**DOI:** https://doi.org/10.54393/pbmj.v5i6.573



# PAKISTAN BIOMEDICAL JOURNAL

https://www.pakistanbmj.com/journal/index.php/pbmj/index Volume 5, Issue 6 (June 2022)



### **Orignal Article**

Role of Vitamin B6 and Folic Acid in Decreasing Diabetic Peripheral Sensory and Motor Neuropathy

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## ARTICLE INFO

#### Key Words:

Diabetes, Peripheral neuropathy, Vitamin B6, Folic acid, Homocysteine

#### How to Cite:

Iqbal Ranjha , N., Azeem, M. ., Khan Malik, M. ., & Ahmed, K. .(2022). Role of Vitamin B6 and Folic Acid in Decreasing Diabetic Peripheral Sensory and Motor Neuropathy : Role of Vitamin B6 and Folic Acid in Decreasing Diabetic Peripheral Sensory and Motor Neuropathy. Pakistan BioMedical Journal, 5(6), 182–185. https://doi.org/10.54393/pbmj.v5i6.573

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Received Date: 20<sup>th</sup> June, 2022 Acceptance Date: 25<sup>th</sup> June, 2022 Published Date: 30<sup>th</sup> June, 2022

## INTRODUCTION

## ABSTRACT

Diabetic peripheral neuropathy is a disease of diabetic patients in which nerves of peripheral nervous system got degenerated and unable to transmit any signals. Diabetic peripheral neuropathy occurs due to decreased serum level of B type vitamins in the body among which vitamin B6 and folic acid are more important. Objective: To determine the role of Vitamin B6 and folic acid in decreasing peripheral neuropathy. Methods: This study was conducted in the Hospital of Sargodha from 2018 to 2020. This study was carried on 250 type 2 diabetic patients. Both males and females were included. Subjects were submitted to detailed medical history about the duration of diabetes and symptoms of peripheral neuropathy. Complete examination of nervous system was conducted. Laboratory examination was done to find out mean fasting glucose. The control group comprised of 50 potentially healthy males and females was made. Serum level of vitamins was checked before and after treatment. Results: The main symptom which was present in all the patients was severe pain in lower legs Distal numbness was reported in 200 patients. Distal sensory neuropathy was reported in 150 patients. Distal motor neuropathy was reported in 52 patients. 157 patients had demyelinating neuropathy, 57 had axonal and 44 had mixed neuropathy. Peripheral diabetic neuropathy decreased after supplementations of homocysteine, folic acid and vitamin b6. Conclusions: Vitamin B6 and folic acid are known for their role to support healthy nervous system. Vitamin B6 and folic acid improved glycemic control through decreasing homocysteine . B6 relieves nerve pain and transmits nerve impulses correctly. The risk of peripheral neuropathy increased as serum folate decreased. Their supplementations are effective strategies for the treatment of peripheral diabetic neuropathy.

Diabetic mellitus (DM) is a disease in which there is higher concentration of glucose in the blood than usual. DM occurs due to disturbance in production and release of insulin. Insulin is a hormone which decreases the concentration of glucose in the body. Due to low production of insulin, concentration of glucose in blood increases. According to WHO, almost 9-10% population of this world is diabetic. Neuropathy is a disorder of nervous system in which transmission of signals from brain to spinal cord or from spinal cord to brain got disturbed [1]. In this disorder, nerves of central and peripheral nervous system got damaged and unable to transmits signal [2]. Peripheral neuropathy is a disorder in which nerves of peripheral nervous system got damaged. Almost 30% patients of peripheral neuropathy are positive to diabetes as well. It means diabetes is related to destructive and damage of nerves of peripheral nervous system. Peripheral neuropathy has many symptoms among which most common are restless leg syndrome and burning foot syndrome [3]. Diabetic peripheral neuropathy is a disease of diabetic patients in which nerves of peripheral nervous system got degenerated and unable to transmit any signals. As we discussed, diabetes is a disorder related to hyperglycaemia (high concentration of glucose in blood). Hyperglycaemia causes increased deposition of protein kinase C and polyol (compound that contains multiple

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hydroxyl groups) in neurons. It leads to damage of neurons. It also leads to oxidative stress. One third of patients of diabetic peripheral neuropathy shows symptoms (Burning, Lancing, paraesthesia) that are extremely painful [4]. After several studies, researchers stated that vitamins had strong effect on the normal functioning of brain [5]. It was also observed that due to surgeries, level of many vitamins got decreased in the body and it led to disorders of nervous system [6]. For the treatment of diabetic peripheral neuropathy, several vitamins and nutrients are required.

