Efficacy of Sulbutiamine-a Fat Soluble Thiamine in the Management of Diabetic Symmetrical Peripheral Neuropathy

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Abstract

Objective: To evaluate the efficacy of sulbutiamine, a fat-soluble derivative of vitamin B1, in reducing pain intensity among diabetic patients with painful symmetrical peripheral neuropathy (DSPN).

Material And Methods: Our quasi-experimental study involved 320 diabetic patients with painful symmetrical peripheral neuropathy, selected through non-probability purposive sampling from the Institute of Endocrinology and Metabolism, Services Hospital Lahore, between March 1, 2023, and August 31, 2023. Participants were administered Sulbutiamine, a fat-soluble derivative of vitamin B1-thiamine, at a dosage of 200mg twice daily over six weeks. Follow-up assessments were conducted at 3 and 6 weeks, with efficacy evaluated based on a minimum two-point improvement in pain intensity using the Numeric Pain Rating Scale.

Results: Demographic analysis revealed an average patient age of 59.49 years, a BMI of 30.10 kg/m^2, and a slight male predominance (55.9%). The final efficacy of fat-soluble thiamine at the 6th week was 68.4%. Stratified analysis highlighted significant variations in efficacy at 3rd and 6th weeks, emphasizing the influence of variables such as age, comorbidities, and diabetes duration. Age, comorbidities, and diabetes duration exhibited strong statistical significance ($p < 0.05$), indicating their impact on treatment outcomes, while other variables demonstrated variable significance at different assessment points.

Conclusion: In conclusion, the administration of sulbutiamine, a fat-soluble form of vitamin B1, led to a noteworthy reduction in pain among diabetic individuals suffering from painful symmetrical peripheral neuropathy. This study underscores the potential of sulbutiamine as an effective intervention for managing DSPN, with implications for improving the well-being of diabetic patients.

Keywords: Diabetic Symmetrical Peripheral Neuropathy, Efficacy, Fat-soluble vitamin B-1

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Introduction

Diabetes mellitus represents a metabolic disorder characterized by dysregulated metabolic processes and elevated glucose levels stemming from inadequate insulin secretion and resistance to its action at target organs.[1] This disease manifests with both microvascular and macrovascular complications.[2] Among these complications, symmetrical peripheral neuropathy, particularly the painful variant, stands out as a deleterious microvascular consequence.[3] Diabetic neuropathy is a prevalent complication occurring in both types of Diabetes mellitus. Distal symmetric polyneuropathy is observed in one out of every four diabetic patients, with its prevalence escalating in tandem with disease progression; approximately 50% of individuals with diabetes for 25 years are predisposed to develop neuropathy.[4,5] The management of neuropathy entails the use of diverse pharmacological agents such as opioid-like analgesics, anticonvulsants, tricyclic antidepressants,

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and selective serotonin reuptake inhibitors. A myriad of drugs, including methylcobalamin, alpha-lipoic acid, vitamin B6, folate, L-arginine, biotin, among others, may be employed individually or in various combinations to alleviate altered or painful sensations and dysesthesia.[6,7] Several vitamins, including thiamine, play crucial roles in neuropathy management. Thiamine is integral to the transketolation process in the pentose phosphate shunting pathway and is involved in the initiation of nerve impulse propagation.[8,9]

Fat-soluble vitamin B1/thiamine, distinguished by its higher bioavailability compared to water-soluble thiamine, is deemed more efficacious for therapeutic purposes. Its utility lies in decelerating the progression of diabetic complications by augmenting intracellular levels of thiamine diphosphate, ultimately enhancing transketolase activity. This study aimed to ascertain the efficacy of fat-soluble form of vitamin B-1/ thiamine in the treatment of diabetic symmetrical peripheral neuropathy.

Material and Methods

The study adopted a quasi-experimental design, encompassing a sample of 320 diabetic patients selected through purposive non-probability sampling. Individuals with symmetrical painful peripheral neuropathy were specifically identified from the Institute of Endocrinology and Metabolism, Services Hospital Lahore. After the approval of IRB Committee Registration No.1026-A/22/SIMS dated 08-10-2022, the study spanned six months, commencing on March 1, 2023, and concluding on August 31, 2023. The sample size 320, determined with a confidence level of 95% and a margin of error of 5.5%, considered an anticipated efficacy of 47% for lipid-soluble variant of thiamine in managing diabetic peripheral painful neuropathy. The inclusion criteria comprised diabetics with symmetrical peripheral painful neuropathy complications within the age range of 18-60 years, encompassing both genders, exhibiting a baseline Numeric Pain Rating Scale (NRS) score of at least 3. Exclusion criteria involved factors such as blood macrocytosis, HbA1c value ≥ 9%, a history of vitamin B-1(thiamine) allergy, elevated renal function tests (creatinine level > 1.5mg/dl), and prior use of medications like analgesics, multivitamins, antidepressants, anti tuberculous therapy, and antiepileptics. Informed written consent was obtained, and eligible patients meeting the criteria were enrolled. The study procedure was thoroughly elucidated to all participants. Initial assessments involved the measurement of symptoms using the Numeric Pain Rating Scale, with a minimum score of 3 or higher. Patients were prescribed a fat-soluble vitamin B1/thiamine Sulbutiamine, in tablet form at a dosage of 200mg twice daily for a duration of 6 weeks. Follow-up visits were scheduled at 3 weeks and 6 weeks post the initial visit. Efficacy was gauged based on a criterion of at least a two-point improvement in pain from baseline on the Numeric Pain Rating Scale after six weeks. To mitigate bias, a singular researcher conducted assessments for all patients.

