# Efficacy of mecobalamin (Methylcobalamin) in the treatment of diabetic peripheral neuropathy

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## Abstract

Eleven diabetic patients with painful peripheral neuropathy were included in this study. They were selected according to certain criteria, interviewed, information taken, pain score recorded according to the visual analogue scale (VAS) and electromyography (EMG) done for them. Then, they put on mecobalamin for 5 months (initial 3 months as I.M injections 3 times/week and then for 2 months as tablet 3 times a day), then pain score recorded, EMG done and any reported adverse effects recorded.

The study concluded that mecobalamin not only reduces pain sensation ($P<0.001$) but also improves nerve conduction velocity (NCV) in EMG in the tibial, peroneal and sural nerves without any reported adverse effects.

## الخلاصة

احد عشر مريضا مصاب بداء السكر مع التهاب الاعصاب المحيطية المؤلم ادخلوا في هذه الدراسة. تم انتقاء المرضى وفق معايير خاصة وضعت للدراسة . تم مقابلتهم ، اخذ المعلومات منهم وقياس حالة الالم وفق معيار النظير البصري واجري لهم تخطيط العضلات الكهربائي . وضع المرضى على علاج ميكوبولامين ( اولا لمدة 3 اشهر بشكل حقن عضلية ثم لمدة شهرين على شكل حبوب عن طريق الفم ) في نهاية فترة العلاج تم قياس حالة الالم واجراء تخطيط العضلات الكهربائي وسجل أي عارض جانبي للدواء بتقرير المريض .

اظهرت هذه الدراسة ان عقار الميكوبولامين لايسبب فقط تحسن في حالة الالم بشكل كبير وانما ايضا تحسن في سرعة الانتقال العصبي حسب تخطيط العضلات الكهربائي للاعصاب : الظنبوبي ، الشظيي، والعصب الجلدي لباطن الساق ( الربري) مع ملاحظة عدم تسجيل أي عارض جانبي للدواء.

## Introduction

Diabetic neuropathy occurs with type I and type II diabetes mellitus (DM), and is associated with pain, numbness and considerable morbidity[1]. It can be diffuse or focal; the diffuse type can be peripheral (i.e affecting the extremities) or autonomic (e.g cardiovascular, gastrointestinal, genitourinary). Focal neuropathy is relatively uncommon and include cranial, truncal, proximal motor and compression neuropathy[2]. Diagnosis is based on the neurologic history and examination, prevention and management focus on glucose control, foot care and pain relief using pharmacologic and non-pharmacologic agents[3].

Mecobalamin or methylcobalamin (methyl $B_{12}$) (Fig 1) is the neurologically active, most

bioavailable and best utilized form of vit $B_{12}$, actually has some metabolic and therapeutic applications not shared by other forms of vit $B_{12}$, has been proven clinically to improve some cases with diabetic painful peripheral neuropathy[4]. This drug is used in this study to evaluate its effect in selected cases of diabetic peripheral neuropathy.

## Patients and Methods

The study was conducted from Apr 2003 to Mar 2005. Patients with painful diabetic peripheral neuropathy were interviewed, examined clinically and according to certain criteria, only 13 patients were included in this study, of which only 11 completed the study. They were 5 males and 6 females with a mean age of 53.18 ± 5.07 year (ranged between 45 and 60 year).

All patients have type II DM, on oral hypoglycemic agents. Their mean duration of DM was 12.72 year ± 4.24 and with a mean duration of pain in the lower extremities of 3.5 year ± 2.03.

Criteria for patient's selection:

1. Diabetic patient with painful peripheral neuropathy in the lower extremities.
2. Not receiving any drug for the painful neuropathy (oral. Topical or injectable ) or any medication beside the oral hypoglycemic therapy .
3. Not alcoholic or having renal or hepatic disorders.
4. Cooperative, educated and compliant patient.

After patient's selection, pain score recorded according to the visual analogue scale (VAS) (Fig 2), EMG done for tibial, peroneal and sural nerves, and the drug given to patients with the following instructions:

1. Initially the drug mecobalamin (500µg) is given as injection I.M 3 times / week for the initial 3 months.
2. The injections are susceptible to photolysis and must be used promptly after the package of each ampule is opened.
3. Repeated injection at the same site should be avoided.
4. To be continued after the initial 3 months, on mecobalmin ( 500µg) tablet 3 times / day for 2 months.
5. During course of treatment, patient should consult to report any adverse effect.

