

Comparative Study of Paracetamol vs Paracetamol Plus Acupressure for Pain Relief in Diabetic Neuropathy Patients

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ABSTRACT

Background: Diabetes Mellitus (DM) is a chronic metabolic disorder that causes neuropathy. Diabetic neuropathy causes severe pain and needs therapy to relieve its pain. In Indonesia, the therapy uses paracetamol, sometimes combined with acupressure. However, the efficacy of the combination therapy needs to be better understood. **Purpose:** This study aimed to elucidate the efficacy of paracetamol vs paracetamol combined with acupressure for pain relief in diabetic neuropathy patients. **Materials and methods:** This study used a cross-sectional study design. Total of 70 participants were agreed to involved in this study. The patients were then interviewed, and their visual analogue scale was assessed. The data was then analysed statistically using Pearson's correlation. **Result:** Out of the 70 patients diagnosed with type II DM, 40 had *Diabetic Neuropathic Pain* (DNP). Shockingly, most of the patients with type II DM and DNP were females, accounting for 33 out of 40 cases (82.50%). The study found a significant correlation between the type of therapy and the decrease in VAS scores for diabetic patients with neuropathic pain ($p \leq 0.05$). Patients treated with paracetamol and acupressure showed more improvement in the VAS score than those treated with only paracetamol. **Conclusion:** The study suggests that the combination treatment could benefit DNP as an analgesic for type II DM patients. Advanced study is required to be performed using larger samples so that accurate data can be obtained.

Keywords: Acupressure, Diabetic neuropathic pain, Paracetamol, Type II diabetes mellitus, Visual analogue scale.

INTRODUCTION

Diabetes Mellitus (DM) is one of the chronic metabolic disorders in humans. DM is characterized by persistent hyperglycemia. DM is classified into three types: type I, II, and III, based on its etiological and clinical signs.¹ Type I occurs in humans with autoimmune disease, while type II occurs in humans with impaired insulin secretion and its mechanism of action. In addition, type III is a gestational type. Of all of them, type II DM is the most prevalent in humans.² It most commonly occurs in adults, and during the last decades, it has also developed in young and adolescents. Type II DM is significantly associated with beta-cell dysfunction, leading to insulin resistance.³

Insulin resistance is correlated to the insulin receptor substrate (IRS) protein mutation and phosphorylation. The previous study described that the increase of phosphorylation of IRS-1 tyrosine impairs downstream effector in beta cells in an insulin-resistant rat model.⁴ Moreover, serine phosphorylation leads to the disintegration of various insulin receptors, such as IRS-1 and P13-kinase. Thus, disintegrations of IRS-1/P13 kinase promote circulating free fatty acid (FFA) and TNF that impair the signal of transduction of insulin.⁵ Moreover, FFA contributes to increased lipid metabolism intracellularly (including diacylglycerol and fatty acyl CoAs) and leads to insulin resistance.⁶ The pathophysiology of this disease has a lot of negative impacts on various organs. Several impacts are nephropathy, retinopathy, and neuropathy.⁷

Neuropathy in diabetic patients is called diabetic neuropathy. Diabetic neuropathy (DN) is a common disorder caused by peripheral nerve dysfunction. Diabetic neuropathy is often accompanied by severe pain released spontaneously and or with stimulus.⁸ Diabetic neuropathic pain (DNP) occurs chronically; its pain increases at night, and the pathogenesis is poorly understood. In DNP, the sensory loss manifests in foot, skin ulcer, gastrointestinal, and genitourinary.⁹

The therapy against DNP uses anticonvulsants, antidepressants, opioids, and sometimes analgesics. In Indonesia, the analgesic used as the treatment against DNP is paracetamol. However, paracetamol cannot always relieve the pain caused by DN.¹⁰ In addition, several public health centres modify the therapy using a combination of paracetamol and acupressure to increase the success of therapy. A previous review study described that acupressure is a complementary treatment that can be used for a patient with chronic pain.¹¹ Moreover, Smith *et al.*¹² described that acupressure combined with a standard pain treatment with usual care effectively reduces pain intensity. Unfortunately, the efficacy of acupressure as a therapy and the risk factor of therapeutic success in DNP is not well understood.

This study aimed to elucidate the efficacy of paracetamol vs paracetamol combined with acupressure for pain relief in diabetic neuropathy patients and its risk factors using a cross-sectional study.

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MATERIALS AND METHODS

Ethic approval

The ethic approval is not applicable for this study because all the therapy were conducted by medical specialist from Ngoro Public Health Centre, Mojokerto, Indonesia. The authors only collected the data from interview during anamnesis.

Study period, location and study design

This study was performed from September 2022 until September 2023 in Ngoro Public Health Centre, Mojokerto, Indonesia. The location of the study was between latitude -7.551559359132314 and longitude 112.6178308288363. The cross-sectional approach study design was used in this study. This study was an analytical comparative that compared two types of therapy, including paracetamol oral with paracetamol plus acupressure. The data on risk factors were individually collected by face-to-face interview.

