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Role of Vitamin D Deficiency on The Onset and Prognosis of Bell's Palsy

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Abstract

Objective: To investigate the role of vitamin D on the etiology and the prognosis of Bell's Palsy (BP).

Methods: A prospective controlled clinical study was conducted on patients diagnosed as BP and healthy volunteers as control group. Vitamin D levels were measured in all subjects. In a homogenous group, effects of vitamin D on the etiology and prognosis were evaluated according to House-Brackmann (HB) grades of participants.

Results: Vitamin D levels were similar in the BP and control groups. In BP group, patients with advanced HB grades had lower vitamin D levels. Moreover poorer outcomes (p=0.01) were achieved in patients who had <10ng/ml vi-tamin D, regardless the initial HB grade.

Conclusion: Our results demonstrated a possible role of vitamin D levels on the prognosis of BP. Lower vitamin D levels may have a negative effect on recovery particularly in patients with advanced grades.

Keywords: Vitamin D, facial paralysis, Bell palsy

Introduction

Bell's palsy (BP) is the most common acute mono-neuropathy of the facial nerve without any detectable causes.[1] This phenomenon was named with respect to the famous anatomist Sir Charles Bell. It is a rapid and usually unilateral weakness or paralysis of the 7th cranial nerve. Although BP is typically a self-limited disease, poor long-term outcomes have been reported which can be devastating to the patient.[2] According to epidemiological studies the disease is more common during pregnancy, in patients with compromised immune systems, diabetes mellitus or upper airway infections.[3,4] Previous reports describe a number of prognostic factors such as age, accompanying pain, diabetes, initial grade of the palsy or electrophysiological test results.[5-7]

Vitamin D is a key hormone in the skeletal physiological actions by regulating the calcium and phosphorus metabolism. In recent years there is a great interest on the

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role of vitamin D on the extraskeletal actions. Emerging evidence suggests that the deficiency of vitamin D is associated with a wide range of disorders like multiple sclerosis, hypertension, cardiometabolic diseases, diabetes and related complications.[8, 9, 10] In addition to this, recent studies indicate a relationship between vitamin D and peripheral neuropathy.[11,12]

In this study we aimed to investigate the role of vitamin D on the etiology and the prognosis of BP which is actually a peripheral neuropathy.

Materials and Methods

The present work is a prospective controlled clinical study. The protocol was approved by the ethics committee (EC) of the Kecioren Research and Training Hospital (EC number: 897). All patients signed an informed consent before the study and the principles in the Declaration of Helsinki were followed.

The study subjects comprised of adult patients diagnosed as BP in the otolaryngology outpatient clinic of our hospital within 72 hours from onset and age and sex matched healthy volunteers. The exclusion criteria were any metabolic disorders which can change the metabolism of vitamin D, central or peripheral nervous system diseases, use of drugs known to decrease 25-hydroxy vitamin D such as anticonvulsants, cardiovascular, liver or kidney diseases, pregnancy, any kind of malignancy and individuals receiving vitamin D supplement therapy. Patients with any detectable situations that can cause facial palsy such as previous otologic operation, head and neck tumors or head trauma were also excluded.

All of the diagnosis, staging, evaluation, treatment and follow-up protocols were implemented according to the clinical practice guideline of American Academy of Otolaryngology Head and Neck Surgery.[2] After detailed otolaryngological examination facial nerve evaluation of the patients was carried out via the House-Brackmann (HB) grading system.[6] After the diagnosis, every subject received a 10-day course of oral prednisolone therapy (60 mg per day for 5 days than tapered over for 5 days).[13] All patients were followed-up at 3 months after the initial diagnosis. Full recovery was noted as HB grade 1 at the final examination.

Serum vitamin D (25-hydroxy vitamin D), parathormone, calcium, albumin and phosphate levels were measured in all subjects. Vitamin D deficiency was considered as levels <20ng/ml in accordance to WHO definition.[14]

Participants were divided into 2 groups as BP and control. Vitamin D levels of both groups were compared. In addition to this, effects of vitamin D levels on prognosis were evaluated separately in all BP patients and BP patients with different vitamin D levels. Participants in the study group (patients with Vitamin D Deficiency) were given a standart theraphy with a loading dose of 50,000 IU cholecalciferol per week for 8 weeks, and continued to 1,500 IU maintenance therapy.

Statistical analysis

All the statistical analyses were performed by using the Statistical Package for Social Sciences 22.0 (SPSS Inc., Chicago, IL). The descriptive values were given as number (n), percent (%), mean ($\bar{x}$), standard deviation (SD), median and minimum-maximum. The normality of data distribution was evaluated by using Shapiro-Wilk or Kolmogorov-Smirnov tests. A two-tailed Student's t test was used to compare the differences in the mean values of normally distributed variables between patient and control. The Wilcoxon test was used to compare vitamin D levels and BP recovery rate in 3rd month. A p value off less than 0.05 was considered to show a statistically significant result.

Results

A total number of 91 patients were included in the study. BP group consisted of 43 patients (23 female and 20 male) with a mean age of 41.88 years (range 18-91) while the control group consisted of 48 patients (20 female and 28 male) with a mean age of 38.77 years (range 18-66). The groups were statistically similar in terms of age and gender.

