

Characteristics of neuropathic pain in patients with diabetes mellitus

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Abstract

Aim: Epidemiological data on the frequency, quantity, and consequences of symptomatic diabetic neuropathy remain poor. We conducted this study to examine the characteristic of neuropathic pain in patients with diabetes mellitus (DM).

Materials and Methods: Average daily pain intensity was measured using a 100 mm visual analog scale (VAS). Localization of the pain, position that aggravated pain, frequency of the pain, duration of the pain, pain's influence on daily living activities were examined.

Results: The average patient age was 62.56 years and the number of males was 21 (42%). 29 Patients had only DM and 13 patients had hypertension (HT) plus DM, 4 patients had DM+HT+heart disease. The mean of pain according to VAS was 6.86±2.79. Thirty-two patients defined that the pain affected their daily living activities negatively; 30 patients' pain localization was lower extremity, 12 patients' was upper and lower extremity; mostly pain was aggravated by standing and 40 patients' pain frequency was as every day; 24 patients' pain duration was less than 1 year and 18 patients' was between 1-5 years.

Conclusion: Studies on diabetic neuropathy are important drivers to improve the treatment of these patients. Neuropathic pain is considered to be more serious than other types of pain. So patients diagnosed with DM should be examined for neuropathic pain and the treatment plan should include pain decreasing medication and/or neurosurgical interventions.

Keywords: Diabetes mellitus; neuropathic pain, pain; spinal cord stimulation

INTRODUCTION

Diabetes mellitus (DM) is estimated to affect around 415 million adults worldwide (1). Neuropathic pain (NP) is defined as pain caused by a lesion or disease of the somatosensory system. The somatosensory system allows for the perception of touch, pressure, pain, temperature, position, movement, and vibration (2,3). Neuropathy is one of the most common long-term complications of DM (4). Diabetic neuropathic pain (DNP) is characterized by tingling, burning, sharp, shooting, and lancinating or even as electric shock sensations (5,6). Several theories have been proposed to explain the pain related to diabetic neuropathy, such as worsening glucose tolerance, older age, longer diabetes duration, drinking alcohol, and cigarette smoking (5,7). Anesthetic management is important in patients with diabetic neuropathy, as serious intraoperative and postoperative

complications can be observed. Safe anesthesia can be provided in patients with diabetic neuropathy by extensive preoperative evaluation, close monitoring of intraoperative and postoperative vital signs (8,9).

Although many prevalence studies on the frequency of neuropathic pain in patients with diabetes mellitus are available in the literature, very few studies have focused on the characteristics of pain, frequency, duration, localization, conditions that increase and decrease pain, and its effect on daily activities. Epidemiological data on the quantity, and consequences of symptomatic diabetic neuropathy remain poor due to inconsistent definitions, poor ascertainment, and a lack of population-based studies (8,10). In this study, we aimed to emphasize the characteristics of diabetic neuropathic pain, which have not been emphasized before in the literature.

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MATERIALS and METHODS

This study conducted at Hatay Mustafa Kemal University School of Physical Therapy and Rehabilitation. The diagnoses were made based on patients' history and signs and the results of neurological examinations by a neurologist. Demographic characteristics (age, gender, marital status) and medical histories of the patients were recorded. The number of female patients included in the study was 29 (58%), and the number of male patients was 21 (42%). Patients aged over 18, and that have neuropathic pain plus DM were included. Those with a disease other than diabetes (traumatic injuries, infections, metabolic problems, inherited causes, and toxic exposure, etc.) that could cause peripheral neuropathy were excluded from the study. Patients who had an adequate level of understanding of the questions were enrolled and written informed consents were obtained. This study was approved by the Clinical Study Ethics Committee of Mustafa Kemal University Tayfur Ata Sokmen Medical Faculty (Approval no: 07/32).

Evaluations: Average daily pain intensity was measured using a 100 mm visual analog scale (VAS) (11). Localization of the pain, position that aggravated pain, frequency of the pain, duration of the pain, pain's influence on daily living activities were examined.

