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Original Article

The relationship between therapeutic modalities and itch intensity in patients with diabetes mellitus

Desy Sahara Putri Simanjuntak[1], Ariyati Yosi[1]*, Dina Arwina Dalimunthe[1]

[1] Department of Dermatology and Venereology, Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia

* Correspondence to: Ariyati Yosi, Department of Dermatology and Venereology, Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia. E-mail: ariyati.yosi@usu.ac.id

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Abstract

Diabetes mellitus (DM) is a metabolic disorder characterized by chronic hyperglycaemia that can lead to various complications, including pruritus. The severity of pruritus in DM patients may vary and is influenced by factors such as blood glucose control, diabetic neuropathy, and skin conditions. Both pharmacological and non-pharmacological approaches are utilized to manage DM and its associated skin conditions. This study aims to analyze the relationship between treatment modalities and pruritus intensity in DM patients. This study employed an observational design with a cross-sectional approach. All eligible study participants were DM patients aged 18–60 years experiencing pruritus. The severity of pruritus was assessed using the Numerical Rating Scale (NRS). Statistical analysis was performed using the Chi-square test, with significance set at $p<0.05$. Among 76 participants, 46.1% received oral antidiabetic medications, 44.7% received injectable antidiabetic medications, and 9.2% received a combination of both. The majority of patients reported moderate pruritus intensity. Statistical analysis revealed no significant association between treatment modalities and pruritus intensity ($p=0.157$). There was no significant relationship found between treatment modalities and pruritus intensity in DM patients.

Keywords: diabetes mellitus, treatment modalities, pruritus intensity

Introduction

Diabetes Mellitus (DM) is a metabolic disease characterized by chronic hyperglycemia due to impaired insulin production or action. One of the complications often experienced by DM patients is skin disorders, including pruritus or itching. The intensity of itching in DM patients can vary, influenced by various factors such as uncontrolled blood sugar levels, diabetic neuropathy, and changes in skin conditions due to dehydration or infection [1–3].

The severity of pruritus, as well as the intensity of itching, can be evaluated using a simple tool called the Numerical Rating Scale (NRS), which ranges from 0 to 10. which is done by asking the patient to choose the number that corresponds to the intensity of pruritus they experience to assess the severity of pruritus and how much it interferes with their daily life. Pruritus is a common manifestation of DM and affects sleep patterns and circadian rhythms in DM patients, as patients experience itching more frequently during sleep [4–8]. Various therapeutic modalities have been used in the management of DM, ranging from pharmacological therapies such as insulin and oral antidiabetic drugs to non-pharmacological therapies such as lifestyle changes and dietary management. However, there are still differences in the effectiveness of various therapeutic modalities in reducing pruritus symptoms in patients with DM [9, 10]. Therefore, it is important to understand the relationship between the therapeutic modalities applied and the intensity of itching experienced by patients.

This study aims to analyze the relationship between therapeutic modalities and itch intensity in patients with DM. The results of this study are expected to provide deeper insight into therapeutic strategies

that are more effective in reducing pruritus complaints in patients with DM and improving their quality of life.

Material and methods

Study design and patients

This study is an observational study with a cross-sectional design to assess the relationship between therapeutic modalities and itching intensity in patients with DM. This study was conducted from May 2024 to July 2024 at the outpatient unit of the Department of Internal Medicine of Prof. Dr. Chairuddin Panusunan Lubis Hospital, University of North Sumatra. The inclusion criteria of this study were DM patients aged ≥18–60 years, DM patients with dermatological manifestations in the form of pruritus or itching symptoms. All patients who are willing to participate in the study have signed an informed consent form. Exclusion criteria in this study were pregnant, suffering from primary skin disorders such as psoriasis, atopic dermatitis, or skin infections, and patients with comorbidities, such as liver and kidney function abnormalities, and malignancies.

Laboratory, anthropometric and clinical data collection

Therapeutic modalities were categorized based on the type of therapy the patient received. Itch intensity is measured using a simple tool called the Numerical Rating Scale (NRS), which ranges from 0 to 10. The assessment is conducted by asking the patient to choose the number that corresponds to the intensity of pruritus they experience, thereby evaluating the severity of pruritus and its impact on daily life.

Statistical analysis

Data were collected and statistically analyzed using the Statistical Product and Service Solutions computer program (SPSS v. 26.0; SPSS Inc., Chicago, IL, USA). Data processing was carried out by univariate analysis to analyze the characteristics of one variable by conducting descriptive tests, followed by bivariate analysis to analyze the relationship between variables, in this case to determine the relationship between therapeutic modalities and itching intensity in DM patients using the Chi-square test and said to be statistically significant if the p-value<0.05.

This study was conducted after obtaining an ethical permit from the Research Ethics Committee of the University of North Sumatra (Number 595/KEPK/USU/2024) and the Research Permit of the University of North Sumatra Prof. Dr. Chairuddin Panusunan Lubis Hospital (Number 2491/UN5.5.6.D2/PPM/2024). All procedures were conducted in accordance with the Declaration of Helsinki, as revised in 2013.

Results

The type of treatment most widely used in patients in this study was oral antidiabetics, with 35 people (46.1%), and the least common combination treatment was used by 7 people (9.2%). The characteristics of the study subjects, categorized by treatment type, are presented in Table 1.