The mean vitamin D levels were 15.96 and 18.61 ng/ml in BP and control groups respectively (p=0.956) (table 1). Parathormone, calcium, albumin and phosphate levels

Table I. The Comparison of Vitamin D Levels Between Bell's Palsy and Control Groups.

	n	Vitamin-D levels x̄±SD	Median (min-max)
BP	43	15.96 ± 9.00	14.90 (4.70-58.10)
Control	48	18.61 ± 19.01	13.35 (4.40-133.70)
p		0.956*	

BP: Bell's Palsy, *: Non-significant, Independent sample t-test

Table II. The mean vitamin D levels and recovery rates of Bell's Palsy group according to House-Brackmann grading system.

HB grade	n	Vitamin-D levels x̄±SD	Full recovery*
2	16	19.67 ± 11.65	93.8%
3	17	17.12 ± 5.40	94.1%
4	10	8.06 ± 1.89	10%

HB: House-Brackmann, *: HB grade 1 at 3 months.

were similar between the two groups. In BP group, numerical distribution of patients according to their HB grades were 16 for HB grade 2, 17 for HB grade 3 and 10 for HB grade 4. There were no patients with HB grade 5 or 6. The mean vitamin D levels and recovery rates of BP group were summarized in table 2. Most of the patients with an initial HB grade 2 and 3 recovered successfully (93.8% and 94.1%). On the other hand the vast majority of cases with HB grade 4 recovered to HB grade 2 (80%) after 3 months with a statistical significance (p<0.001). Regardless of vitamin D deficiency status of the patients, the patients were divided into 3 subgroups depending on different vitamin D levels (table 3). When all BP patients were evaluated in terms of vitamin D levels, poorer outcomes (p=0.01) were achieved in patients who had <10ng/ml vitamin D, regardless the initial HB grade (table 3).

Discussion

BP has a self-limiting character but in cases where full recovery can not be achieved, the disease may have dramatic impact on patient's quality of life. Therefore proper and prompt treatment is necessary as soon as the diagnosis is made. Prognostic factors in BP were investigated in previous studies. Lee et al studied the prognostic effect of age on BP and found no major correlation.[15] Baba et al reported the presence of an identifiable response in ENoG may indicate a favorable outcome in children with BP.[16] Another study in which the role of diabetes mellitus in the clinical presentation and prognosis of BP was investigated, the authors did not find any differences on prognosis in diabetic and nondiabetic patients.[17] In two recent studies, neutrophil to lymphocyte ratio (NLR) was indicated as a prognostic factor. An association between higher NLR levels and worse prognosis of BP was reported.[18,19] Apart from those, numerous factors have been indicated as prognostic markers such as procalcitonin, blink reflex, vestibular evoked myogenic potentials or high-frequency ultrasonography of the facial nerve. [20-23]

Table III. The mean vitamin D levels and recovery rates of Bell's Palsy group.

Vitamin-D level	n	Full recovery*	p
<10 ng/ml	17	58.8%	0.014**
10-30 ng/ml	18	83.3%	NS
>30 ng/ml	8	87.5%	NS

*: HB grade 1 at 3 months, **: Statistically significant, NS: non-significant, Wilcoxon test

Despite the recent interest on the role of vitamin D levels in many extraskeletal diseases, relationship between BP and vitamin D levels is less well studied. There are two forms of vitamin D in circulation; 25-hydroxy vitamin D and 1,25-dihydroxy vitamin D. The latter one is referred as the active form while the measurement of 25-hydroxy vitamin D concentration reflects total body vitamin D reserves.[24] Rather than skeletal effects, it is now well known that vitamin D plays a role in the regulation of neurotrophine levels.[25] Studies demonstrated that ergocalciferol (vitamin D2) and cholecalciferol (vitamin D3) promoted axon sparing/regeneration and induced a significant elec-

trophysiological nerve recovery.[26,27] It is well established that neurons and glial cells express vitamin D receptors which stimulates the expression of neurotrophines.[28] Vitamin D is also involved in the regulation of genes which are relevant to myelination process. *Prx* plays a role in peripheral nerve myelin maintenance. [29] *Tspan2* is required for the oligodendrocyte terminal differentiation into myelin forming glia.[30] It is undoubtly that vitamin D is one of the key molecules in the complex process of nerve regeneration. In an animal model of traumatic facial nerve injury, Montava et al demonstrated the positive effect of vitamin D3 on the myelination and recovery. [31]

According to our results, vitamin D levels did not have an impact on the onset of BP as the mean levels were similar between the study and control group. On the other hand in BP group, patients with HB grade 4 have lower vitamin D levels when compared to the rest of the group. The recovery rate was also lower in patients with HB grade 4 in BP group. Moreover, patients with higher vitamin D levels tend to recover better than those with lower vitamin D levels (Table 3). These results suggested that vitamin D may have a role on the prognosis of BP. Lower vitamin D levels may have a negative effect on recovery particularly in patients with advanced grades.

The limitations of the study are the lack of electrophysiological tests, limited number of patients and the lack of subjects with HB grade 5 and 6. In the present work our aim was to determine the effect of vitamin D levels on the prognosis regardless the other factors. Thus further electrophysiological tests were avoided. To our knowledge, this is the first study directly evaluating the relationship of vitamin D and the prognosis of BP. Studies with more patients with homogenous HB groups are planned.

Our results demonstrated a possible role of vitamin D levels on the prognosis of BP. Further studies with larger groups will provide more information on the issue.

The effect of vitamin D supplementation on the prognosis of the disease at such a short period was not evaluated in this study. Further studies involving larger patient groups and longer periods are needed to evaluate the effect of vitamin D supplementation on the BP prognosis.

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