By the end of treatment period, pain score recorded according to VAS, EMG done and any reported adverse effects recorded.

**Materials**

1. Mecobalmin injection 500µg (Methycobal) Eisai co., Ltd, Tokyo, Japan.
2. Mecobalamin tablet 500µg (Methycobal) Eisai co., Ltd, Tokyo, Japan.

Statistical Analysis

Paired t-test was used to compare between measurements before and after therapy and the results were considered significant at $p \leq 0.05$. Mean and standard deviation was used.

## Results

By comparing pain score before and after mecobalmin therapy, there was a highly significant reduction in pain score ($P<0.001$), (table 1).

With regard to EMG record:

The NCV showed a highly significant improvement in the sural ($p<0.001$) and peroneal nerve ($P<0.01$), with a significant improvement in NCV of tibial nerve ($P< 0.05$), while improvement in distal latency (DL) was significant only for peroneal nerve (tables 2-4).

## Discussion

Diabetic peripheral neuropathy is a common complication of DM and its frequent clinical symptoms are pain and numbness in the lower extremities. Its occurrence is related to control and

duration of DM, but the pathogenesis of diabetic neuropathy is still not clear[5]. The most important factor of treatment of diabetic neuropathy is a good control of the diabetic state and pharmacological approaches, and although several drugs have been advocated none has proved consistently effective[6].

Methylcobalamin, one form of vit B12, occurring in blood and cerebrospinal fluid, also developed as a drug by Eisai., Co, Ltd, reported in several clinical studies to have the efficacy in slowing down or even reversing the effects on nerve tissue and in experiments using glia cells, it was reported to enhance the synthesis of lecithin a major component of the myelin sheath[7].

Our study results reflect a highly significant improvement in pain and NCV component of EMG of sural, tibial and peroneal nerves which are the parameters usually looked for in evaluating patients with peripheral neuropathy especially the demyelinating type as seen in diabetic patients. In contrast, the less conspicuous improvement in DL seen in our study is reflecting the fact that increase in DL is pathophysiologically due to localized conduction block, a phenomenon mainly seen in compressive neuropathy and some other types of peripheral neuropathy as chronic inflammatory demyelinating polyneuropathy and not in diabetic neuropathy[8,9]. The fact that responses are lost first in the tibial and later in sural and peroneal nerves could give an explanation to our results in that sensitive nerves affected or damaged first are last to be improved[10]. The small number of patients included in this study can be attributed to the high cost of therapy (for each patient drug cost for injections and tablets about 134 $), the criteria of selection of our patients and the long duration of patients therapy (5 months).

Methylcobalamin was reported by Yamatsu *et al*. (1976) to possess a stimulating effect on proteosynthesis in Schwann cells at the initial stage of axon regeneration and it may facilitate neural regeneration in rats[11].

Methylcobalamin has been observed in rats to be taken up into nerve cell organelles more actively and extensively than cyanocobalamin and experimentations using sciatic nerve cells from rats with experimental diabetes has demonstrated that mecobalamin helps maintain axonal function by promoting the synthesis of protein that is the major structural component of the axon and by normalizing transport velocity of the protein[12]. Tanaka *et al*. (1982) in studying relation of partial deficiency of mecobalamin to occurrence of diabetic neuropathy suggested that partial deficiency of methylcobalamin in the peripheral nerve tissue might be related to the pathogenesis of diabetic neuropathy,he found that total serum cobalamin levels in patients with diabetic neuropathy, were slightly decreased as compared with those in healthy control and that total cobalamin content in the diabetic peripheral nerve tissues from autopsied materials was moderately lower as compared with that in controls and there was a marked fall in methlycobalamin content[13]. In a multicentre study conducted by yamada et al. (1982) regarding the usefulness of methylcobalamin in diabetic neuropathy, the results showed that the improvement rate of pain in the lower extremities was 78% and the symptoms disappearance rate of pain was 42%, the improvement in motor nerve conduction velocity was 36% and the general improvement rate was 68.7% after 8 weeks of treatment[14].

A recent study comparing 2 groups of patients with diabetic peripheral neuropathy, one receiving mecobalamin initially for 3 weeks as

injection and later 8 weeks as tablet, and a 2nd group receiving vitamin B12 served as a control. The study which was conducted by Li (1999), concluded that spontaneous pain and numbness of the limbs were improved by 73% and 75% in the mecobalamin group as compared to 36% and 45% in the control group respectively[15].

