INTRODUCTION

The most frequent entrapment neuropathy of the upper limbs is carpal tunnel syndrome (CTS). There are several conservative or surgical options available for the treatment of CTS. The most common conservative treatments include wrist splinting, non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroid injection into the carpal tunnel, systemic steroids, pyridoxine (Vitamin B6), and diuretics. Some researchers have suggested that Vitamin B6 deficiency can lead to CTS, and that pyridoxine is a suitable conservative option for the treatment of CTS. However, other researchers have not found any obvious benefit with pyridoxine in CTS.

ABSTRACT

Objective: Carpal tunnel syndrome (CTS) is a common disorder that can be treated with surgery or conservative options. There have been several studies of Vitamin B6 as a conservative treatment for CTS, but its effectiveness remains controversial. Our objective was to compare the efficacy of splinting and placebo with splinting and Vitamin B6 in patients with CTS.

Methodology: We conducted a randomized case-control trial in the neurology clinic of Alzahra hospital, Isfahan, Iran, between March 2009 and March 2010. Ninety outpatients who were at least 18 years old and who had clinically and electrophysiologically confirmed idiopathic CTS were included in the study. The patients were randomly allocated to two groups: placebo plus wrist splinting (control) or Vitamin B6 supplementation (for six months) plus wrist splinting (case) for at least three months. Eighty-six patients (95%) completed the study. The primary endpoint was improved sensory nerve conduction by the median nerve.

Result: Evaluations performed at three months follow up revealed a significant difference in the mean peak sensory latency between the case and control groups (p=0.002). A total of 65% of patients in the case group reported subjective symptom relief compared with 58% of patients in the control group. These data suggest that splinting combined with Vitamin B6 supplementation is more effective than splinting alone in improving electrophysiological parameters and subjective symptoms of CTS.

Conclusion: Vitamin B6 is an effective treatment in mild and moderate CTS and could be considered as a conservative treatment.

KEY WORDS: Vitamin B6, Carpal tunnel syndrome, Splinting, Electrodiagnosis.
To the best of our knowledge, there have been no randomized clinical trials comparing splinting alone with splinting plus Vitamin B6 for the treatment of CTS.

The aim of this study was to compare the effect of splinting alone with splinting plus Vitamin B6 in CTS.

**METHODOLOGY**

This randomized clinical trial was performed at the neurology clinic of Alzahra Hospital, Isfahan, Iran, between March 2009 and March 2010. The study was approved by the ethics committee of Isfahan University of Medical Sciences. Written informed consent was obtained from all patients who participated in the study. Out patients with clinically and electrophysiologically confirmed CTS who attended our health center and who met the selection criteria for the trial were enrolled. Clinical confirmation of CTS was achieved by noting compatible symptoms such as numbness, burning, and tingling or pain in the wrists, hands, or fingers, which are suggestive of median nerve involvement.7 Electrodiagnostic confirmation of CTS was based on the guidelines of the American Association of Electrodiagnostic Medicine. 4 Inclusion and exclusion criteria were specified with the aim of ensuring a relatively uniform group of patients with idiopathic CTS.

**Inclusion criteria were:**
* Clinically and electrophysiologically confirmed CTS
* Patients age ≥ 18 years
* Available for the three-month period of the study

**Exclusion criteria were:**
* Pregnant women
* Previous treatment with a wrist splint
* History of previous carpal tunnel release
* Currently receiving other treatment for CTS
* History of wrist or median nerve injury due to trauma (e.g. contusion, fractures) or prior wrist surgery
* History suggestive of possible underlying causes of CTS such as diabetes mellitus, thyroid disease, rheumatoid arthritis, anatomic abnormalities of the wrist or hand, and pregnancy
* Clinical signs and symptoms or electrodiagnostic studies suggesting conditions that could mimic CTS or interfere with its validation, such as cervical radiculopathy, brachial plexopathy, polyneuropathy, among others.

A group of 90 CTS cases was selected for the trial based on the inclusion and exclusion criteria. Afterward, a primary evaluation of baseline electrophysiological values and possible prognostic factors such as age, sex, dominant side, and bilateral symptoms was made.

The patients were then randomly divided into two groups. The first group of patients (case group) were treated with 80 mg/day Vitamin B6 plus splinting, and the second group (control group) received a placebo along with splinting. The placebo and Vitamin B6 tablets were the same shape, color, and size.

In patients with bilateral symptoms, splinting was prescribed for the most affected hand. At present, there are no standard guidelines for the wearing of splints, but in this study, the patients were directed to wear the splint continuously at night for at least three months. The only other therapy allowed during the study was Naproxen 250 mg/day, which was prescribed by the neurologist for pain relief if required. To avoid wrist and finger stiffness, patients were educated in the performance of a number of mild range-of-motion exercises throughout the study.

The patients were permitted to continue their normal activities without any limitations. They were followed up by telephone throughout the study to see if they had continued with their prescribed therapy or not, and to ask about possible side effects. After three months, 86 patients completed the study. The electrophysiological assessments were repeated at the end of the trial. Based on the nerve conduction study (NCS) findings, patients were divided into three categories: Mild (3.5< distal sensory latency <4.5); Moderate (4.5< distal sensory latency<5.5); and Severe (distal sensory latency ≥ 5.5). In addition, the patients were asked about subjective symptom relief.