For the statistical analysis, SPSS for Windows Release SPSS 22 was used. The results are presented as mean±standard deviation and percent.

RESULTS

Fifty two patients who accepted participating in the study were included. Fifty patients had diabetes mellitus and two patients had stroke additional DM. Stroke is a condition that can cause central neuropathic pain, therefore these 2 patients were excluded from the study (Figure 1).

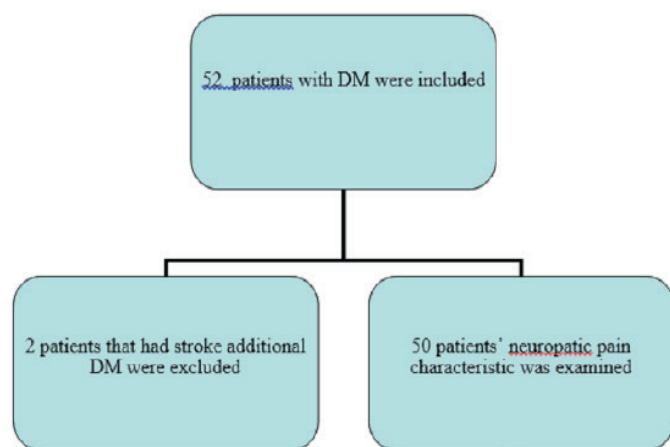


Figure 1. Study design

The demographic and clinical characteristics of the patients are listed in Table 1. The average patient age was 62.56 years. The youngest patient participating in

the study was 23 years old and the oldest patient was 80 years old. The number of males was 21 (42%). 29 Patients had only DM and 13 patients had hypertension (HT) plus DM, 4 patients had DM+HT+heart disease.

Table 1. The demographic characteristic of the patients

		X±SD	
		62.56±11.26 (23-80)	
		n	%
Marital Status	Married	44	88
	Single	6	12
Gender	Male	21	42
	Female	29	58
History	DM	29	58
	DM+HT	13	26
	DM+HT+Heart Disease	4	8
	DM+CVA	1	2
	DM+Asthma	1	2
	DM+HT+Asthma	2	4

DM: Diabetes mellitus, HT: Hypertension, CVA: Cerebrovascular Accident

The mean of pain according to VAS was 6.86±2.79. Thirty-two patients defined that the pain affected their daily living activities negatively; 30 patients' pain localization was lower extremity, 12 patients' was upper and lower extremity; mostly pain was aggravated by standing and 40 patients' pain frequency was as every day; 24 patients' pain duration was less than 1 year and 18 patients' was between 1-5 years (Table 2).

Table 2. Features of the pain

		X±SD	
		6.86±2.79	
		n	%
Localization of the Pain	Lower Extremity	30	60
	Upper Extremity	4	8
	Trunk	1	2
	Upper and Lower Extremity	12	24
	Upper Extremity and Trunk	2	4
	Neck	1	2
Position Aggravated the Pain	Standing	10	20
	Sitting	4	8
	Supine	7	14
	Walking	6	12
	Standing and Sitting	1	2
	Standing and Walking	4	8
	Sitting and Supine	5	10
	No Position	13	26

Frequency of the Pain	Everyday	40	80
	More than 3 times in a week	3	6
	2-3 times in a week	3	6
	1 time in a week	2	4
	3-4 times in a month	1	2
	1 time in a month	1	2
Duration of the Pain	1-12 month	24	48
	1-5 years	18	36
	6-10 years	2	4
	11-20 years	4	8
	>21 years	2	4
Influence of the Pain on Daily Living Activities	Yes	32	64
	No	18	36

DISCUSSION

We conducted this study to investigate the characteristics of DNP and to take attention to pain treatment in patients with DM and found that pain intensity was high, pain affects daily living activities and patients have pain every day. So pain is an important problem in DM and clinicians should consider NP in DM treatment.

