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The Efficacy of Acyclovir in Childhood Bell's Palsy

Çocukluk Çağı Bell Paralizisinde Asiklovirin Etkinliği

Gürkan Gürbüz

Cengiz Gokcek Maternity and Children's Hospital, Clinic of Child Neurology, Gaziantep, Turkey

Abstract

Objective: Bell's palsy is an acute onset, unilateral, self-limiting paresis or paralysis of the facial nerve. The objective in treatment is to increase facial functions and to accelerate recovery by suppressing this inflammatory process. Steroids and acyclovir (singly or in combination) are used in medical treatment. The objective of this study was to determine the clinical profile of Bell's palsy in childhood and to compare the efficacy of combined acyclovir-prednisolone therapy with that of prednisolone therapy alone.

Materials and Methods: Eighty-six patients diagnosed as having Bell's palsy were enrolled in the study. All patients were assessed in terms of facial nerve dysfunction and recovery time using the House-Brackman Facial Nerve Grading scale (HBFNGS) at initial presentation and at the 15th day, and the first, third, and sixth months. Grade 4 and above was assessed as severe, and lower grades were regarded as mild.

Results: The mean age of the patients was 9.5 (±2.4) years. Forty-six (57.6%) patients received prednisolone therapy only, and 34 (42.4%) were started on a combination of oral acyclovir and prednisolone therapy, 29 of whom were in the severe category. Analysis of HBFNGS at one month revealed that the addition of acyclovir to treatment had no effect on the recovery period. However, combination therapy seems more beneficial in severe cases.

Conclusion: Bell's palsy frequently resolves entirely in childhood, and an acyclovir plus prednisolone combination is not superior to prednisolone alone except in severe cases.

Keywords: Acyclovir, Bell's palsy, childhood, peripheral facial paralysis

Öz

Amaç: Amaç çocukluk döneminde Bell paralizisinin klinik profilini belirlemek ve kombine asiklovir-prednizolon tedavisinin etkinliğini tekli prednizolon tedavisiyle karşılaştırmak.

Gereç ve Yöntem: Çalışmaya Bell paralizisi tanısı konan 86 hasta dahil edildi. Tüm hastalar ilk sunumda ve 15. günde ve birinci, üçüncü ve altıncı aylarda House-Brackman Yüz Sinir Sınıflandırma (HBYS) ölçeği kullanılarak fasiyal sinir disfonksiyonu ve iyileşme süresi açısından değerlendirildi. Dördüncü derece ve üstü şiddetli, düşük dereceler ise hafif olarak kabul edildi. Tüm bulgular, hasta dosyalarının retrospektif incelemesi ile yapıldı.

Bulgular: Hastaların yaş ortalaması 9,5 (±2,4) idi. Kırk altı (%57,6) hasta sadece prednizolon tedavisi alırken, 34 (%42,4) hasta kombine tedavi aldığı gözlendi. Kombine tedavi alanların 29'u ağır kategorideydi. Bir aylık HBYS skorlarının analizi, tedaviye asiklovir ilavesinin iyileşme süresi üzerinde bir etkisi olmadığını ortaya koydu. Ancak ciddi olgularda, kombinasyon terapisi daha faydalı görünmektedir.

Sonuç: Bell paralizisi sıklıkla çocuklukta tamamen geçer ve asiklovir- prednizolon kombinasyonu, ağır olgular haricinde, tekli prednizolondan daha üstün değildir.

Anahtar Kelimeler: Asiklovir, Bell paralizisi, çocukluk, periferik fasiyal paralizi

Introduction

Bell's palsy was first described in 1821 by the Scottish surgeon Sir Charles Bell as weakness of the facial nerve (1). The condition is an acute onset, unilateral, self-limiting paresis or paralysis of the facial nerve. The reported incidence in childhood is 6.1 per 100.000 (2). It is the most frequently seen mononeuropathy and the most common disease associated with paralysis of the facial nerve in both childhood and adulthood. Motor loss is unrelated to any congenital, genetic or acquired diseases (3). Bell's palsy is a diagnosis of exclusion, and infections, trauma, systemic diseases, vasculitis, and neoplasms must all be ruled out (4). Although the

Address for Correspondence/Yazışma Adresi: Gürkan Gürbüz MD, Cengiz Gokcek Maternity and Children's Hospital, Clinic of Child Neurology, Gaziantep, Turkey
Phone: +90 530 696 67 84 E-mail: drgurkangurbuz@hotmail.com ORCID: orcid.org/0000-0001-6640-636X
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etiopathogenesis of Bell's palsy is still unclear, the main focus is on inflammatory processes (5,6). The objective in treatment is to increase facial functions and to accelerate recovery by suppressing this inflammatory process. Steroids and acyclovir (singly or in combination) are used in medical treatment, and physiotherapy and electrical nerve stimulation are used in complementary therapy (7). Surgical decompression can be applied in refractory cases (8).

