

Effect of Vitamin B6 on Clinical Symptoms and Electrodiagnostic Results of Patients with Carpal Tunnel Syndrome

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ABSTRACT

Purpose: Carpal tunnel syndrome (CTS) refers to a cluster of signs and symptoms that stems from compression of the median nerve traveling through carpal tunnel. Surgery is a definite treatment for CTS; however, many conservative therapies have been proposed. The present study set out to assess the effect of vitamin B6 in patients with CTS. **Methods:** Forty patients (67 hands) with mild-moderate CTS were initially selected and randomly assigned into two groups as follows: 1) Case group with 20 subjects (32 affected hands) receiving vitamin B6 (120 mg/day for 3 months) and splinting. 2) Control group with 19 subjects (35 affected hands) only received splinting. One subject from the control group dispensed with continuing participation in the research. Daily symptoms and electrodiagnostic (NCV-EMG) results were assessed at baseline and after 3 months. **Results:** Nocturnal awakening frequency due to pain, daily pain, daily pain frequency, daily pain persistence, hand numbness, hand weakness, hand tingling, severity of nocturnal numbness and tingling, nocturnal awakening frequency owing to hand numbness and tingling, and clumsiness in handling objects improved significantly in the vitamin B6-treated patients; even so, only problem with opening a jam bottle and handling phone significantly reduced in the control group. The median nerve sensory latency mean decreased following the treatment; and the median nerve sensory amplitude mean and sensory conduction velocity mean increased. **Conclusion:** The present study suggests that vitamin B6 treatment improves clinical symptoms and sensory electrodiagnostic results in CTS patients, and thus is recommended for CTS treatment.

Introduction

Carpal tunnel syndrome (CTS) refers to a constellation of signs and symptoms that stems from compression of the median nerve traveling through the carpal tunnel.¹ It accounts for approximately 90% of entrapment neuropathies² and is more prevalent amongst females.³ Paget first described the clinical manifestation of CTS.⁴ CTS is classified into acute and chronic forms. Acute CTS is not prevalent and results from radius fractures, burns, coagulopathies, infections and local injections; however, chronic CTS is rather prevalent and patients present with its symptoms for several months or years.² CTS is also divided into primary and secondary forms. Secondary CTS can result from pregnancy,^{5,6} rheumatoid arthritis,⁷ acromegaly⁸ and type 2 diabetes mellitus.⁹ Furthermore, career is said to be involved in CTS. For instance, dentistry was suggested to be associated with CTS.¹⁰ CTS is clinically diagnosed by Phalen's,¹¹ Hoffmann-Tinel's,¹¹ and Durkan¹² tests. In spite of the fact that conservative therapies are

proposed,¹³ surgery is a definite treatment for CTS.¹⁴ Initial therapies for CTS incorporate oral or local injection of corticosteroids,¹⁵ splinting¹⁶ and activity modification.¹⁷ Moreover, vitamin B6 has been demonstrated to be effective in CTS treatment.^{18,19} Vitamin B6 contributes to multiple metabolic pathways of neuronal function for instance, production of neurotransmitters, amino acid metabolism, synthesis and destruction of sphingolipids. Administration of vitamin B6 as add-on therapy for CTS has been introduced into western communities since 1980.²⁰ CTS is a common cause of patients' referral to neurology clinics and electrodiagnostic wards and patients with mild to moderate CTS do not necessitate surgery but to require treatment. Hence, it is difficult to ignore CTS conservative therapies such as vitamin B6 treatment. On the other hand, a literature search has offered contradictory results pertaining to impact of vitamin B6 upon CTS. Moreover, the preceding

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published research suffered major pitfalls, that is to say, limitation in sample size and methodology, uncontrolled CTS severity and difference in dose and duration of treatment. The present study attempted to iron out all aforesaid drawbacks of the preceding research and have a novel approach in order to achieve reliable results. Therefore, our aim was to assess the effect of vitamin B6 upon CTS. More to the point, the present study was designed in order to specifically identify the effect of vitamin B6 treatment upon clinical symptoms and electrodiagnostic results in CTS patients presenting with mild to moderate clinical symptoms. It was hypothesized that vitamin B6 treatment can improve CTS and specifically patients' electrodiagnostic results.

