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# The Comparison between Effects of 12 weeks Combined Training and Vitamin D Supplement on Improvement of Sensory-motor Neuropathy in type 2 Diabetic Women

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## Abstract

### Background:

Peripheral neuropathy is a common complaint of diabetes. This study aimed to determine the effects of 12 weeks combined training with Vitamin D supplement on improvement of sensory-motor neuropathy in women with diabetic neuropathy.

### Materials and Methods:

This clinical trial study conducted on 90 patients were selected and randomly divided into two groups. Finally, 81 adult females with diabetes type II (20–55 years old) were interred in this study. The control group had no training, but received Vitamin D. The experimental group received Vitamin D and 12 weeks training program (3 days a week, 60 min/session) including aerobic exercises, strength, and flexibility. Aerobic exercise intensity was set at 60–70% maximum heart rate and resistance training intensity was determined by 10 R.M. Michigan neuropathy questionnaire, reflex hammer and tuning fork 128 Hz used to screening tense of neuropathy (Michigan Neuropathy Screening Instrument) that were used for pretest and posttest.

### Results:

Following 3 months combined training and supplementation with Vitamin D, had observed a significant reduction in numbness ($P = 0.001$), pain (0.002), tingling ($P = 0.001$), and weakness ($P = 0.002$) in the lower limb and also increases in sense of touch intervention ($P = 0.005$), detects the position of the fingers ($P = 0.001$) and vibration perception ($P = 0.001$) in tissues. Knee reflexes ($P = 0.77$) and ankles reflexes ($P = 0.47$) did not significantly change after interventions.

### Conclusion:

It seems that taking part in combined training and supplementation with Vitamin D can improve the symptoms of sensory-motor neuropathy.

**Keywords:** Combination training, diabetes, sensory-motor neuropathy, Vitamin D supplement

## Introduction

Over 150 million people in all over the world have type II of diabetes, and a large number of cases are still unidentified.[1] The spread of this disease in Iran has been reported between 5% and 8%. Due to many complications and disabilities caused by diabetes, it is known as a disabling disease. Diabetic neuropathy (DP) is one of the most common complications of diabetes that is seen in 50% of all patients. This complication in type I of diabetes access late and in type II of diabetic patients is an early phenomenon.[2]

The main characteristic of DP is the progressive destruction of neural tissues that is directly related to the period of time that the patient had been affected by the disease. Depending on location and type of neurotic tissues involved, the clinical demonstration of disease will be different. From all different types of DPs, the chronic poly-neuropathic sensory-motor or diabetic peripheral neuropathy (DPN) is more common than the other. DPN can lead to acute pain, lack of feeling in the feet, an increasing risk for leg wounds or amputation, instability and disordering in stability that leads to trouble in deep sensory-body system performance.[2,3]

Physical activities and healthy diet can play an important role in controlling of diabetes and its harmful effects. The studies have been shown that physical activities could decrease blood sugar levels.[4] In addition, reduction of heart problems and cardiovascular malfunction,[5] delay in diabetic retinopathy,[6] better functioning in muscles,[7] and an improvement in life quality and anxiety.[1,8] Physical activities also cause an improvement in controlling HbAlC.[9] Kluding *et al*. concentrated on the effect of sport on improving the DP complications and expressed that 10-week aerobic exercise program has a very good effect on performance of the neural fibers and leads to reduction in neuropathic symptoms.[10] Akbari *et al*. (2011) had also revealed that balancing exercises could improve the balancing indexes in diabetic patients with neuropathy.[11]

There are some varied studies have focused on the effect of physical activities on reducing the neuropathic complications. Therefore, such important is the type of exercise that must be prescribed. It is shown that the best type of exercises for patients is some combined exercises (aerobic, resisting, and flexibility).[12,13]

In addition, in some studies about Vitamin D, as a calcium hemostat factor, osteopathic metabolism which is the natural requirement of insulin excretion in treating the complications caused by diabetes.[14] Although its exact mechanism is not known, these studies have shown that an intake of Vitamin D and calcium has a reverse relation with weight gaining and the spread of the metabolic syndrome.[15] Soderstrom *et al*. (2010) in a study titled “the correlation between Vitamin D and neuropathic diabetes” explains that an insufficient level of Vitamin D will increase the self-expression of the people with neuropathic diabetes. Therefore, we can use Vitamin D supplements as a therapeutic method in patients with neuropathic diabetes.[16] Considering the given explanations, the goal for the present study is to study the simultaneous effect of combined exercises and Vitamin D intake in reducing the adverse effects of the neuropathy diabetes.