**Outcome Assessment:** Although there is currently no agreement on the best means of assessing treatment effects, in this study, the results of the electrodiagnostic study were considered the primary endpoint. Subjective assessments of symptom improvement were based on the patients reporting of their symptoms as ‘improved’ (complete recovery or significant recovery) or ‘not improved’ (mild recovery, no change, mildly worse, or much worse), and were considered the secondary end point.

**Statistical Analyses:** The results are presented as mean ± standard deviation (SD). The mean NCS values were calculated before and after the intervention. Independent sample t tests were used to
identify differences between the analyzed case and control groups. A P-value ≤ 0.05 was considered statistically significant. Statistical analyses were performed using SPSS 14 for Windows (SPSS, Inc., Chicago, IL, 1996).

RESULTS

Eighty-six patients completed the study. They ranged in age from 38 to 67 years. The mean age of the patients in the case and control groups was 48.18±2.93 years and 45.89±3.56 years, respectively; there was no significant difference between the groups in terms of age (p=0.25). Thirty patients in the case group (69.87%) and 33 patients in the control group (76.7%) were women; there was no significant difference between the groups in terms of sex (p = 0.47) as summarized in Table-I.

The mean sensory peak latency of the median nerve before and after the intervention was 5.2±1.1 and 4.8±1.2, respectively, in the case group (p =0.002), and 5.1±1.1 and 4.9±1.3, respectively, in the control group (p = 0.98). Improvement in median distal sensory latency was observed in both groups; however, the improvement was not statistically significant in the control group. Furthermore, a significant difference in mean peak sensory latency was found between the case and control groups (p=0.002).

A total of 65% of subjects reported subjective symptom relief (improved) after the use of a splint plus Vitamin B6 whereas only 58% of patients reported symptom improvement from the splint alone. No serious side effects were reported by the patients.

DISCUSSION

CTS is the most common entrapment neuropathy, with a total lifetime risk of 10%. It usually occurs after the third decade of life, and tends to affect more women than men (3: 1 ratio). The majority of CTS cases are idiopathic; however, many predisposing factors for CTS have been suggested, including diabetes mellitus, thyroid dysfunction, pregnancy, and some rheumatologic diseases. Slow but progressive ischemia and mechanical deformation of the median nerve as a consequence of elevated pressure within the carpal tunnel is believed to be the underlying pathophysiology of CTS. Symptoms consist of sensory complaints such as tingling, a burning sensation, and numbness in the territory of the median nerve, pain in the hand, and motor deficits such as weakness and atrophy of the thenargroup of muscles, and reduction in the dexterity of hand movements.

Electrodiagnostic studies and clinical findings are both essential for diagnosing CTS. The most sensitive electrodiagnostic test for CTS is the median nerve sensory conduction study, which provides evidence of a distal delayed sensory latency in 70–90% of cases. Several conservative and surgical alternatives have been used for the treatment of CTS. There is currently no agreement on the selection criteria for each treatment methodology, but in severe cases the recommended treatment is often surgery. Patients with mild symptoms are usually managed with nonoperative and alternative options. Initially, conservative treatments are effective in approximately 80% of cases of CTS; however, the rate of recurrence of symptoms is reported to be close to 80% after one year.

Conservative options should be tried for those who are not able to undergo surgery or for those who do not wish to undergo surgery. The most frequently used conservative treatments are splinting, corticosteroid injection into the carpal tunnel, NSAIDs, systemic steroids, pyridoxine (Vitamin B6), and diuretics. To the best of our knowledge, few well-designed trials have evaluated and compared these treatments, and high quality...
supporting evidence is only available for splinting and steroids. There is conflicting evidence as to the benefits of oral pyridoxine in the treatment of CTS. It has been assumed that idiopathic CTS may be a manifestation of Vitamin B6 deficiency, and some investigators have declared that Vitamin B6 supplementation can reduce symptoms and others have claimed that pain alleviation is a consequence of Vitamin B6’s anti-nociceptive nature.

In 1973, Ellis and Presley suggested a relationship between Vitamin B6 deficiency and CTS. Thereafter, several additional studies emerged that were suggestive of a causal association in many CTS patients. However, numerous reports have failed to prove an exact causal relation between Vitamin B6 deficiency and CTS. Indeed, the connection between pyridoxine deficiency and CTS is multifaceted and remains poorly understood. The cause of this complexity may be the fact that pyridoxine has numerous biological functions and separating the contributions of these to CTS is not easy.

Our data suggest that combined treatment with splinting and Vitamin B6 is more effective than splinting alone in terms of the effects on electrophysiological parameters and subjective improvement in clinical status, especially among patients with mild and moderate forms of CTS. The main concern regarding the therapeutic use of Vitamin B6 in CTS is its safety as it can be toxic. Vitamin B6-related sensory neuropathy has been reported several times and was most often associated with dosages >1000 mg/day.

Overall, most studies recommend a dose of between 40 and 500 mg/day for safety, and to avoid the development of neuropathy. In our study, the assessment of side effects was not well designed, but oral questioning of patients during follow-up revealed no significant side effects related to the use of Vitamin B6, suggesting that doses < 200 mg/day can be safe. Finally, the findings of this trial are supported by the results of several studies that have used Vitamin B6 for CTS. A large, well-designed study should allay concerns as to the effectiveness and safety of Vitamin B6 in CTS.

CONCLUSION

Although the effectiveness of Vitamin B6 in CTS is controversial, our clinical trial results indicate that Vitamin B6 is a suitable conservative treatment for CTS, especially among patients with mild and moderate symptoms.

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REFERENCES