Materials and Methods

The whole study lasted for 18 months from 2009, Mar 21 to 2010, Jun 23. Forty patients with idiopathic CTS were initially recruited from Neurosciences Research Center, Tabriz University of Medical Sciences. Patients were randomly assigned into 2 groups as follows: 1) Case group including 20 patients with 32 affected hands 2) Control group involving 20 patients with 35 affected hands. Case group received splinting and was orally treated by vitamin B6 at a dose of 120 mg/day during 3 months; be that as it may, the control group received only splinting. Symptoms and electrodiagnostic results (Nerve Conduction Velocity [NCV] and Electromyography [EMG]) results were compared prior and subsequent to the treatment in both groups. All participants gave informed consent for the research. All the procedures were approved by ethical committee of Tabriz University of Medical Sciences. Of the study population, one subject from the control group dispensed with continuing participation in the research. Hence, we were ultimately studied a total number of 39 subjects with CTS. It is worth noting that we applied inclusion criteria of mild to moderate CTS for the study. Mild, moderate and severe CTSs were defined based upon electrodiagnostic results as follows: a) Mild: increased median nerve sensory latency of more than 3.1 ms or median-ulnar sensory latency difference of more than 0.5 ms b) Moderate: increased median nerve sensory latency and decreased median nerve sensory amplitude or increased median nerve motor latency c) Severe: decreased median nerve sensory amplitude or EMG results.^{2,9} Moreover, patients with severe CTS, diabetes mellitus, acromegaly, wrist burns, wrist sesamoid fracture, pregnancy, hypothyroidism, cervical neuropathy and radiculopathy resulting in hand numbness and paresthesia were excluded from the study. It should also be noted that patients' hands, but not patients, were assessed in the present study. Therefore, at least 10 hands with mild or moderate CTS were assessed in each group. Electrodiagnostic tests including NCV and EMG tests, Phalen's and Tinel's tests and symptom assessments (standard Boston questionnaire) were

carried out prior to commencing the treatments. Aforesaid tests and assessments were repeated again 3 months later and changes were recorded. Splinting and activity modification were performed as usual. Patients' responses were scored from 1 to 5 in terms of severity of clinical symptoms. Ultimately, collected data incorporated age, gender, career, side of involvement, CTS severity, positive Phalen's and Tinel's tests, clinical symptoms and electrodiagnostic findings. Statistical analyses were performed using the SPSS statistical software package (Version 17.0). More precisely, statistical significance was analyzed for categorical variables using contingency tables, Chi-Square test, Fisher's exact test and McNemar test. In addition, comparisons were drawn for numerical variable using independent samples T-test, paired samples T-test and Wilcoxon test. The results were significant at P-value<0.05 level.