## METHODS

In this case control study, 250 diabetic patients of both genders were enrolled in the hospital of Sargodha from 2018 to 2020. Data was collected from the record sheets of each verified case. Following procedures were done on the admitted patients: A detailed medical history about the duration of diabetes, Complete examination of nervous system, Symptoms of peripheral neuropathy present in the patients, Electro physiological studies were conducted Laboratory examination to find out blood group and mean fasting glucose. Control group of 50 healthy males and females was made. Their age ranged from 28-58 years. The mean and standard values of vitamins before and after treatment. Both male and females who are positive to diabetic peripheral neuropathy with age 20 years or above was included. Pregnant women, patients with psychiatric disorders, patients with contraindications to folic acid, pyridoxine, methylcarbylamine were removed from our study.

### RESULTS

The main symptom which was present in all the patients was severe pain in lower legs Distal numbness was reported in 200 patients. Distal sensory neuropathy was reported in 150 patients. Distal motor neuropathy was reported in 52 patients (Table 1). Total 157 patients had demyelinating neuropathy, 57 had axonal and 44 had mixed neuropathy. Peripheral diabetic neuropathy decreased after supplementations of homocysteine, folic acid and vitamin b6 (Table 1). Serum level of homocysteine, pyridoxine and folic acid in diabetic patients before and after treatment is shown in table 2.

Characteristics	Diabetic Patients, N=250	Control Group, N=50	
Gender			
1.Males	110	25	
2.Females	140	25	
Age	35-60	28-58	
Characteristics:			
1.Distal numbness	200	nil	
2.Distal sensory neuropathy	150	nil	
3.Distal motor neuropathy	52	nil	

4.Demyelinating neuropathy	157	nil
5.Axonal neuropathy	57	nil
6.Mixed neuropathy	44	nil
7. Fasting blood glucose mg/L	110-260	70-102
8.Post prandial blood glucose mg/L	157-360	90-118
Serum level of various vitamins in diabetic patients or control group		
9.Glycosylated haemoglobin	5-10%	3-5%
10. Serum level of homocysteine umol/L1	2.3-2.6	2.5-6.4
11.Serum level of vitamin B6 nmol/L	6-25	6-50
12. Serum level of folic acid nmol/L	3-12.5	3-14.5

**Table 1:** Comparison of characteristics between diabetic patients

 and control group

Variables	Before treatment Mean ± SD	After treatment Mean± SD	p- value
Homocysteine umol/L	8.46 ± 5.18	7.55±4.51	0.604
Vitamin B6 nmol/L	24.2±0.52	51± 2.52	24.8
Folic acid ng/L	5.17± 1.41	6.720±2.76	0.196

**Table 2:** Serum level of homocysteine, pyridoxine and folic acid in diabetic patients before and after treatment

### DISCUSSION

Diabetic neuropathy is analogous to neuropathy which occurs due to chemotherapy [7] and peripheral neuropathy which occurs due to high concentration of glucose in diabetic patients [8]. Sources of this vitamin are carrots, spinach, peas, potatoes, milk, cheese, eggs, fish, meat, and wheat. Isoniazid is a drug which causes deficiency and decreased serum level of this vitamin in the body [9,10]. When deficiency of this vitamin occurs in the body, then ability of body to convert tryptophan to nicotinic acid will lost. In this way, peripheral neuropathy occurs. Folic acid plays a very important role in one carbon metabolism. It is used to produce several compounds in our body. Its active form is tetrahydrofolate. It plays crucial role in metabolism of cell [11]. It leads to differentiation of stem cells of neurons of nervous system and lengthening of their axons as well [12]. Regular intake of folic acid prevents neural tube defects in pregnant women and diabetic peripheral neuropathy as well [13,14]. Folic acid is required for the proper and rapid growth of Schwann cells. Researchers observed that when the nerves of peripheral nervous system got damaged, Schwann cells returned to its early parent state. Then Schwann cells formed some specific bands which had ability to grow axons [15]. Harma et al. observed that when proper supplementation of folic acid was given to the injured model of sciatic nerve, then this nerve became able to increase the volume of its axon and its viscosity and myelination as well. It means this vitamin is able to cause healing of nerves of peripheral nervous system [16]. Hyperhomocysteinemia is a disorder which

occurs due to decreased serum level of vitamin b6 and b9. This disorder is responsible for diabetic peripheral neuropathy as well [17]. Oxidative stress also causes demyelination of neurons and leads to neuronal damage [18]. For the treatment of diabetic peripheral neuropathy, aldose reductase inhibitors are used [19,20]. It is very difficult to understand the exact pathophysiology of pain which happens in patients of neuropathy. But there are several central and peripheral mechanisms that try to explain the pathophysiology of this pain[21].

## CONCLUSIONS

Vitamin B6 and folic acid play crucial role in normal and proper functioning of nervous system. These vitamins decrease the serum level of homocysteine. They also maintain normal concentration of glucose in blood. Pyridoxine causes proper transmission of nerve impulses. The risk of peripheral neuropathy increased as serum level of folic acid decreased. Proper and regular intake of vitamin B6 and B9 are required to treat diabetic peripheral neuropathy.

## $\mathsf{R} \to \mathsf{F} \to \mathsf{R} \to$

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