



Efficacy of antiviral therapy in the treatment of peripheral facial paralysis: A tertiary institution experience

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Abstract

Aim: For the treatment of peripheral facial paralysis, the superiority of the use of steroid alone and the use of steroid + antiviral over each other has not been clarified in the literature. In this study, the efficacy of using steroid treatment alone and using a combination of steroid+antiviral treatment in patients we followed up with peripheral facial paralysis in our clinic was questioned retrospectively. It was aimed to clarify the efficacy and superiority of steroid alone and steroid+antiviral therapy in patients with peripheral facial paralysis.

Materials and Methods: One hundred and ten patients who received only steroids and 62 patients who received combination therapy were included in the study. Age, gender, regular drug use, smoking, previous history of facial paralysis, comorbid diseases, initial stage of the disease (House-Brackman/HB staging), treatment protocol and response to treatment were recorded from the files examined. Patients with HB stage ≤ 2 at the 6th month follow-up were considered to have responded well or completely to the treatment.

Results: When the group receiving only steroid treatment and the group receiving steroid + antiviral treatment were compared in terms of age, chronic drug use, gender, and previous facial paralysis, no statistically significant difference was observed. The groups were compared in terms of response to treatment, 88.2% improvement was observed in the steroid group (HB stage ≤ 2), and 91.9% improvement was observed in the combined treatment group. No statistically significant difference was observed ($p=0.605$).

Conclusion: For the treatment of peripheral facial paralysis, the superiority of steroid use alone and combined antiviral + steroid use has not been proven. In the light of the literature, it is recommended that the patient be treated with steroids at the earliest stage.



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Introduction

Idiopathic peripheral facial paralysis, also known as Bell's palsy, is a clinical entity whose etiopathogenesis is not fully elucidated, with an incidence of 11-40 / 100 000 per year [1,2]. It is known that 71% of the patients recover completely if not intervened, and 84% of the patients recover completely and near completely. The remainder continue their lives with permanent facial paralysis sequelae, synkinesis or facial contracture if not intervened [3,4].

Many studies have provided evidence that viral pathogens, especially viruses such as Herpes Simplex Virus (HSV), Epstein-Barr Virus (EBV), Varicella Zoster Virus (VZV), may play a role in the etiopathogenesis of Bell's palsy [5,6]. The strongest of these evidences is the isolation of the HSV genome from the geniculate ganglia and facial nerve en-

doneural fluid of patients with Bell's palsy [7,8]. Inflammations caused by reactive viral latent infections in the facial nerve and immune response secondary to inflammation are accepted as the starting point of Bell's palsy [9]. Edema due to viral reactivation causes compression of the facial nerve, which runs along an anatomically narrow and long bone canal, and thus causes ischemia [9].

Steroids are used as the first-line treatment option in the treatment of peripheral facial paralysis due to their known strong anti-inflammatory activity and edema-reducing effect [10]. Although it is thought that the inflammatory process is due to viral factors, the effectiveness of antiviral agents in the treatment is still controversial. While there are studies showing that the combination of antiviral and steroid therapy is superior to steroid therapy alone, on the other hand there are articles that argue these two modalities do not have any superiority over each other [11].

In this study, the efficacy of steroid treatment alone and

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a combination of steroid + antiviral treatment in patients we followed up with peripheral facial paralysis was questioned retrospectively, and it was aimed to contribute to the consensus in the literature on this issue.

Materials and Methods

In our study, it was aimed to compare steroid (methylprednisolone) and steroid (methylprednisolone) + antiviral (valacyclovir) protocols used in the treatment of peripheral facial paralysis. Permission for the study was obtained from the Inonu University Health Sciences Non-Interventional Clinical Research Ethics Committee with a protocol number 2023/4678. The patients who applied to the Inonu University Otorhinolaryngology clinic between January 2021 and June 2022 with peripheral facial paralysis and whose treatment processes were followed up constituted the pool of the study. The files of the patients who were followed up with the diagnosis of peripheral facial paralysis were reviewed retrospectively, and a total of 172 patients were included in the study after being considered fit for the study. Age, gender, regular drug use, smoking, previous history of facial paralysis, comorbid diseases, initial stage of the disease (House-Brackman/HB staging), treatment protocol and response to treatment were recorded from the files examined. Patients with HB stage ≤ 2 at the 6th month follow-up were considered to have complete or near complete response to the treatment. Patients with a history of temporal trauma, chronic otomastoiditis, patients with vesicular eruption in the facial nerve dermatome, patients with tumors affecting the facial nerve, patients whose drug administration was interrupted while their treatment was ongoing were not included in the study. Among the patients included in the study, only methylprednisolone treatment was applied to 110 patients and combined treatment (methylprednisolone + valacyclovir) was applied to 62 patients. All patients were started on methylprednisolone 1mg/kg (maximum 80 mg/day) as the basic treatment. In all patients, this treatment was started in the first 48 hours and the treatment was continued by decreasing 10 mg at 2-day intervals. In addition, patients who received valacyclovir were treated for 5 days at a daily dose of 1000 mg. Valacyclovir, like steroids, was started within 48 hours of the onset of the facial paralysis. In addition to systemic steroid and antiviral treatment, patients were given eye protection with artificial tears.