Results

In the present study, 40 participants including 20 cases and 20 controls were studied. Howbeit, one subject from the control group dispensed with continuing participation in the research. The recruitment was carried out for 3 months starting at 2009, June 20. Comparing the two results, no significant difference was found in the average age of the patients in the case and control groups which were 42.7 ± 12.0 years (25 to 65 years) and 43.8 ± 13.1 years (22 to 62 years), respectively ($p=0.805$). No significant difference was found in gender between the case and control groups (male cases [$n=4$; 20%], female cases [$n=16$; 80%], male controls [$n=1$; 5%] and female controls [$n=19$; 95%]) ($p=0.342$). The case group included 16 homemakers and 4 employed patients who constituted 80 % and 20%, respectively. To be more precise, the employed patients involved a carpet weaver and 2 self-employed individuals. However, the control group included 15 homemakers and 5 employed patients who made up 75% and 25%, respectively. More precisely, the employed patients involved a carpet weaver and 4 self-employed individuals. No significant difference was found in patients' career between these groups ($p=0.647$). In the case group, 19 subjects showed right hand involvement (59.4%), however, 13 subjects presented with left hand involvement (40.6%). In the control group, 24 subjects showed right hand involvement (68.6%); nonetheless, 11 subjects presented with left hand involvement (31.4%). In this regard, there was no significant difference between these groups ($p=0.339$). No significant difference was found between the case and control groups in the severity of CTS (22 [68.8%] and 10 [31.2%] controls with mild and moderate CTS, respectively, and 19 [54.3%] and 16 [54.7%] cases with mild and moderate CTS, respectively ($p=0.177$)). In the case group, 14 hands with positive Phalen's and Tinel's tests were detected prior to treatment (43.8%) which were more than those observed subsequent to the treatment (11

[32.4%]). This difference was not statistically significant ($p=0.727$). In the control group, 12 hands with positive Phalen's and Tinel's tests were found prior to the treatment (43.3%) which were less than those detected following the treatment (16 [45.7%]). This difference was not statistically significant ($p=0.359$).

Table 1 provides a comparative breakdown pertaining to questionnaire responses of the patients in terms of clinical symptoms in the case and control groups. As can be decidedly noted, in the case group, nocturnal

pain severity, nocturnal awakening frequency due to pain, daily pain, daily pain frequency, daily pain persistence, hand numbness, hand weakness, hand tingling, severity of nocturnal numbness and tingling, nocturnal awakening frequency owing to hand numbness and tingling, and clumsiness in handling objects decreased significantly following the treatment (amelioration). According to the table, problem with opening a jam bottle and handling phone significantly reduced in the control group (amelioration).

Table 1. A comparison of CTS patients' responses in the control and case groups in terms of distribution of clinical symptoms before and after treatment.

Variables	P value (Before and after treatment)	
	Case group	Control group
Nocturnal pain	0.040*	0.544
Nocturnal awakening frequency due to pain	0.027*	0.579
Daily pain	0.027*	0.865
Daily pain frequency	0.035*	0.725
Daily pain persistence	0.023*	0.185
Hand numbness	0.045*	0.936
Hand weakness	0.029*	0.675
Hand tingling	0.030*	0.865
Severity of nocturnal numbness and tingling	0.030*	0.253
Nocturnal awakening frequency owing to hand numbness and tingling	0.040*	0.166
Problem with handling objects	0.035*	0.558
Problem with writing	0.080	0.506
Problem with buttoning	0.287	0.344
Problem with holding book	0.306	0.075
Problem with holding phone	0.502	0.018*
Problem with opening bottle	0.223	0.029*
Problem with daily household chores	0.506	0.776
Problem with holding bag	0.306	0.258
Problem with bathing and dressing	0.333	0.644
* $p<0.05$		

Table 2 depicts a comparison of electrodiagnostic results in the case and control groups. It is apparent from the table that in the case group, median nerve sensory latency mean significantly diminished following the treatment; even so, median nerve sensory amplitude mean and median nerve sensory conduction velocity mean went up subsequent to the treatment (amelioration). It is apparent from the table that there was no significant difference amongst electrodiagnostic results in the control group.

Discussion

The present study was designed to assess the effect of administration of vitamin B6 with a dose of 120 mg/day for 3 months upon clinical symptoms and electrodiagnostic results in patients with mild to

moderate CTS. Treatment with vitamin B6 in CTS patients in the case group alleviated several clinical symptoms such as nocturnal pain severity, nocturnal awakening frequency due to pain, daily pain, daily pain frequency, daily pain persistence, hand numbness, hand weakness, hand tingling, severity of nocturnal numbness and tingling, nocturnal awakening frequency owing to hand numbness and tingling, and clumsiness in handling objects. Moreover, there were improvements in sensory electrodiagnostic results incorporating increased median nerve sensory latency mean, increased median nerve sensory amplitude mean and increased sensory conduction velocity mean in this group. However, none of these results was observed in the control group. There were no significant differences in the results of Phalen's and Tinel's tests before and

