**ORIGINAL ARTICLE**

# Efficacy of Combination of Vitamin B1, B6 and B12 in Management of Diabetic Peripheral Neuropathy

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## ABSTRACT

**Aim:** To determine the efficacy of combination of vitamin B1, B6 and B12 in the management of diabetic peripheral neuropathy.

**Methods:** It was a descriptive case series with the sample size of 310 patients collected by non-probability purposive sampling technique. Patients of diabetes mellitus with diabetic peripheral neuropathy were selected from Department of Endocrinology and Metabolism, Services Hospital Lahore. The duration of study was six months from 04-03-2013 to 03-09-2013. Patients were prescribed Tab Neurobion (vitamin B1 100mg, vitamin B6 100mg, Vitamin B12 200mcg) twice a day for a period of 4 weeks (28 days). Follow up visit was scheduled on 28th day of the initial visit. Efficacy was judged by documenting improvement in pain of at least 2 points from the baseline as assessed by numeric pain rating scale.

**Results:** Mean age of the patients was observed 46.7±8.6 years. Out of 310 cases, 177 patients (57.0%) were male and remaining 133 patients (43.0%) were female. Duration of diabetes as follows: 83 patients (26.8%) had duration of 0-10 year, 139 patients (44.8%) had 11-20 year, 77 patients (24.8%) had 21-30 year and 11 patients (3.6%) had >30 years of duration. Combination of vitamin B1, B6 and B12 in the management of diabetic peripheral neuropathy was found to be efficacious in 271 patients (87.4%).

**Conclusion:** Treatment with combination of vitamin B1, B6 and B12 appeared to improve pain relief among patients with diabetic peripheral neuropathy.

**Keywords:** Diabetic peripheral neuropathy, Vitamin B1, B6 and B12, Efficacy

## INTRODUCTION

Diabetes mellitus is a syndrome with disordered metabolism with inappropriate hyperglycemia due to either a deficiency of insulin secretion or resistance to its action.[1] Its complications may be macrovascular or microvascular[2]. Painful Diabetic peripheral neuropathy is one of the microvascular complications of diabetes mellitus.[3] Diabetic neuropathy is a very common and disabling complication of diabetes and is associated with significant morbidity[4]. It affects patients with both Type 1 and 2 diabetes mellitus. At least one of the four diabetic patients is affected by distal symmetric polyneuropathy[5]. The prevalence increases as the disease progresses; approximately 50% of patients who have had diabetes for 25 years will develop neuropathy[6].

Treatment of symptomatic neuropathy may include opioid or opioid-like analgesics, tricyclic antidepressants, selective serotonin reuptake inhibitors, serotonin norepinephrine reuptake inhibitors, or anticonvulsant medications. A variety of agents may be used as individual therapy or in combination therapy to reduce symptomatic paraesthesia, pain, or dysesthesia. These agents include methylcobalamin, pyridoxine, folate, biotin, taurine, L-arginine, alpha-lipoic acid, and others[7]. Vitamin B12 plays a vital role in the metabolism of fatty acids essential for the maintenance of nerve myelin. Thiamine has a role in initiation of nerve impulses propagation that is independent of its coenzyme. Pyridoxal phosphate, a form of Vitamin B6 is involved in sphingolipid biosynthesis and neurotransmitter synthesis so they all play a role in neuropathy[8]. Although both monotherapy and combined therapy can lower plasma/serum homocysteine levels and improve the neuropathic symptoms, combination therapy with other B complex vitamins seems to be more effective[9].

## METHODOLOGY

It was a descriptive case seriesstudy of 310 patients collected by non probability purposive sampling technique. Patients of diabetes mellitus with diabetic peripheral neuropathy were selected from Department of Endocrinology and Metabolism, Services Hospital Lahore. The duration of study was six months from 04-03-2013to 03-09-2013. The calculated sample size was 310 patients, 95% confidence level, 3.5% margin of error taking efficacy of Vitamin B1, B6 and B12 in the treatment of diabetic neuropathy i.e. 88.9%. Patients of diabetes mellitus with diabetic peripheral neuropathy having Age 18-60 years of both genders and numeric pain rating scale (NRS) with score 3 or more were selected.While patients with HbA1c more than 9%,

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creatinine more than 1.5 mg/dl, known history of allergy to water soluble vitamin B1, B6 or B12 on available medical record, patients already taking multivitamins and pain killers on available drug history were excluded from study.After written informed consent, patients fulfilling the inclusion and exclusion criteria were recruited. Each patient was explained the importance and procedure of the study. Before putting them on intervention, researcher gauged the patient symptoms by using numeric pain rating scale [NRS] with score of 3 or more. Patients were prescribed Tab Neurobion (vitamin B1 100mg, vitamin B6 100mg, Vitamin B12 200mcg) twice a day for a period of 4 weeks (28 days). Follow up visit was scheduled on 28th day of the initial visit. Efficacy was judged by documenting improvement in pain of at least 2 points from the baseline as assessed by numeric pain rating scale. All the patients were assessed by NRS by researchers to avoid bias. Effect modifiers like duration of diabetes was dealt with stratification.

## RESULTS

Regarding age distribution, 16 patients (5.1%) were <20 years of age, 77 patients (24.9%) were 20-40 years old, 217 patients (70.0%) were 41-60 years old with mean age of 46.7±8.6 years (Table 1).