The steroid group and the combined treatment group were compared in terms of age, gender, regular drug use, smoking, history of previous facial paralysis, diabetes and hypertension comorbidity, disease stage and response to treatment. Contrast-enhanced ear magnetic resonance imaging (MRI) was performed in patients with peripheral facial paralysis as a clinical protocol for our patients. Patients with mass pathology in MRI were not included in the study because they ceased to be Bell's palsy.

Statistical analysis

Data were evaluated using the SPSS Statistical Package Program (v22.0; SPSS Inc. Chicago IL, USA). Normality analysis of numerical data was evaluated by Kolmogorov-Smirnov test. It was determined that all numerical data

showed normal distribution. As descriptive statistics, mean and standard deviation values of numerical data and percentage values of categorical data are given. For normally distributed data; Independent groups t-test was used for group comparisons, and chi-squared test was used for comparison of categorical data. Significance level was determined as $p < 0.05$.

Results

One hundred and ten patients in the steroid group and 62 patients in the steroid+antiviral treatment group were included in the study. 54.5% of the patients using steroids and 46.8% of the patients receiving combined therapy were women. While the mean age was 49.3 ± 18.6 years in the monotherapy group, it was 51.4 ± 19.7 years in the combined treatment group. It was observed that there was statistical similarity between the groups in terms of age and gender. The data were compiled in Table 1.

Chronic drug use, comorbidities (diabetes mellitus, hypertension), smoking and history of previous facial paralysis were questioned between the groups. While chronic drug use was 38.2% in the monotherapy group, it was 32.3% in the combined treatment group ($p=0.509$). Smoking frequency was 28.2% in the monotherapy group and 24.2% in the combined group ($p=0.596$). When the groups were questioned in terms of the frequency of previous facial paralysis and comorbidities, it was observed that there was no statistical difference between the two groups (Table 1).

The HB stage of the patients was evaluated at the time of first admission, when the two groups were compared in terms of response to treatment, 88.2% complete or near-complete recovery was observed in the steroid group (HB stage ≤ 2), and in the combined treatment group 91.9% complete or near-complete recovery was observed. No statistically significant difference was observed ($p=0.605$). In both groups, HB stage 4 facial paralysis was the most common at the time of admission, and there was no statistically significant difference between the groups according to the distribution of stages ($p=0.704$). The data were compiled in Table 2.

When patients' MRI data were retrospectively compiled, enhancing was observed in 5 patients in the combined group and 9 patients in the monotherapy group along the facial nerve tracing. Control MRI was performed in patients with contrast enhancement in the first MRI, and it was observed that all enhancements were resolved.

Discussion

Idiopathic peripheral facial paralysis remains a clinical entity whose etiopathogenesis is not fully explained and its treatment modality is still unclear [11]. Although various treatment modalities have been tried, a complete consensus on the treatment has not been achieved. Surgical opening of the narrow fallopian canal of the facial nerve and relieving the compression of the nerve, steroid applications to reduce edema and the use of antiviral therapy to reduce viral replication or the use of some of these modalities together are some of the treatment methods [10,12,13]. While some reports argue that corticosteroid alone is sufficient, some articles report that corticosteroid+antiviral

Table 1. Sociodemographic characteristics of participants.