In Table 2, it can be seen that DM patients who experience itching with injection and oral antidiabetic treatment types have moderate itching intensity, specifically 71.4% of each group. Based on the chi-square test, the p-value of 0.157 (p>0.05) indicates that there is no significant relationship between therapeutic modalities and itching intensity in DM patients.

Discussion

The results of our study showed that the majority of DM patients were treated with injectable antidiabetics. The results of this study are in line with the research of Merdin *et al.*, who found that pruritus was experienced

Table 1: Characteristics of study subjects based on treatment type.

Type of treatment	n	%
Injectable antidiabetics	34	44.7
Oral antidiabetics	35	46.1
Combination of injectable and oral antidiabetics	7	9.2
Total	76	100

Table 2: Relationship between therapy modalities and itch intensity.

Type of treatment	NRS								P-value
	Mild		Moderate		Severe		Very severe		
	n	%	n	%	n	%	n	%	
Injectable antidiabetics	12	35.3	21	61.8	0	0	1	2.9	0.157
Oral antidiabetics	16	45.7	18	51.4	1	2.9	0	0	
Combination of injectable and oral antidiabetics	2	28.6	5	71.4	0	0	0	0	
Total	30	39.5	44	57.9	1	1.3	1	1.3	

Note: * – significant if P-value<0.05 by Chi-Square test.

by DM patients with oral antidiabetic treatment by as many as 215 people (86.3%) [11].

The majority of DM patients in our study had a moderate degree of itching intensity. Research by Boonsiri *et al.* also found that the majority of patients with type 2 DM experienced moderate pruritus (49%) [12]. Similar findings were obtained in the study of Stefaniak *et al.*, with the majority of patients experiencing moderate pruritus (54.26%) [13]. The pathogenesis of pruritus in DM is not fully understood, and various factors are described as contributing to the development of this symptom. There are two main factors associated with itching in DM: skin xerosis and diabetic neuropathy, which is associated with sweat gland dysfunction caused by sympathetic nervous system disorders. Prolonged hyperglycemia leads to changes in insulin levels, which can result in an altered hydration state of the stratum corneum and reduced sebaceous gland activity [14].

Our study did not find a statistically significant association between treatment modality and itch intensity in DM patients, with a p-value of 0.157. Patients on combined injectable and oral antidiabetic therapy tended to report moderate itching intensity compared to patients taking only oral or injectable antidiabetic drugs. Pruritus can occur with sulfonylurea, metformin, dipeptidyl peptidase 4 (DPP-4) inhibitor, and insulin treatments used in DM patients. In addition, other drugs that most often cause pruritus include heparin, calcium channel blockers, beta blockers, angiotensin-converting enzyme inhibitors, statins, and cotrimoxazole antibiotics [15]. Diabetes mellitus is a systemic disease that affects multiple organs, including the dermatologic system. The relationship between DM and dermatological problems stems from the disease itself, its complications, and treatment [16, 17]. Skin barrier disruption underlies dry skin, so that impaired skin barrier function and integrity in DM patients will eventually trigger pruritus.18,19 Several studies have shown that patients undergoing combination therapy tend to experience improvement in itching symptoms compared to those taking only oral antidiabetic drugs, possibly due to more stable glycemic control. However, in some cases, the intensity of itching remains high despite blood sugar control, indicating that other factors, such as neuropathy or inflammatory responses, play a role in pruritus [18, 19].

Research specifically examining the relationship between therapeutic modalities and itch intensity in patients with DM is limited. However, some studies have addressed related aspects that may provide insight into this topic. A study by Ko *et al.* reported a DM patient who experienced symptoms of itching all over the body, accompanied by uncontrolled hyperglycemia. Although this study did not explicitly examine the relationship between therapeutic modalities and itch intensity, these findings suggest that poor glycemic control may contribute to the appearance of pruritus in DM patients [20]. The state of hyperglycemia in DM patients is a precursor to the formation of advanced glycation end products (AGEs) [21]. The accumulation of AGEs will cause skin tissue damage through the regulation of gene expression, damage to structural proteins, and activate various molecular pathways (such as the NF-κβ pathway). The presence of AGEs decreases lipid production, reduces the amount of ceramide, cholesterol, and filaggrin structural proteins in the epidermis, and disrupts skin barrier integrity, resulting in dry skin and pruritus [22]. The study by Novena *et al.* also discussed various therapeutic modalities for pruritus, including topical and systemic therapies. The management of pruritus depends on the underlying etiology, and the success of therapy is also influenced by the patient's compliance with treatment [23]. However, our

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study did not find a statistically significant relationship between therapeutic modalities and itch intensity in DM patients. Further research, including multicenter studies and larger sample sizes, is needed to identify the relationship between therapeutic modalities and itch intensity in patients with DM on a broader scale.

Conclusion

There was no significant association between therapeutic modalities and itch intensity in patients with DM. Further research, including multicenter studies and larger sample sizes, is needed to confirm the relationship between therapeutic modalities and itch intensity in patients with DM on a broader scale. Combination therapy modalities may be beneficial for blood sugar control to reduce the intensity of itching in patients with DM.

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Conflict of interest

The authors declare no conflict of interest.

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