Table 1: Distribution of cases by age (n = 310)

| Age (Year) | =n | %age |
|---|---|---|
| < 20 | 16 | 5.1 |
| 20-40 | 77 | 24.9 |
| 41-60 | 217 | 70.0 |
| Mean±SD | 46.7±8.6 | |

Table 2: Distribution of cases by gender (n = 310)

| Gender | =n | %age |
|---|---|---|
| Male | 177 | 57.0 |
| Female | 133 | 43.0 |

Table 3: Duration of diabetes

| Duration of diabetes (Year) | =n | %age |
|---|---|---|
| 0-10 | 83 | 26.8 |
| 11-20 | 139 | 44.8 |
| 21-30 | 77 | 24.8 |
| > 30 | 11 | 03.6 |

Table-4: Distribution of cases by efficacy

| Efficacy | =n | %age |
|---|---|---|
| Yes | 271 | 87.4 |
| No | 39 | 12.6 |

Out of 310 cases, 177 patients (57%) were male and remaining 133 patients (43%) were female (Table 2). Duration of diabetes as follows: 83 patients (26.8%) had duration of 0-10 year, 139 patients (44.8%) had 11-20 year, 77 patients (24.8%) had 21-30 year and 11 patients (3.6%) had >30 years of duration (Table 3).Combination of vitamin B1, B6 and B12 in the management of diabetic peripheral neuropathy was found to be efficacious in 271 patients [87.4%] (Table 4).

## DISCUSSION

Painful diabetic peripheral neuropathy (PDPN) is one of the most significant symptoms experienced by patients presenting with diabetic peripheral neuropathy[10]. PDPN occursin about 50 percent of patients with diabetic peripheral neuropathy and it substantially impairs patients' quality of life ; interferes with sleep as well as leads todepressive and anxiety disorders[11]. Pharmacological treatment of PDPN with agents like tricyclic antidepressants (TCAs), anticonvulsants, serotonin-norepinephrine reuptake inhibitors (SNRIs) and opioid analgesics have been proved to be effective[12].

The main goal lies in acquiring optimal glycemic control with a purpose to slow down the further worseningof the complication.Studies conducted to evaluate diabetic patients' compliance to their oral antidiabetic (OAD) drugs demonstrated that adherence to OAD medications has been suboptimal[13]. Earlier conductedstudies comparing adherence amongst diabetic patients found more advantageous adherence while using a single tablet per day as compared to the everyday of multiple pills[14]. Subjects on monotherapy have also been proven to be more adherent with their regimen in comparison to those on polytherapy[15]. Simpler dosage regimens have been associated with better adherence rates and a switch to a fixed-dose combination therapy has also been associated with improvement in adherence[16].

Nowadays, there are few options for neuropathic patients. However, the most frequent treatment options are short term and mostly involve the usage of prescription medicine, injection therapy, as well as physical therapy. Surgical procedure could also be helpful in treating some causes of neuropathy (e. g. carpal tunnel syndrome)[17].

Early diagnosis and management of the underlying cause can reduce the risk for continuing nerve damage. For example, controlling diabetes may reduce diabetic neuropathy and in lots ofcases renal dialysis usually improves neuropathy that develops because of chronic renal failure.

Medicines are only able to decrease the pain temporarily, and do minor or almost nothing to completely cure the underlying condition. They may provideshort-term remedy, however as the disease advances, the efficacious dosage of the drug may be required to keep going suppressing the pain boosts concurrently. The side effects of these types of drugs is not easy to overcome and even add to the patient's discomfort. Withthe higher drug dosage, the patient may become confused, ataxic, constipated, confined to a wheelchair or may become bedridden. Signs or symptoms much like Alzheimer's can follow[17].

Vitamin B12 has been evaluated in diabetes as remedy for neuropathies. Now vitamin B12 isdiscovered to be an effective treatment for diabetic peripheral neuropathy with pain and paraesthesias reduced the most from the treatment[18].

In present study, efficacy of combination of vitamin B1, B6 and B12 in the management of diabetic peripheral neuropathy found to be in 87.4% patients.

These results are close to the findings of Abbas and Swair where they proved efficacy in 88.9%[19].

In one double-blind study of 24 diabetic patients who suffered from peripheral neuropathy, a high-dose B-Complex regimen was used. The dosages were: Thiamin, 320 mg/d for the first 2 weeks, and 120 mg/d thereafter; Vitamin B6, 720 mg/d for the first 2 weeks, and 270 mg/d thereafter; and Vitamin B12, 2,000 mcg/day for the first 2 weeks and then 750 mcg/day thereafter. The treatment resulted in significant improvement in nerve conduction velocity in the peroneal nerve and an improvement of the vibration perception threshold[20].

Because of very little data available for combination of vitamin B1, B6 and B12 in the management of diabetic peripheral neuropathy, we are unable to quote more studies for comparison.

The strength of the present study is as follows: A larger sample size is used in comparison with previous studies. Study design is simple and therapy used is cost effective, well tolerated, and easily available and has almost no side effects when used in appropriate doses. The method used to assess improvement in neuropathy i. e. numeric pain rating scale is easy to understand by the patients.

Drawbacks of the present study are as follows: Sample size was small compared to the prevalence of diabetes mellitus. Vitamin B1, B6 and B12 levels were not done before and at the end of therapy to see whether patients had any deficiency of these vitamins or not and whether improvement in pain was due to improving the deficiency state or was an independent effect. In present study, only patients with painful neuropathy were studied and effects on symptoms of numbness, tingling and reduced sensations were not studied. Furthermore, assessment of improvement in neuropathy was done by using numeric pain rating scale which is only subjective more objective assessment of improvement in neuropathy by using electrophysiological parameters was not done.

## CONCLUSION

In conclusion, treatment with combination of vitamin B1, B6 and B12 seemed to improve relief from the pain amongst patients with diabetic peripheral neuropathy.Nevertheless, further high quality, double-blind RCTs are required to establish the clinical effectiveness of combination of vitamin B1, B6 and B12 and its active coenzyme.

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