Patients with diabetes-induced peripheral neuropathy over the age of 18 were included in the study. Those with a disease other than diabetes (traumatic injuries, infections, metabolic problems, inherited causes, and toxic exposure etc.) that could cause peripheral neuropathy were excluded from the study. Those with a disease that could cause central neuropathy such as vascular (ischemic or hemorrhagic), infectious (abscess, encephalitis, myelitis), demyelinating, traumatic (brain or spinal cord), or neoplastic disorders in the central nervous system were also excluded.

There have been many studies on the prevalence of neuropathic pain in DM since neuropathic pain is common. We examined the intensity of the NP additional, position aggravated the pain, pain frequency, the influence of the pain on daily living activities.

Age, body mass index, hypertension, smoking, and waist circumference influence the development of DNP (11-13). In our study, we found that 19 patients have HT. These patients have a risk factor for DNP.

High blood sugar (glucose) can injure nerves throughout the body. Diabetic neuropathy most often damages nerves in legs and feet as it is found that DNP causes pain mostly in lower extremities (9,13). We found that the pain localized mostly in lower extremity and pain is aggravated mostly while standing. So standing position is the most painful position. When we think patients are working mostly while standing, pain's effect on daily living activities is inevitable and we figure out NP affects patients' daily living activities negatively.

Bouhassira et al. found that the prevalence of chronic pain with neuropathic characteristics was 20.3%, and only

38.6% of the patients had received appropriate treatment for neuropathic pain (14,15). Most of our patients have pain every day in high intensity. So pain decreasing medication always should be considered for patients with NP.

Abbot et al. found a significantly greater proportion of females (38%) than males (31%) reported painful neuropathy symptoms. After adjustments for age, DM's duration and, differences in clinical neuropathy, women still had a 50% increased risk of painful symptoms compared with men (10). In our study, a neurologist diagnosed patients that have NP additional DM and found that 29 female patients and 21 male patients admitted to the clinic in 6 months.

Aguiar et al. included 129 patients in their study and found that 67 (51.9%) of them reported pain. 34.1% of these were detected with the pain of NP characteristics, with a predominance of pain in lower limbs and moderate intensity. The most reported symptoms were: tingling, pinching/needling, and numbness (16). Most of our patients had pain every day and the intensity of the pain was moderate ($x=6.86$). Patients that have DM, have multiple symptoms and problems depending on DM, additional problems such as NP cause the patients to feel more helpless.

Studies on DNP are important drivers to improve the treatment of these patients. Due to the restriction of daily living activities, diagnosing and treating diabetic neuropathy is an important subject. Novel treatment options are classified as a medical and medical plus neurosurgical intervention. DNP's medical treatment options include regulation of blood glucose levels, non-steroidal anti-inflammatory drugs, anticonvulsants, antidepressants, opiates, Vit.B12 replacement therapy, etc. (17,18).

Neurosurgical interventions such as peripheral nerve stimulation and spinal cord stimulation alone or in addition to medical treatment are among the treatment options when the response to medical treatment is insufficient (19).

Spinal cord stimulation is a DNP effective and safe method for the treatment of chronic pain caused by diabetic neuropathy,

Serious cardiovascular complications such as bradycardia, hypotension, cardiopulmonary arrest after anesthesia induction are seen in diabetic patients with neuropathy (20).

LIMITATIONS

As the limitations of the study, the duration could be kept longer and more patients could be included in the study. Scoring systems other than VAS could also be used to assess and compare pain intensity. The effect of blood glucose control on diabetic peripheral neuropathy and its characteristics could be evaluated.

CONCLUSION

NP is considered to be more serious than other types of pain. So patients diagnosed with DM should be examined for NP and the treatment plan should include pain decreasing medication and/or neurosurgical interventions.

Conflict of interest : The authors declare that they have no competing interest.

Financial Disclosure: There are no financial supports.

Ethical approval: This study was approved by the Clinical Study Ethics Committee of Mustafa Kemal University Tayfur Ata Sokmen Medical Faculty (Approval no: 07/32).