## Materials and Methods

This is a clinical study that conducted in Isfahan province during 2013–2014. The target of the study was patients with DPN. Inclusion criteria were females who suffered from type II of diabetes, suffered from diabetic neuropathy and more than 5 years suffering from diabetes. Patients were without another comorbidity and ranged between 20 and 55 years old. In this study, the exclusion criteria were Michigan


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Neuropathy Screening Instrument (MNSI) questionnaire, a reflection hammer and a diapason (128 Hz) that were used to test the patients for neuropathic symptoms (before and after the experiment). At first, the signs of self-expression for having and not having pain, numbness, tingling, weakness, and disability in lower body limbs were recorded by researcher and then the patients were standby to do the other stages of the test (reflex recordings, sense of touch, realizing fingers positions, and vibration sensing). To measure the reflexes, the reflection hammer was used. Some strokes were delivered on kneecap and Achilles tendons to check the existence or lack of existence of reflection in knee and ankle. The meaning of touch in patients was having a light sense of touch in a way that the person would feel and report the rubbing of a piece of cotton on their legs. Realizing the fingers positioning was performed by the researcher by putting one of the patient's big toes in three different positions and asking him to guess the position without looking at it. Diapason was used to produce vibration and putting it in touch with a point on the patient's leg (the big toe was chosen for all the patients) to measure his or her level of neural conduction in the leg (all of these examinations were repeated for the posttest stage).

The samples were divided into two groups that each group had 45 persons (later in the study, the number of control and experiment groups were reduced to 41 and 42 persons). The control group did not perform any exercises and only received some Vitamin D supplements, but the experiment group performed some combined exercises in addition to Vitamin D intakes. Vitamin D was provided in the form of tablets (500 mg carbonated calcium + 200 units of Vitamin D) for every 12 h. Patients were between 20 and 55 years old and they have been diabetes for at least 5 years. The patients with cardiovascular disease, retinopathy, hypoglycemic attacks, and diabetic foot ulcer were denied from taking part in this study.

### Exercise protocol

The first experimental session took 20 min. By the end of 3 months ($36^{th}$ session), it had increased to 60 min. The first sessions started with low-intensity exercises, and the intensity was growing up gradually. The American College Protocol was used to determine the intensity of the aerobic and resistance exercises. To measure the intensity of the aerobic exercises, the maximum heart beat (50–70% of the heart beat) was used. Furthermore, to measure the intensity of resistance exercises, the maximum repetition was 10–12 with 50% of maximum intensity. An exercise session included: Light stretches to warm up, simple aerobic exercises for everyone, resistance exercise movements with dumbbells and stretches for cooling down. Exercises lasted for 12 weeks and 3 sessions/week and 60 min/session.

### Statistical analysis

The data were analyzed by (SPSS) version 21.0 for Windows (SPSS Inc., Chicago, IL, USA). Chi-square and *t*-test were used to determine the mean differences.

## Results

In Table 1, the demographic characteristics of patients are given; here is no significant difference between control and experimental groups.

To analyze the data, Chi-square test was used. The table data are related to variables of pain, sense of touch, and knee ankles' reflexes [Tables 2 and 3].

In Table 2, the complications by neuropathy diabetes are shown. It is divided according to pretest and posttest results.

Table 3 is about the existence of reflection in ankles and knees. The reflection for pretest and posttest was not recoded significantly.

## Discussion

The purpose of this study was: The effects of 12 weeks combined training with Vitamin D supplementation on improvement of sensory-motor neuropathy in women with diabetic neuropathy.

The results show the simultaneous effects of Vitamin D and combined exercises on neuropathy motor-sensory components. Although, the effects were insignificant for knee and ankle reflection, the intake of Vitamin D with combined exercises could have significant effects on numbness, pain, tingling, weakness and disability, increase in sense of touch, position of fingers, and vibration sensing were significant.

The solutions for improving neuropathy in patients with type II diabetes have been the focus for studies by researchers. Kluding *et al*. in a study titled "the effect of sport exercises on neuropathy symptoms, neural performance and skin stimulations in patients with DPN" during 10-week aerobic and resisting exercise programs observed a reduction in neuropathy symptoms (MNSI on 1.24 ± 1.8, $P = 0.01$) and pain (Michigan Neuropathy on − 8.1 ± 35.5 on a 100, $P = 0.05$).[12] Richardson *et al*. in their studies titled "exercise diets for balance improvement in neuropathy patients" studied 20 patients with type II diabetes with neuropathy symptoms. In this study, it was shown that the people in the experiment group with 3 weeks of physical education had a considerable improvement in their balance.[17] Eventually, the evidences have shown that a sport exercise program intervention can improve the quality of life and disorders in patients with neuropathy.[18] Therefore, sport therapy is one of the factors has been the focus of researchers in treating neuropathy and reducing the complications caused by it throughout the years.[19,20,21,22]