Participants

The participants of this study were all diabetic type II patients undergoing therapy in Ngoro Public Health Centre during the study period. The number of patients with type II DM was 70 peoples. This study focused on the patients with pain clinical signs, so the patients without DNP were excluded. Several inclusion criteria in this study are only patients willing to undergo an interview, are conscious, willing to sign informed consent, undergoing therapy for DNP, able to communicate using Bahasa Indonesia, and do not have mental disorders

Visual analogue scale (VAS)

VAS was used to assess the pain in a patient, including no pain at all until the worst. The standardization of VAS was explained to the patients before the assessment. VAS is a self-report measurement. The participants were asked to report the pain intensity before treatment and 72 hours after treatment. The score was designed using a scaling system from 0 to 5. The absence of pain was scored 0, and the worst scored 5.¹³

Analysis data

The data was analysed using SPSS version 26 (IBM Corp, USA). The association between age, sex, work, educational background, period in suffering type II DM, type of treatment, obedience, and VAS was tested using Pearson's correlation. The statistical analysis used $p < 0.05$ as statistically significant.

RESULTS

Out of the 70 patients diagnosed with type II DM, 40 of them had DNP. From all criteria, 40 (57.15%) patients were used in this study (Figure 1).

Shockingly, most of the patients with type II DM and DNP were females, counting for 33 out of 40 cases (82.50%). The most common age group suffering from DNP was between 25 to 64 years old, representing 62.50% of the total cases. Among the patients with DNP, 70% of them worked for a living, while the remaining did not. It is concerning to note that the highest educational background of the patients was senior high school, followed by elementary, bachelor, and junior high school, respectively. They usually had been suffering from type II DM for over five years, and an alarming 36 out of 40 patients had DNP. However, it is even more concerning to observe that only 17 patients were treated with a single treatment using paracetamol. In contrast, the rest were treated with paracetamol combined with acupressure. Nonetheless, it is reassuring to note that all the patients had high compliance with the treatment procedure they followed (Table 1 and Table 2).

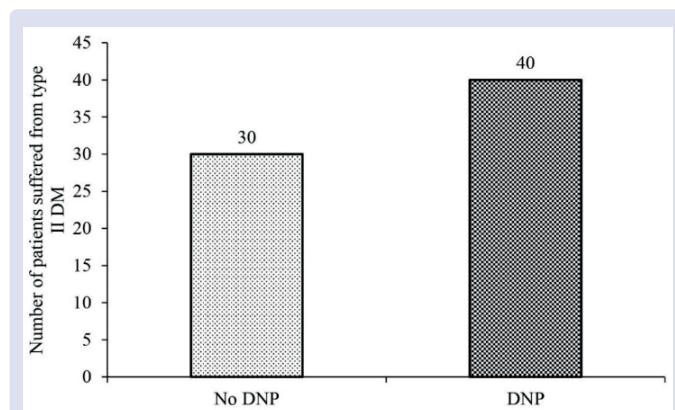


Figure 1. The number of patients used in this study.

Table 1. Demographic data of the type II DM patient with DNP.

Variables	Categories	Frequency (n)	Percentage (%)
Sex	Female	33	82.50
	Male	7	17.50
Age	0 – 15 years	-	-
	16 – 24 years	-	-
	25 – 64 years	25	62.50
	≥65 years	15	37.50
Work	Yes	12	30.00
	No	28	70.00
Educational background	Elementary school	5	12.50
	Junior high school	3	7.50
	Senior high school	26	65.00
Period in suffering type II DM	Bachelor	6	15.00
	≤5 years	4	10.00
Obedience in drug consumption	>5 years	36	90.00
	Yes	40	100.00
Type of treatment	No	-	-
	Paracetamol	16	40.00
	Paracetamol + acupressure	24	60.00

Table 2. The collected data during an interview.

Variables	Categories
Sex	Male, female
Age	0 – 15 years, 16 – 24 years, 25 – 64 years, ≥65 years
Work	Yes, no
Educational background	Elementary school, junior high school, senior high school, bachelor
Period in suffering type II DM	Less than or equal to 5 years (≤5 years), more than 5 years (>5 years)
Type of treatment	Single (paracetamol), combination (paracetamol + acupressure)
Obedience in drug consumption	Yes, no

The structured questionnaire was used as a medium during face-to-face interviews. Several collected data were embedded in Table 2. After the interview, the visual analogue scale (VAS) score was assessed.

The study found a significant correlation between the type of therapy and the decrease in VAS scores for diabetic patients with neuropathic pain ($p \leq 0.05$). Patients treated with paracetamol and acupressure showed more improvement in the VAS score than those treated with only paracetamol. The study suggests that the combination treatment could benefit as an analgesic for DNP in type II DM patients (Table 3).

Table 3. Correlation between types of treatment with VAS score in type II DM patient with DNP.