after treatment in both studied groups. To date, a large body of literature has investigated the effect of vitamin B6 upon symptoms and electrodiagnostic results in patients with CTS; nonetheless, the controversy about scientific evidence has raged unabated. Ellis *et al.* reviewed the literature concerning impact of vitamin B6 upon CTS and found that the influence of vitamin B6 upon CTS symptoms was demonstrated in 8 studies, although 6 studies did not corroborate these findings.²¹ The authors also mentioned that the most important limitation for these studies lied in the relatively small sample size. Kasdan and Janes studied 1075 patients with CTS over 12 years symptoms were alleviated in 14.3 % of patients treated conservatively before 1980, with one or a combination of splinting anti-inflammatory drugs, job or activity modification, and steroid injections. Subsequent to vitamin B6 (pyridoxine) usage as a conservative treatment in 1980, Satisfactory improvement was achieved in 68 % of 494 patients treated with vitamin B6 at a dose of 100 mg.²⁰ Predicated upon this study, a course of treatment at aforementioned dose was recommended,²⁰ even so, two sources of uncertainty lied in this investigation. Firstly, it was a retrospective study. Secondly, it lacked a control group. These findings corroborated our results with respect to alleviation of CTS symptoms. On the other hand, Stransky *et al.* studied 15 patients with CTS receiving vitamin B6 and placebo for 10 weeks and reached different conclusions, finding no difference in symptoms and electrodiagnostic results before and after treatment in the cases and controls.²² Spooner *et al.* reported that administration of vitamin B6 at a dose of 200 mg/day for 12 weeks did not exert any effect upon pain severity, nocturnal numbness and tingling in CTS patients.¹⁹ Laso Guzman *et al.* traced the effect of vitamin B6 treatment with a dose of 150 mg/day for 3 months upon 12 CTS patients requiring surgery and observed that clinical symptoms and electrodiagnostic results improved in half of them.²³ The authors finally concluded that administration of vitamin B6 is beneficial for patients with CTS.²³ In contrast to these findings, the present study exhibited an improvement exclusively in sensory diagnostic results. Bernstein and Dinesen investigated the impact of vitamin B6 on and electrodiagnostic results and highlighted beneficial changes in pain severity and sensory latency results.²⁴ The authors also pointed to concurrent improvement of symptoms and electrodiagnostic results following vitamin B6 treatment.²⁴ Aufiero *et al.* reviewed the literature regarding administration of vitamin B6 for treatment of CTS and reported that in some studies the treatment produced positive effects upon symptoms and electrodiagnostic results; although they showed that some studies did not accord with the influence of vitamin B6 upon CTS.²⁵ The authors finally emphasized the administration of vitamin B6 to treat CTS.²⁵ They also recommended two mechanisms by which vitamin B6 treatment affects CTS as follows: 1) mitigation of vitamin B6 dependent-neurological

problems 2) vitamin B6 effect as analgesic bringing about decreased pain threshold.²⁵ It is worth noting that there has been little agreement in the literature on the alleviation of vitamin B6 dependent-neurological problems. Lack of vitamin B6 in CTS patients has been demonstrated in a study;²¹ howbeit, the association between lack of vitamin B6 and CTS was rejected elsewhere.²³ Results of the present study in terms of symptoms and electrodiagnostic assessments confirmed therapeutic effect of vitamin B6 upon CTS and were consistent with those of Bernstein and Dinesen.²⁴

