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Original Article *Özgün Araştırma*

EVALUATION OF THE EFFECTIVENESS OF ALPHA LIPOIC ACID IN THE TREATMENT OF BELL'S PALSY

Bell Paralizi Tedavisinde Alfa Lipoik Asitin Etkinliğinin Değerlendirilmesi

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ABSTRACT

Objective: This study aims to evaluate the efficacy of alpha-lipoic acid in the treatment of Bell's palsy by using the House-Brackmann grading system and electromyography.

Material and Methods: A total of 33 patients were included in this retrospective study. Patients were divided into two groups. Group 1 included 18 patients who received 300 mg daily alpha-lipoic acid in addition to Bell's palsy treatment. Group 2 included 15 patients who only received Bell's palsy treatment. House-Brackmann grading score at admission, 21st day and at 3rd month were noted in both groups. The results of electromyography performed at 21st day were also scanned. Patients were classified as good prognosis (neuropraxia) and poor prognosis (axonotmesis and neurotmesis) according to electromyography results. The two groups were compared according to House-Brackmann grades and electromyography results.

Results: Group 1 consisted of 10 women and 8 men, while Group 2 consisted of 6 women and 9 men. There was no difference between the two groups according to whether Bell's palsy was on the right or left side. House-Brackmann grading score of the groups at 21st day and 3rd month were significantly lower than House-Brackmann grading score at admission. There was no significant difference between the two groups according to House-Brackmann grades. There was no difference between the groups in terms of compound muscle action potential ratio and prognosis.

Conclusion: Although alpha-lipoic acid is used for nerve regeneration in various diseases, it did not demonstrate a significant effect on Bell's palsy treatment in our study.

***Keywords**: Alpha-lipoic acid, Bell's palsy, electromyography, House-Brackmann Grading System*

ÖZ

Amaç: Bu çalışma, Bell paralizisi tedavisinde alfa-lipoik asidin etkinliğini House-Brackmann derecelendirme sistemi ve elektromyografi kullanarak değerlendirmeyi amaçlamaktadır.

Gereç ve Yöntemler: Bu retrospektif çalışmaya toplam 33 hasta dahil edildi. Hastalar iki gruba ayrıldı. Grup 1, Bell paralizisi tedavisine ek olarak günde 300 mg alfa-lipoik asit alan 18 hastayı içeriyordu. Grup 2, sadece Bell paralizisi tedavisi alan 15 hastayı içeriyordu. Her iki grupta da kabulde, 21. günde ve 3. ayda House-Brackmann derecelendirme skoru kaydedildi. 21. günde yapılan elektromyografi sonuçları da tarandı. Hastalar elektromyografi sonuçlarına göre iyi prognoz (nöropraksi) ve kötü prognoz (aksonotmezis ve nörotmezis) olarak sınıflandırıldı. İki grup House-Brackmann dereceleri ve elektromyografi sonuçlarına göre karşılaştırıldı.

Bulgular: Grup 1, 10 kadın ve 8 erkekten, Grup 2 ise 6 kadın ve 9 erkekten oluşuyordu. Bell felcinin sağda veya solda olmasına göre iki grup arasında fark yoktu. Grupların 21. gün ve 3. aydaki House-Brackmann derecelendirme skoru, başvuru sırasında House-Brackmann derecelendirme skorundan anlamlı derecede düşüktü. House-Brackmann derecelerine göre iki grup arasında anlamlı fark yoktu. Gruplar arasında bileşik kas aksiyon potansiyeli oranı ve prognoz açısından fark yoktu.

Sonuç: Alfa-lipoik asit çeşitli hastalıklarda sinir rejenerasyonu için kullanılmasına rağmen çalışmamızda Bell paralizisi tedavisine anlamlı bir etki göstermemiştir.

***Anahtar Kelimeler**: Alfa-lipoik asit, Bell paralizi, elektromyografi, House-Brackmann Derecelendirme Sistemi*

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INTRODUCTION

Bell's palsy is the most common cause of facial paralysis. It may manifest as unilateral acute peripheral paresis or paralysis. Bell's palsy is a neuropathy that is also referred to as idiopathic peripheral facial paralysis. Its incidence ranges between 11.5-53.3 per 100,000 individuals. Bell's palsy is diagnosed after known causes of facial paralysis are ruled out. Since its etiology in unknown, there is no definitive treatment. Steroid therapy, steroid and antiviral combined therapy, surgical decompression, hyperbaric oxygen therapy and alternative treatment methods such as acupuncture are currently available (1-4).

Alpha-lipoic acid (ALA) is an antioxidant naturally synthesized in plants and animals. In humans, it plays a role in scavenging free radicals, reduction of lipid peroxidation, regeneration of damaged tissues, chelation of metals, and as a cofactor in the ketoglutarate dehydrogenase complex, which is an antioxidant enzyme (5,6). Alpha-lipoic acid is used in the treatment of diabetic neuropathy, neuropsychiatric diseases, and cardiovascular diseases. Alpha-lipoic acid has been shown to reduce oxidative stress and improve distal nerve conduction by increasing nerve blood flow (7,8).