Variables	Indicator	VAS score		X ²	p-value
		Stable	Decline		
Type of treatment	Paracetamol	11	5	9.18	0.02*
	Paracetamol + acupressure	5	19		

*p<0.05 indicates significant differences.

Table 4. Correlation between variables of DNP with VAS score in type II DM patient with DNP.

Variables	Indicator	VAS score		X ²	p-value
		Stable	Decline		
Sex	Female	15	18	2.33	0.12
	Male	1	6		
Age	0 – 15 years	0	0	0.44	0.50
	16 – 24 years	0	0		
	25 – 64 years	9	16		
	≥65 years	7	8		
Work	Yes	5	7	0.20	0.88
	No	11	17		
Educational background	Elementary school	4	1	8.24	0.04*
	Junior high school	2	1		
	Senior high school	10	16		
	Bachelor	0	6		
Period in suffering type II DM	≤5 years	2	2	0.18	0.66
	>5 years	14	22		

*p<0.05 indicates significant differences.

Further, there is no correlation between sex, age, work, and period in suffering type II DM against the decrease of VAS score ($p \geq 0.05$). However, there is a significant correlation between educational background and the VAS score ($p \leq 0.05$) (Table 4). It showed that educational background influenced the decreased pain in the diabetic type II patient. The correlation may be caused by several factors not observed in this study.

DISCUSSION

As a chronic metabolic disease, DM seriously impacts the patients. One of the significant impacts of this disease is DNP. DM causes DNP due to the damage of peripheral and autonomic nerves that occur in the patients. The DNP can present several injury patterns, such as distal symmetric polyneuropathy, radiculoplexopathy, mononeuropathy, and small fibre predominant neuropathy. DNP is a unique neurodegenerative disorder that targets the axon of the nerve. The progressive mechanism of DNP involves dying back and reflecting damage.¹⁴ Further, it causes severe and continuous pain within the area that suffers tissue damage.¹⁵

According to the study, DNP occurred more frequently in females than males, as well as in unemployed adults. This finding is consistent with a previous study that reported females at a higher risk than males.¹⁶ Additionally, unemployed individuals with less physical activity showed a higher prevalence of DM with DNP than employees. The same previous study reported a significant correlation between demographic parameters such as employment status, educational background, age, and the occurrence of DM and its comorbidities.¹⁷ Higher educational status may be associated with greater awareness of a healthy lifestyle, including sanitation, health management after sickness, and compliance with drug consumption. Interestingly, the duration of DM does not appear to correlate with the occurrence of DNP, as this study found DNP to occur in individuals who had suffered

from DM for less than five years and those who had suffered for more than five years.

The pain during DN can be treated using various therapies such as anticonvulsants, opioids, and analgesics. The analgesic can be applied either topically or systemic. The systemic application of the analgesic can use paracetamol.¹⁸ Paracetamol, also known as acetaminophen, is the first active metabolite identified. Since it is prevalent, either as an analgesic or antipyretic. Paracetamol has been recognised as a drug with minimum adverse effects, although it has been reported to promote hepatotoxicity. This drug can be used to treat chronic pain, including DNP.¹⁹ The previous study by Hovaguimian and Gibbons²⁰ reported that paracetamol combined with tramadol shows high inhibitory effects against pain receptors via its demethylated mechanism through cytochrome P-450 2D6. It is correlated to this study that showed a decrease in VAS score in DNP after using paracetamol. However, the number of patients with decreased VAS scores is minimal (Table 2). Furthermore, using paracetamol over a long period may pose a risk of chronic use.²¹ So, finding an alternative therapy that decreases the potential chronic use of paracetamol is required.

Acupressure is an alternative treatment for various diseases, including pain management. It is a traditional Chinese medicine that involves applying hand pressure on the acupuncture points in the body.²² This pressure stimulates specific neurons that promote the synthesis of endorphins, which have pain-relieving effects, reduce muscle tension and cortisol, and increase oxygen concentration in the treated area.²³ A study has shown that acupressure may increase the analgesic effects of paracetamol in DNP patients. The treated group using paracetamol + acupressure showed a decrease in VAS score. The demethylation mechanism may cause this synergistic effect during forming the active metabolite of paracetamol, supported by the activation of the sympathetic nervous system.²⁴ The activation initiates nociception, which increases the synthesis of serotonin, endorphin, enkephalin, and norepinephrine.²⁵ Additionally, acupressure promotes increased circulatory oxygen within the treated area, decreasing oxidative stress in the pain mechanism.²⁶⁻²⁷ The study found no correlation between sex, age, work, and period of suffering DM against VAS score, indicating that DNP occurs spontaneously during DM without being controlled by those variables. However, educational background correlates to the decrease in VAS score, which may be caused by sanitation and healthy life management after being sick during DNP.

CONCLUSION

The study suggests that the combination treatment could benefit DNP as an analgesic for type II DM patients. Further, the decrease of VAS score is not correlate to the sex, age, work, and period of suffering DM. Advanced study is required to be performed using larger samples so that accurate data can be obtained.

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