As mentioned above, preceding research findings into role of vitamin B6 has been inconsistent. There would be several plausible explanations for the disagreement in the following order: 1) Difference in sample size: some previous studies suffered from a serious drawback, that is, small sample size. This may result in erroneous or indefinite conclusions.²⁴ 2) Problems with methodology: a major weakness with the previous studies was old methods. Indeed, questions have raised about preciseness of preliminary studies. Moreover, it appears that conducting controlled and non-retrospective studies is essential in this regard. In fact, taking these issues into account was a strong point in the present study. 3) Difference in dose and duration of treatment with vitamin B6: in present study, CTS patients received a treatment at a dose of 120 mg/day for 3 months. Efficacy and safety of this dose of vitamin B6 have been demonstrated in the literature.⁹ 4) Uncontrolled CTS severity: patients with mild to moderate CTS were exclusively assessed in the present study on the grounds of surgery indication for severe CTS. To clarify, Laso Guzman *et al.* investigated the impact of vitamin B6 upon CTS patients requiring surgery and observed that vitamin B6 treatment mitigated the symptoms, although it did not obviate the need for surgery.²³ Another study conducted by Folkers *et al.*²⁶ produced results which corroborated the findings of Laso Guzman *et al.*²³ Thereby, selection method is of crucial importance. Indeed, this was a benefit considered in the present study. 5) Method of investigation of symptoms: In order to assess the effect of vitamin B6 treatment upon CTS symptoms, a questionnaire was used that firstly covered all aspects of patients' life and secondly was simple and comprehensible and thirdly facilitated statistical comparison by quantifying answer choices (increasing the scores indicated symptom exacerbation).

Returning to the hypothesis posed at the beginning of this study, it is possible to state that administration of vitamin B6 in patients with mild to moderate CTS alleviates many clinical symptoms incorporating nocturnal pain severity, nocturnal awakening frequency due to pain, daily pain, daily pain frequency, daily pain persistence, hand numbness, hand weakness, hand tingling, severity of nocturnal numbness and tingling, nocturnal awakening frequency owing to hand numbness and tingling, and clumsiness in handling objects. The results of this study indicate that

administration of vitamin B6 in patients with mild to moderate CTS ameliorates sensory diagnostic results. On another reading, it decreases median nerve sensory latency average, increases average of median nerve sensory amplitude and median nerve conduction velocity. Taken together, these results suggest that vitamin B6 treatment at a dose of 120 mg/day does not exert deleterious side effect and mitigates clinical symptoms. Thus, vitamin B6 at this dose is

recommended for CTS treatment. Additionally, a limitation of the current study was the relatively limited number of participants precluding us from studying the effect of different doses of vitamin B6 upon CTS. Hence, further investigation with various vitamin B6 doses, having more sample size and analysis of serum pyridoxine yields illuminating insight into treatment of CTS.

Table 2. A comparison of electrodiagnostic (NCV-EMG) results of CTS patients in the case and control groups before and after treatment.

Variables	P value (Before and after treatment)	
	Case group	Control group
Median nerve distal motor latency	0.178	0.879
Median nerve proximal motor latency	0.290	0.386
Median nerve distal motor amplitude	0.397	0.572
Median nerve proximal motor amplitude	0.506	0.518
Median nerve motor conduction velocity	0.498	0.514
Median nerve motor F	0.080	0.095
Median nerve sensory latency	0.001*	0.818
Median nerve sensory amplitude	0.008*	0.178
Median nerve sensory conduction velocity	0.034*	0.846
Ulnar nerve distal motor latency	0.592	0.732
Ulnar nerve proximal motor latency	0.427	0.921
Ulnar nerve distal motor amplitude	0.628	0.685
Ulnar nerve proximal motor amplitude	0.250	0.124
Ulnar nerve motor conduction velocity	0.948	0.278
Ulnar nerve motor F	0.159	0.299
Ulnar nerve sensory latency	0.642	0.737
Ulnar nerve sensory amplitude	0.072	0.752
Ulnar nerve sensory conduction velocity	0.892	0.579
Median nerve distal motor latency	0.178	0.879
* p<0.05		

Conflict of interest

We declare that we do not have any conflict of interest.

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