		Methylprednisolone		Methylprednisolone+Valacyclovir		X^2	p
		n	%	n	%		
Gender	Female	60	54.5	29	46.8	0.959	0.345
	Male	50	45.5	33	53.2		
Regular drug use	Yes	42	38.2	20	32.3	0.604	0.509
	No	68	61.8	42	67.7		
Smoking	Yes	31	28.2	15	24.2	0.322	0.596
	No	79	71.8	47	75.8		
History of facial paralysis	Yes	7	6.4	10	16.1	4.245	0.060
	No	103	93.6	52	83.9		
Diabetes	Yes	24	21.8	10	16.1	0.809	0.429
	No	86	78.2	52	83.9		
Hypertension	Yes	33	30	20	32.3	0.095	0.864
	No	77	70	42	67.7		
		Mean±SD		Mean±SD			
Age		49.3±18.602		51.40±19.695		0.145	0.704

SD: Standard Deviation.

Table 2. Treatment responses of patients receiving monotherapy and combined therapy.

		Methylprednisolone		Methylprednisolone+Valacyclovir		X^2	p
		n	%	n	%		
Response to treatment	Yes	97	88.2	57	91.9	0.596	0.605
	No	13	11.8	5	8.1		
Initial HB stage	Stage 2	17	15.5	5	8.1	3.881	0.275
	Stage 3	34	30.9	18	29.0		
	Stage 4	39	35.5	21	33.9		
	Stage 5	20	18.2	18	29.0		

HB: House-Brackmann staging.

therapy is more effective than steroid administration alone [14,15]. In this study, we compiled the data of our own cases in order to show whether the combined corticosteroid + antiviral therapy we use in the treatment of Bell's palsy is superior to corticosteroid alone.

In our clinic, 110 patients with idiopathic facial paralysis were followed up with steroid therapy alone, and 62 patients were given steroid+antiviral therapy. While 88.2% satisfactory response was obtained in the monotherapy group, 91.9% satisfactory response was obtained in the combined therapy group. Although more successful results were obtained in the combined therapy, it was not statistically significant. The data we obtained from this study supported the idea in the literature that combined therapy is not better than steroid administration alone.

The effect of steroid therapy in the treatment of Bell's palsy has been questioned in many studies. In studies comparing steroid alone with placebo, cure rates have been proven to be statistically better [16]. For Bell's palsy, it has been proven by strong evidence that steroid alone reduces unsatisfactory recovery by 9% and reduces synkinesis and autonomic dysfunction by 14% [17]. It has been reported that the use of steroids does not increase the risk in terms

of side effects [17].

The use of antiviral therapies alone in the treatment of Bell's palsy is not recommended by the current literature. Acyclovir, famciclovir and valacyclovir are the most commonly used pharmacological agents for this purpose. In the study of Engström et al., it was shown that the efficacy of valacyclovir and placebo in the treatment of Bell's palsy was not different from each other [16]. According to another study, it has been claimed that antiviral therapy alone is not beneficial in the treatment of Bell's palsy [17].

There are many studies evaluating whether steroid+antiviral therapy is better or not than steroid therapy alone. In a controlled randomized study by Engström et al., it was shown that prednisolone+valacyclovir treatment was not superior to prednisolone treatment alone [16]. There are different studies with valacyclovir+steroid and acyclovir+steroid that support the study of Engström et al. and they report that they are not superior to steroid alone [11,18,19] Kang et al., on the other hand, argued that combined therapy may be better in steroid administration alone, especially in patients with comorbidity and/or more severe facial paralysis at the time of first admission [20]. De almedia et al. reported

the possible increased benefit of combined steroid and antiviral use and a synergistic effect when these two agents are used in combination [17]. Our study also showed that steroid+antiviral therapy was not superior to steroid therapy alone, in line with the data reported by Engstöröm et al [18].

The most important limitations in our study are that it was retrospective, the patients were not homogeneous, and the placebo group did not exist. Another limitation is that; blinding (masking) was not done in any part of our study, this may have caused bias in terms of results. Although facial paralysis is a common clinical entity, its spontaneous occurrence and long follow-up make it difficult to conduct studies on facial paralysis. The limited number of patients forming the groups prevents our statistical data from being strong. Prospective controlled studies in which patients are homogeneous will enlighten us more on this issue.

Conclusion

As a result, in the treatment of Bell's palsy, the superiority of steroid use alone and combined antiviral + steroid use has not been proven. In the light of the literature, it is recommended that the patient be treated with steroids at the earliest stage.

Ethical approval

Permission for the study was obtained from the Inonu University Health Sciences Non-Interventional Clinical Research Ethics Committee with a protocol number 2023/4678.

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