In this study, we aimed to demonstrate the regenerative capability of ALA on neuropathy in patients with Bell's palsy. The effect of ALA on Bell's palsy was evaluated using the House-Brackmann (HB) grading system and needle electromyography (EMG).

MATERIALS AND METHODS

This study was carried out with the approval of the local ethics committee (Toros University Scientific Research and Publication Ethics Board Committee, date: 19.08.2020, issue number: 46.). Informed consent was obtained from all patients. The data of 33 patients between January 2015 and June 2018 were retrospectively evaluated.

Among the patients with available records, 18 were Bell's palsy patients receiving 300 mg daily ALA for other reasons (Group 1). The remaining 15 patients were Bell's palsy patients who were not receiving ALA treatment (Group 2). Patients of both groups received 150 mg IV methylprednisolone (Prednol-L®, Mustafa Nevzat, Istanbul) on the first day, which continued as 1 mg/kg systemic steroid treatment, then dosage was gradually decreased then discontinued. In addition to methylprednisolone treatment, 250 mg daily vitamin B1 + 250 mg vitamin B6 + 1 mg vitamin B12 (Nerox-B12®, Abdi Ibrahim, Istanbul) were given to both groups daily. Group 1 received additional 250 mg daily vitamin B1 + 250mg vitamin B6 + 1 mg vitamin B12 + 300 mg alpha-lipoic acid (Beneday®, Takeda, Istanbul).

Patients with Bell's palsy, between ages 18-75, who were admitted within the first 72 hours, and received alpha-lipoic acid treatment for at least three months without polyneuropathy were included in Group 1. In group 2, Bell's palsy patients, between ages 18-75, without any comorbidity were included in the study. Children, pregnant women, diabetics, recurrent Bell's palsy, and patients with contraindications for vitamin B and ALA were excluded from the study.

Age and gender of the patients were noted. House-Brackmann grades at the time of admission, 21st day, and 3rd month of both groups were accessed from archive records (Table 1). Differences in HB grades were used when comparing both groups.

Results of needle EMG conducted on 21st day were obtained. Compound muscle action potential (CMAP) amplitudes in EMG were used to calculate affected orbicularis oris CMAP/non-affected orbicularis oris CMAP ratios. Patients were classified as good prognosis (neuropraxia) and poor prognosis (axonotmesis and neurotmesis) according to needle EMG results and were compared.

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Table 1: House-Brackmann (HB) grading system

Grade	Characteristics
I	Normal facial function
II	Slight weakness on close inspection
	Complete eye closure with minimal effort
III	Obvious weakness, but not disfiguring
	Complete eye closure with effort
IV	Obvious weakness or disfiguring asymmetry
	Incomplete eye closure
V	Motion barely perception
	Asymmetry at rest
VI	No movement

Statistical Analysis

SPSS Statistics 21.0 (IBM SPSS Inc, Chicago) program was used for statistical analysis. Descriptive statistics related to continuous data were expressed as mean±standard deviation. Kolmogorov–Smirnov test and Shapiro–Wilk test was used to assess whether or not the data had normal distribution. Age, initial HB and CMAP values were normally distributed. Other values were not normally distributed in Group 1 and Group 2. Normally distributed data were compared with Paired Sample t test. Comparison of not normally distributed data between the groups was assessed with Mann-Whitney U test. Prognosis between groups was performed with Chi-Square test. The value of $p<0.05$ was considered statistically significant.

RESULTS

A total of 33 patients were included in the study, consisting of 18 patients in Group 1 and 15 patients in Group 2. In Group 1, 10 patients were female (55.6%) and 8 patients were male (44.4%). Group 2 consisted of 6 females (40.0%) and 9 males (60.0%). Mean age was 48.39±17.51 in Group 1 and 43.73±18.46 in Group 2. There was no significant difference between the groups in terms of age and gender ($p=0.102$ and $p=0.231$).

In Group 1, mean HB at admission was 3.78±1.11, was 2.17±0.92 on 21st day and 1.22±0.54 at 3rd month. In Group 2, mean HB at admission was 3.67±0.90, was 2.20±0.77 on 21st day and 1.27±0.45 at 3rd month. In both groups, 21st day HB and 3rd month HB scores were significantly lower compared to initial HB scores ($p<0.001$). In addition, 3rd month HB scores were significantly lower than 21st day scores in both groups ($p<0.001$).

There was no significant difference between Group 1 and Group 2 in terms of the difference between initial HB, 21st day HB and 3rd month HB values (Table 2).

CMAP ratios and the number of patients with good and poor prognosis are shown in Table 3. There was no significant difference between the groups in terms of CMAP ratio ($p>0.05$) (Table 3). Although there were more patients with poor prognosis in Group 2, there was no statistically significant difference between the two groups in terms of prognosis ($p>0.05$) (Table 3).