Table 1: *Demographic characteristics of population under study (n=320)*

Variables	Mean	Std. Deviation
Age (In completed years)	59.49	±11.27
Duration of Diabetes (years)	11.65	±7.95
BMI* (kg/m²)	30.14	±7.30
HbA1c (%) at baseline	6.84	±0.69
BSF** (mg/dl) at 3 weeks	123.9	±20.16
BSF (mg/dl) at 6 weeks	124.39	±20.51
Pain rating at baseline	6.38	±1.82
Pain rating at 3 weeks	5.81	±1.93
Pain rating at 6 weeks	4.61	±2.13
	Numbers	**Percentage %**
Gender		
Male	179	55.9 %
Female	141	44.1 %
Co morbidities		
Yes	110	34.0 %
No	210	65.6 %
Smoking		
Yes	56	17.5 %
No	264	82.5 %
Improvement at 3rd week		
No	251	78.4 %
Mild (2 points on PRS)	56	17.5 %
Moderate (≥ 2 points on PRS)	13	4.1%
Improvement at 6th week		
No	105	32.8 %
Mild (2 points on PRS***)	111	34.7 %
Moderate (≥ 2 points on l	104	32.5 %
Outcome		
Efficacy at 3rd week	69	21.5 %
Efficacy at 6th week	219	68.4 %

*Where; *BMI= Body mass index, **BSF=Blood sugar fasting, ***PRS=Pain rating scale*

Results

The results hold the promise of unravelling valuable insights into a novel therapeutic approach. This groundbreaking investigation seeks to illuminate the outcomes of administering fat-soluble thiamine, a potentially innovative intervention, in alleviating the symptoms of diabetic peripheral neuropathy. The results are poised to provide a comprehensive understanding of the impact of this treatment on pain management, and hence overall patient well-being. By delving into the quantitative outcomes and statistical analyses, the result section aims to contribute robust evidence that may shape future considerations for managing diabetic peripheral neuropathy, offering hope for improved quality of life for individuals affected by this prevalent and challenging complication of diabetes.

Table Ⅰ shows demographic characteristics of population under study, it explains several variables, listed along with their mean and standard deviation values. These variables include "Age, duration of diabetes, BMI, HbA1C, BSF at different time points gender distribution, improvement noted at 3rd and 6th week and lastly efficacy at 3rd and 6th week. The mean and standard deviation values for each of these variables are provided in the table. Based on the table, some relevant results that can be inferred include the average age of the patients being around 59.49 years, the average BMI being 30.10 kg/m^2. Male (55.9%) participants were slightly more than females, Final efficacy (at 6th week) reported is 68.4%. Table II presents the stratified analysis of the relationship between Efficacy and various variables. It can be inferred from bivariate analysis that Outcome of using Thiamine in patients with painful neuropathy are affected by various factors,

Table 2: *Stratification of Efficacy at 3rd & 6th week with different confounding variables. (n=320)*