REFERENCES

1. International Diabetes Federation IDF Diabetes Atlas, 7th ed Brussels: International Diabetes Federation, 2015 Available at: <http://www.diabetesatlas.org> Accessed 24/06/2019.
2. Colloca L, Ludman T, Bouhassira D, et al. Neuropathic pain. *Nat Rev Dis Primers* 2017;3:2.
3. Feldman EL, Callaghan BC, Pop-Busui R, et al. Diabetic neuropathy. *Nat Rev Dis Primers* 2019;5:19-92.
4. Boulton AJ, Vileikyte L, Ragnarson-Tennvall G, et al. The global burden of diabetic foot disease. *Lancet* 2005;366:1719-24.
5. Tesfaye S, Boulton AJ, Dickenson AH. Mechanisms and management of diabetic painful distal symmetrical polyneuropathy. *Diabetes Care* 2013;36:2456-65.
6. Gylfadottir SS, Weerachoenkul D, Andersen ST, et al. Painful and non-painful diabetic polyneuropathy: Clinical characteristics and diagnostic issues. *J Diabetes Investig* 2019;10:1148-57.
7. Gore M, Brandenburg NA, Dukes E, et al. Pain severity in diabetic peripheral neuropathy is associated with patient functioning, symptom levels of anxiety and depression, and sleep. *J Pain Symptom Manage* 2005;30:374-85.
8. Lankhorst S, Keet SW, Bulte CS, et al. The impact of autonomic dysfunction on peri-operative cardiovascular complications. *Anaesthesia* 2015;70:336-43.
9. Assunção A, Campos D, Marques R, et al. The impact of demographic and clinical characteristics on diabetic painful neuropathy. *Rom J Intern Med* 2020;58:13-9.
10. Abbott CA, Malik RA, van Ross ER, et al. Prevalence and characteristics of painful diabetic neuropathy in a large community-based diabetic population in the U.K. *Diabetes Care* 2011;34:2220-4.
11. Gould D, Kelly D, Goldstone L, et al. Examining the validity of pressure ulcer risk assessment scales: developing and using illustrated patient simulations to collect the data. *J Clin Nurs* 2001;10:697-706.
12. Meisinger C, Döring A, Thorand B, et al. Body fat distribution and risk of type 2 diabetes in the general population: are there differences between men and women? The MONICA/KORA Augsburg cohort study. *Am J Clin Nutr* 2006;84:483-9.
13. <https://www.mayoclinic.org/diseases-conditions/diabetic-neuropathy/symptoms-causes/syc-20371580> Accessed date: 24.06.2019. Miralles-García JM, de Pablos-Velasco P, Cabrerizo L, Pérez M, López-Gómez V. Prevalence of distal diabetic polyneuropathy using quantitative sensory methods in a population with diabetes of more than 10 years' disease duration. *Endocrinol Nutr* 2010;57:414-20.
14. Bouhassira D, Letanoux M, Hartemann A. Chronic pain with neuropathic characteristics in diabetic patients: a French cross-sectional study. *PLOS ONE* 2013;8.
15. Khdour MR. Treatment of diabetic peripheral neuropathy: a review. *J Pharm Pharmacol* 2020;72:863-72.
16. Aguiar FLXds, Ramos LFP, Bichara CNC. Detection of pain with neuropathic characteristics in patients with diabetes mellitus assisted in primary care units. *BrJP* 2018;1:15-20.
17. Bril V, England J, Franklin GM, et al. Evidence-based guideline: Treatment of painful diabetic neuropathy: report of the American Academy of Neurology, the American Association of Neuromuscular and Electrodiagnostic Medicine, and the American Academy of Physical Medicine and Rehabilitation. *Neurology* 2011;76:1758-65.
18. DUBY JJ, Campbell RK, Setter SM, et al. Diabetic neuropathy: an intensive review. *Am J Health Syst Pharm* 2004;61:160-73.
19. de Vos CC, Rajan V, Steenbergen W, et al. Effect and safety of spinal cord stimulation for treatment of chronic pain caused by diabetic neuropathy. *J Diabetes Complications* 2009;23:40-5.
20. Jermendy G. Clinical consequences of cardiovascular autonomic neuropathy in diabetic patients. *Acta Diabetol* 2003;40:3-122.