The findings of the current study are in compliance with previous studies on the effect of sport and activities on improving the motor-sensory neuropathy symptoms in type II diabetic patients. Balduccia *et al*. (2006) showed the effect of long-term aerobic exercises on improving the neural-muscular motor-sensory parameters.[21] The effect of resistance exercises on DPN symptoms was also shown by Mokshagundam.[23] Baum *et al*. reported the effect of power and flexibility exercises on improving the neuropathy symptoms.[24] As a result of exercise activities, the verified results by this study on the effects of exercise intervention are based on improvement in neuropathy complications due to a reduction in blood sugar levels. In other words, exercise could stimulate the metabolic system of the body. By the increasing in sport activities and blood circulation, the plasma blood sugar level reduced–reciprocally. Lack of exercise causes that the blood sugar level in type II diabetic patient goes up.[24] Studies have shown that by doing regular exercises, the glucose transferring protein (GLUT-4) level in cells will increase.[21,25] In addition, doing an exercise session with muscular contractions causes the transfer of GLUT-4 to the plasma membrane, and this will increase the glucose transfer capacity into muscular and fat cells.[26,27] Insulin increases the glucose transfer to muscular cells directly and indirectly. Insulin receptors are membrane receptors and tyrosine kinesis. Insulin will stimulate tyrosine kinase by connecting to receptors that will cause the autophosphorylation of receptors and produces some messenger molecules such as insulin receptors of types I and II inside the cells. Other proteins will form a complex chain of phosphorylation and dephosphorylation which have extensive metabolic and myotonic effects on insulin. Defects in insulin or resistance against absorption of insulin will cause the reduction in number of transporters, and this will greatly reduce the GLUT-4 activity.[28] Therefore, by increasing the physical activities and controlling the blood sugar level, the motor-sensory neuropathy complications will improve.

Another possibility by observing the current study is about the improvement in neural conductivity in neuropathic patients following an exercise activity. Researchers noted that after an exercise intervention period, the diabetic neuropathy patients had a better neural conductivity. These researchers explained that increasing in neural axons in neuropathic patients will happen after doing some exercises. This increase in axon connections can substantially improve the neural controls in these people.[12]

Reduction in neuropathy pain has also been observed as a result of exercising. This is a guess because of the production of some proteins that are resisting to cellular damages and help to repair the neural damages.[29] In the studies, this protein has been considered as a protector for cells, and it is produced by

skeletal muscular contractions that prevent from pain and damage. On the other hand, it has been reported that exercise activities will lead to a reduction of preinflammatory and inflammatory factors. In addition, they reduce the neurotropic factors which in turn lead to an improvement in sensory neurons.[16]

On the other hand, there is a possibility that the Vitamin D supplement for the experimental group plays a role as a pain reducer factor by having some pain killer's effects.[30] Some evidences show that this vitamin will help to increase the trophic factors such as nerve growth factor (NGF), glial cell-derived neurotrophic factor (GDNF), NT3.[29,30] A reduction in Vitamin D results looking a reduction in NGF and GDNF and a change in p57 receptor level for neurotrophin (NT).[31] The effects of trophic NGF on dopaminergic neurons and forebrain, and the effects of GDNF on dopaminergic neurons of Basal Ganglia have clearly been shown.[32] It is worth-mentioning that the forebrain has an important effect in displaying of painful behaviors.

Vitamin D deficiency has been reported in diabetic patients, and it is probable that the consumption of this supplement can delay the attack of diabetes.[30] In addition, Vitamin D consumption helps to regulate the NT and calcium hemostat. Both of them help to protect the nervous system. In fact, the Vitamin D effects have been reported as a pain reducer.[33] The findings by Soderstrom *et al*. in determining the relation between Vitamin D and neuropathy complications: It became clear that the presence of Vitamin D in the body can reduce the symptoms of numbness, losing the sense of touch, pain, and tingling in diabetic patients. Of course, we should also consider the age, race, geographic and demographic restrictions in our research sampling.