Table 2: Comparison of groups according to House-Brackmann grading scores

Difference (mean±SD)	Group 1 (Alpha-lipoic acid)	Group 2 (Control)	p*
Initial HB – 21st day HB	1.61±0.60	1.46±0.63	0.654
Initial HB – 3rd month HB	2.55±0.98	2.40±0.73	0.552
21st day HB – 3rd month HB	0.94±0.72	0.93±0.70	0.968

*: Mann-Whitney U test was used. HB; House-Brackmann grading scores.

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Table 3: Comparison of groups according to Electromyography results

	Group 1 (Alpha-lipoic acid)	Group 2 (Control)	p
CMAP ratio (%)	62.30±23.84	61.58±18.44	0.925*
Good prognosis	12 (66.7%)	7 (46.7%)	0.421¥
Poor prognosis	6 (33.3%)	8 (53.3%)	

*: One-Way ANOVA test was used. ¥: Chi-Square test was used. CMAP (Compound muscle action potential) ratio: affected orbicularis oris/non-affected orbicularis oris.

DISCUSSION

Bell's palsy is a common mononeuropathy that equally affects both men and women and can occur at all ages, although it is more common in middle and older ages (9). Although many theories have been proposed, the etiology of Bell's palsy is still unclear. It manifests as paresis or paralysis in upper and lower facial muscles. Ear and neck pain, hyperacusis, and altered facial sensation may be present in 50-60% of cases (10). Loss of taste and changes in salivary secretion may occur (11). The House-Brackmann grading system is most commonly used in determining the grade of Bell's palsy and evaluating its progression (12). In this study, there was no difference between the HB scores of patients who received only methylprednisolone + vitamin B treatment and the patients who received additional ALA. However, HB scores on the 21st day and 3rd month in both groups were found to be significantly lower than the HB scores at admission.

The condition is clinically diagnosed. In addition, audiological examinations and topographic examinations (Schirmer's test, stapes reflex, saliva secretion test, and taste test) are used. Electrophysiological tests are also used. Nerve Excitability Test (NET), Maximum Stimulation Test (MST), Electroneuronography (ENoG), and EMG are electrophysiological tests used in diagnosis.

Electromyography indicates the prognosis of Bell's palsy. Low amplitude fibrillation potentials in muscles may appear in EMG 14-21 days later. Increase in polyphasic reinnervation potentials indicate good potential. Jung et al. evaluated the effect of metabolic syndrome on Bell's palsy using House-Brackmann grading system, EMG and ENoG. Patients were classified into favorable and unfavorable groups and it was shown that Bell's palsy patients with metabolic syndrome had lower recovery rates (13). In our study, there was no significant difference between patients who received ALA and patients who did not receive ALA in terms of CMAP ratio. In addition, patients were grouped according to prognosis, and there was no significant difference between the groups in terms of prognosis.

There is no definitive treatment of Bell's palsy. Steroids, antiviral drugs, combination therapies, eye care, physiotherapy, pentoxifylline, hyperbaric oxygen therapy, acupuncture, and surgical decompression are among treatment modalities (1-4). However, in 2013, according to Bell's palsy guidelines, only eye care and oral steroids were "strong recommendations" (1). According to a review published in 2016, randomized controlled trials demonstrated that corticosteroids have significant benefits in the treatment of Bell's palsy (14).

Alpha-lipoic acid is a necessary coenzyme for mitochondrial energy production found in plants and animals (15). Alpha-lipoic acid is a powerful antioxidant that causes a decrease in oxidative stress, an increase in nerve blood flow and conduction velocity, and a decrease in lipid peroxidation (16,17). Alpha-lipoic acid is used in diabetic neuropathy, neuropsychiatric diseases and cardiovascular diseases. The effectiveness of ALA

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in diabetes-induced polyneuropathy and neuropathic pain has been shown in many studies (18,19). In one meta-analysis, 300-600 mg/day ALA for 2-4 weeks increased nerve conduction velocity and improved neuropathic symptoms in patients with diabetic neuropathy (8). However, one study on 460 diabetic neuropathy patients did not find a significant difference at the primary endpoint between patients who received 600 mg/day ALA for 4 years and patients who received placebo. They reported that ALA provided significant improvement in values such as neuropathy impairment score (NIS), neuropathy impairment score of the lower limbs (NIS-LL), and NIS-LL muscular weakness sub-scores compared to the placebo, however the ALA group showed more severe side effects than the placebo group (20). To the best of our knowledge, the efficacy of ALA in the treatment of Bell's palsy has not yet been studied. In our study, ALA effectiveness in Bell's palsy was evaluated using the HB grading system and EMG. Neither method was able to demonstrate the effectiveness of ALA in Bell's palsy. The main limitation of our study was its retrospective study design. In addition, patients received ALA treatment due to different indications and in various time periods.

Although Bell's palsy is a common disease, there is still no definitive treatment. In our study, the efficacy of ALA, which has not been previously investigated for Bell's palsy was investigated. Bell's palsy patients who were given methylprednisolone + vitamin B were compared with those who received ALA (300 mg/day) + methylprednisolone + vitamin B. There was no significant difference between the group receiving ALA and the group that did not receive ALA. However, significant improvement was observed in both groups. Larger series of prospective clinical studies are needed to further investigate the efficacy of ALA in Bell's palsy.

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