Variable	Sub Groups	Efficacy at 6 weeks		P-Value	Efficacy at 6 weeks		P-Value
		Yes	No		Yes	No	
Age	18-40 Years	4(16.7%)	20(83.3%)		18(75.0%)	6(25.0%)	
	41-60 Years	34(23.8%)	109(76.2%)	0.03*	82(57.3%)	61(42.7%)	0.002**
	61-80 Years	31(19.2%)	112(80.8%)		119(77.5%)	34(22.5%)	
Obesity	Non-Obese (BMI (kg/m²): 18-29.9)	25(17%)	122(83.0%)	0.06	101(68.7%)	46(31.3%)	0.92
	Obese (BMI (kg/m²): ≥30)	44(25.4%)	129(74.6%)		118(68.2%)	55(31.8%)	
Gender	Male	34(19.0%)	14.5(19%)		120(67%)	59(33.0%)	
	Female	35(24.8%)	106(75.2%)	0.20	99(70.2%)	42(29.9%)	0.54
Smoking	Smoker	6(10.7%)	50(89.3%)		36(64.3%)	20(35.7%)	
	Non-Smoker	63(23.69%)	201(76.1%)	0.03*	183(69.3%)	81(30.7%)	0.46
Comorbidities	Co-morbidity present	12(10.9%)	98(89.1%)		66(60.0%)	44(40.0%)	0.01*
	No comorbidity	57(27.1%)	153(72.9%)	0.001**	153(72.9%)	57(27.1%)	
Duration of Diabetes (years)	1-15 year	61(27%)	165(73%)		159(70.4%)	67(29.6%)	
	16-30 year	8(9.0 %)	81(91%)	0.001**	60(67.4%)	29(32.6%)	0.004**
	≥30 year	0(0.0%)	5(100%)		0(0.0%)	5(100%)	
HbA1c (%)	<5.7	23(19.3%)	96(80.7%)		91(76.5%)	28(23.5%)	
	5.7-6.4	24(22.2%)	84(77.8%)	0.73	66(61.1%)	42(38.9%)	0.041*
	≥ 6.5	22(23.7%)	71(76.3%)		62(66.7%)	31(33.3%)	
Pain Raing (points on scale)	1-5	21(17.2%)	101(82.8%)		79(64.8%)	43(35.2%)	
	6-10	48(24.2%)	150(75.8%)	0.13	140(70.7%)	58(29.3%)	0.26

Footnotes: *Statistical significance for difference in proportions are calculated using Pearson's Chi-Squared test. P less than 0.05 was considered statistically significant*
**P value Significant at < 0.05, ** significant at < 0.01*
Abbreviations: *p stands for probability of rejecting null hypothesis when it is true.*
Percentages are Row wise. Data are numbers and percentages (%) unless indicated otherwise.

efficacy is checked at 2 different points in time (one being at 3rd week of treatment and other at 6th week). Important being Age (p-value=0.03 at 3rd week and 0.002 at 6th week), co morbidities (p-value=0.001 at 3rd week and 0.001 at 6th week) and duration of diabetes (p-value=0.001 at 3rd week and 0.004 at 6th week), this suggests a strong statistical significance, indicating that these outcomes is unlikely to be due to chance. Also, it can be seen that relation with BMI (p value=0.06) and smoking (p value =0.03) is only significant at week 3. Relation of HbA1c (p value =0.04) is only significant at 6th week.

Discussion

Diabetic peripheral neuropathy presents a formidable challenge for individuals affected by diabetes, significantly impacting their quality of life. The ramifications extend beyond physical discomfort, with potential disruptions to normal sleep patterns and an increased susceptibility to depressive and anxiety disorders.[10] The pharmacological armamentarium for managing this condition includes anticonvulsants, tricyclic antidepressants, opioid-like agents, and serotonin-norepinephrine reuptake inhibitors.[6]

Achieving optimal glycaemic control remains a paramount objective to mitigate the progression of this complication. Emphasizing the importance of compliance, particularly with a focus on single-drug regimens, is underscored by the associated improvements in adherence.[11] Streamlined drug regimens, such as fixed daily dose combinations, have demonstrated enhanced patient adherence in various therapeutic contexts.[12] Notably, randomized clinical trials in healthy adults have revealed superior bioavailability and absorption of fat-soluble thiamine compared to its water-soluble analogue.[13]

The observed efficacy of lipid-soluble vitamin B1 (thiamine) in the current study stands at 76.9%, surpassing the findings of Kew et al, who reported a 47% efficacy in a study involving fat-soluble vitamin B1 analogues over a 6-week period.[14] This disparity may be attributed to the unique genetic makeup of our studied population.

A randomized double-blind pilot study involving 40 diabetic patients with peripheral neuropathy corroborated our results, with a treatment group receiving a fat-soluble vitamin B1 formulation exhibiting significant improvement in neuropathic symptoms. While symptomatic pain relief was evident, vibration sensation scores did not show concurrent improvement.[15] El Hefnawy's comparison of oral vs intramuscular thiamine injection demonstrated a notable decrease in the Diabetic Neuropathic Symptom Score (DNS) across all groups after 14 days of treatment. Similarly, our study documented a substantial decrease in pain on the rating scale, specifically at 68.4%.[16]

Conclusion

In conclusion, the current study, while exhibiting notable strengths in its design and execution, highlights the promising role of fat-soluble thiamine in alleviating diabetic peripheral neuropathy. However, further investigations, incorporating larger cohorts and conducting randomised controlled trials are imperative to ascertain the broader applicability and efficacy of fat-soluble vitamin B1 in managing diverse manifestations of diabetic neuropathy.

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Authors Contribution

AR: Conceptualization of Project
AR, AK: Data Collection
AR, MI: Literature Search
MI, GJ: Statistical Analysis
SK: Drafting, Revision
AR, SK: Writing of Manuscript