Considering the effect of exercise and Vitamin D on neuropathy, the results of this study can be in agreement with previous studies.[12,19,26,29,31] The explanation is that exercise will enlarge the blood vessels, and this will result in higher blood uptake by the peripheral nerves and, therefore, reduction in numbness and tingling. The recovery of the nerves by the proteins in the blood will result in reduction of pain. Therefore, by repairing the peripheral nerves, there is a possibility for axons to shoot out and as a result the feeling of numbness will increase. By increasing in peripheral blood circulation and consumption of Vitamin D, the painkilling effects of Vitamin D will reach the peripheral nerves and eventually there will be a lower pain, numbness and tingling, adding to the effects by exercising.[33] All the effects except the numbness, are in agreement with previous studies. This will cause an increase in peripheral neural axons and also in repairing the destroyed enervation by neuropathy. In crescent and recovery of neurons can improve the sense of feeling that requires further studies. This is an essential role in nerve conduction. Inpatients with diabetic neuropathy, nerve branches of the axons will increase after exercise.[20] After sports activity, a possible increase in recovery of nerve conduction in patients with neuropathy will be observable. An increase in perfusion to nerve cells will repair the myelin.

Therefore, it is likely that a multi-factor mechanism happens, and this may include a direct effect on controlling the blood sugar level of neural fibers, a change in blood vessels function and body composites.

In this study, the effect of combined exercises and Vitamin D intake on reflexes by ankle and knees were found insignificant. One of the restrictions of the present study is lack of any background and scientific information regarding the reflexes in sensory neuropathic patients. The thing that is clear is that the body fluctuation in this type of people is very high, and conversely a little reflection was reported in their body limbs.[17,20] Perhaps the only explanation for this lack of effect is the type of exercises performed. Evidences show the effectiveness of deep sensory exercises on diabetic women.[34] However, the present study showed that combined exercises do not have a significant effect on reflexes of the ankle and knee. Perhaps, this type of exercise (combined) has not been able to improve the deep sensation of these people. Even if the deep sensory exercises were conducted, the positive impact on reflexes could be observed. We recommend a future study on this topic.

We must mention that by considering the conducted studies on animals, it has been shown that this vitamin will have some pain reducing effects during a long run.[22] Therefore, the consumption of this vitamin for

long periods is recommended.

## Results

Briefly, in this study turned out that doing exercises in parallel of Vitamin D supplementation could have an extra effect on decreasing the complication of diabetic neuropathy.


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Nil.


### Conflicts of interest

There are no conflicts of interest.

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## Figures and Tables

**Table 1**

| Group | Variable | | | |
|---|---|---|---|---|
| | Age | Height | Weight | BMI |
| Control | 46.1±7.4 | 160.6±5.5 | 69.1±9.5 | 26.77±3.5 |
| Experiment | 45.2±7.8 | 160.2±5.0 | 68.6±8.9 | 26.68±2.5 |

BMI: Body mass index

Frequency distribution of demographic characteristics

## Table 2

| Variable | Period | Group | *n* (%) | | Statics | |
|---|---|---|---|---|---|---|
| | | | Has | Does not have | $\chi^2$ | *P* |
| Pain | Pretest | Control | 23 (56.1) | 18 (43.9) | 0.99 | 0.32 |
| | | Experiment | 18 (45) | 22 (55) | | |
| | Posttest | Control | 23 (56.1) | 18 (43.9) | 9.56 | 0.002 |
| | | Experiment | 9 (22.5) | 31 (77.5) | | |
| Sense of touch | Pretest | Control | 23 (56.1) | 18 (43.9) | 0.3 | 0.58 |
| | | Experiment | 20 (50) | 20 (50) | | |
| | Posttest | Control | 24 (58.5) | 17 (41.5) | 7.9 | 0.005 |
| | | Experiment | 11 (27.5) | 29 (72.5) | | |

Frequency distribution of diabetic neuropathy

## Table 3

| Variable | Period | Group | *n* (%) | | | Statics | |
|---|---|---|---|---|---|---|---|
| | | | No | Decreased | Yes | $\chi^2$ | *P* |
| Knee reflexes | Pretest | Control | 19 (14.6) | 6 (14.6) | 16 (39) | 0.99 | 0.32 |
| | | Experiment | 16 (17.5) | 7 (17.5) | 17 (42.5) | | |
| | Posttest | Control | 16 (14.6) | 6 (14.6) | 19 (46.3) | 9.56 | 0.002 |
| | | Experiment | 18 (10) | 4 (10) | 18 (45) | | |
| Reflexes ankles | Pretest | Control | 20 (9.8) | 4 (9.8) | 17 (41.5) | 1.08 | 0.3 |
| | | Experiment | 23 (15) | 6 (15) | 11 (27.5) | | |
| | Posttest | Control | 19 (9.8) | 4 (9.8) | 18 (43.9) | 15.4 | 0.001 |
| | | Experiment | 24 (7.5) | 3 (7.5) | 13 (32.5) | | |

Results of Chi-square test in the knee and ankles of reflexes