experienced significantly less pain than the control group²¹.

4. CONCLUSION

Electrical stimulation, low-intensity laser therapy (LILT), repetitive magnetic stimulation, acceptance and commitment therapy (ACT), hydrotherapy, aromatherapy massage, exercise training, acupuncture, and Chinese herbal medicine are complementary therapies that have been shown to reduce neuropathic pain in diabetic patients. The articles found in this systematic review were still varied, so they cannot be used as meta-analyses. The limits of using search engines to access international-based data allow us to miss other studies that cannot be published in this study. Research using an RCT method about types of nonpharmacological therapy to reduce diabetic neuropathy pain with a large sample is necessary to do so that generalization can be achieved.

AUTHORS' CONTRIBUTIONS

The first writing draft was produced by HP. This study was directed and carried out by AS, ES, and SP. This paper was reviewed, revised, and polished by HP, AS, ES, and SP. All authors wrote the essay and agreed to its submission.

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