Our study concluded that mecobalamin could have a major role not only in improving symptomatic pain diabetic peripheral neuropathy, but also could help to improve nerve tissue condition as reflected by the improvement in the NCV component of EMG.

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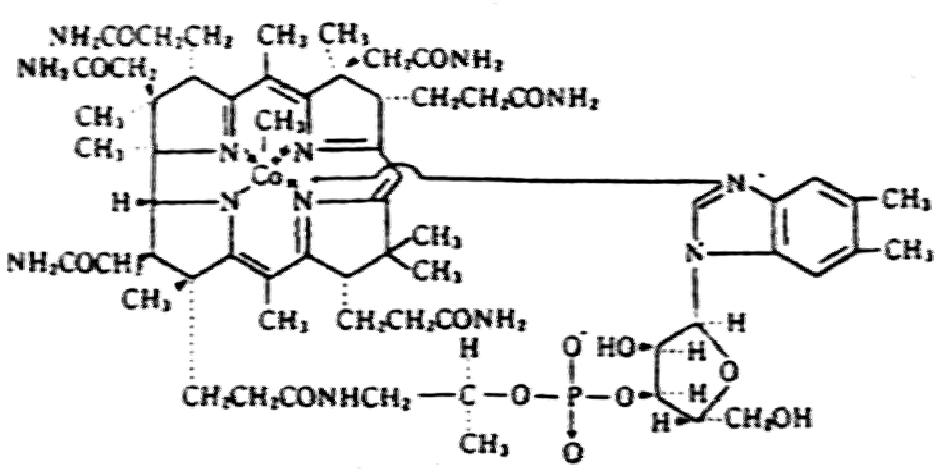

**Figure1** Structure of Mecobalamin.

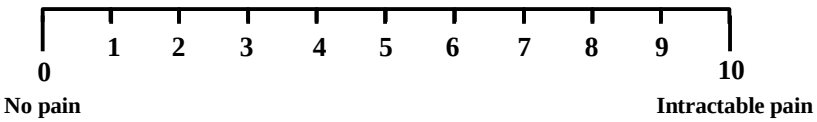


**Figure 2** Visual Analogue Scale (VAS).

**Table 1** Effect of Mecobalamin treatment on pain score in diabetic peripheral neuropathy.

| | Mean ± SD | | p-value | Sig. |
|---|---|---|---|---|
| | Before treatment | After treatment | | |
| **Pain score (n=11)** | 6.09 ± 0.70 | 2.55 ± 1.75 | <0.001 | S |

S = Significant

**Table 2** EMG response of sural nerve before and after treatment with Mecobalamin.

| | Sural nerve (Mean ± SD) | | p-value | Sig. |
|---|---|---|---|---|
| | Before treatment | After treatment | | |
| **DL (msec) (n=11)** | 5.35 ± 1.57 | 5.34 ± 1.60 | >0.05 | NS |
| **NCV (m/sec) (n=11)** | 31.82 ± 2.52 | 41.36 ± 5.52 | <0.001 | S |

S = Significant, NS = Not significant

**Table 3**EMG response of peroneal nerve before and after treatment with Mecobalamin.

| | Pereneal nerve (Mean ± SD) | | p-value | Sig. |
|---|---|---|---|---|
| | Before treatment | After treatment | | |
| **DL (msec) (n=11)** | 4.96 ± 1.09 | 4.59 ± 0.82 | <0.05 | S |
| **NCV (m/sec) (n=11)** | 40.91 ± 5.91 | 44.64 ± 4.52 | <0.01 | S |

S = Significant

**Table 4** EMG response of tibial nerve before and after treatment with Mecobalamin.

| | Tibial nerve (Mean ± SD) | | p-value | Sig. |
|---|---|---|---|---|
| | Before treatment | After treatment | | |
| **DL (msec) (n=10)*** | 5.13 ± 1.11 | 5.03 ± 0.96 | >0.05 | NS |
| **NCV (m/sec) (n=10)** | 38.30 ± 6.04 | 41.70 ± 5.46 | <0.05 | S |

S = Significant, NS = Not significant.

* Number of patients was 10 because one patient have no record on EMG before and after therapy.