The aim of this study was to determine the clinical profile of Bell's palsy in childhood and to compare the efficacy of combined acyclovir-prednisolone therapy with that of prednisolone therapy alone.

Materials and Methods

Eighty-six patients diagnosed with peripheral facial paralysis were enrolled in the study. Patients' examination findings, laboratory tests, and neuroimaging results (if applicable) were retrieved retrospectively from patient file records. No ethics committee approval was needed because of the retrospective nature of the research but hospital manager approval has been taken.

All children were assessed by a pediatric neurologist, an ear nose and throat (ENT) specialist, and a rehabilitation specialist. All neurologic examinations and tests were planned and assessed by a pediatric neurologist. Cases with no etiologic cause were assessed as Bell's palsy and were placed under monitoring for treatment at the pediatric neurology clinic.

Patients were referred to our hospital by various different centers and pediatricians. Some patients were receiving prednisolone only, while others had been prescribed oral acyclovir in addition to prednisolone by other centers on suspicion of accompanying viral infection and/or due to differing practice protocols. Although no evidence of viral infection was determined in clinical findings or laboratory tests aimed at viral etiology in patients started on acyclovir therapy, acyclovir was maintained at a dosage of 80 mg/kg/day. Antiviral therapy was completed and stopped on day 7. Oral prednisolone therapy was administered at a full dose of 1 mg/kg/day (maximum 60 mg/day) for five days, followed by tapering over five days, thus being used for 10 days in total by all patients. All patients were prescribed artificial tears and sleep masks for nocturnal use. A standard rehabilitation protocol was established for all patients, and all were given home exercises for their facial muscles.

Table 1. House-Brackman Facial Nerve scoring system

Grade	Defined by
1	Normal function
2 Mild dysfunction	Slight weakness, normal symmetry at rest, complete eye closure with minimal effort
3 Moderate dysfunction	Obvious but not disfiguring difference between the two sides, noticeable but not severe synkinesis, complete eye closure with effort, and strong but asymmetrical mouth movement with maximal effort.
4 Moderately severe dysfunction	Obvious weakness, and/or disfiguring asymmetry, incomplete eye closure with asymmetry of mouth with maximal effort
5 Severe dysfunction	Only barely perceptible motion, asymmetry at rest, incomplete eye closure, slight movement of corner of the mouth
6 Total paralysis	No movement

All patients were assessed in terms of facial nerve dysfunction and recovery time using the House-Brackman Facial Nerve Grading scale (HBFNGS) at initial presentation and at the 15th day, and the first, third, and sixth months (Table 1, 2) (9). Grade 4 and above was assessed as severe, and lower grades were regarded as mild. Patients with severe facial nerve effects persisting at three months underwent magnetic resonance imaging (MRI) of the brain and temporal bone, and electrical stimulation (ES) of the facial nerve was initiated in order to prevent muscular atrophy. In order to stimulate the facial muscles, interrupted galvanic stimulation was administered at 1 pulse/s 100 ms until 100 contractions were achieved.

Statistical Analysis

Analysis of variables was performed using the SPSS 24.0 (IBM Corporation, Armonk, New York, USA) software. Quantitative variables are expressed in the tables as mean ± standard deviation, and categorical variables are expressed as n (%). Descriptive statistics regarding age, sex, HBFNGS grade, neurologic findings, results of neuroimaging, treatment, and prognosis were calculated. The chi-square test was used to compare categorical data. Numeric data were compared using Student's t-test. Significant relationships between two variables were also analyzed using the Pearson correlation test. Variables were analyzed at a 95% confidence interval, and p values less than 0.05 were regarded as statistically significant.

Results

Eighty-six patients presenting to our hospital with at least one diagnosis of unilateral peripheral facial paralysis and in consultation from another center were included in the study. Otitis media was determined in four patients, hypertension in one, and pontine glioma in one, and these six patients were excluded. The patients' demographic data and classifications based on the severity of disease are shown in Table 2. Forty-nine of the 80 patients with Bell's palsy were girls, and 31 (38.7%) were boys. The mean age of the patients was 9.5 (±2.4) (range=2-17) years. The mean time to presentation to a health institution was 3.5 (±1.7) days. The mean time to presentation was shorter in the mild types than in the severe types with HBFNGS scoring (p=0.047). Sixty-three patients experienced attacks in winter and fall, when viral infections are more common.

Three patients had a previous history of Bell's palsy, and a family history was present in all cases in which recurrence was observed. Full recovery was observed in the first month in 60 (75%) patients. The remaining 20 (25%) patients were all in the severe category based on HBFNGS scoring (p=0.01). Facial paralysis persisted in only one case (1.2%) at the sixth-month follow-up, and this patient was referred to the ENT department for decompression surgery. Forty-six (57.6%) patients received prednisolone therapy only, and 34 (42.4%) patients were started on a combination of oral acyclovir and prednisolone therapy, 29 of whom were in the severe category. Analysis of HBFNGS scores at one month revealed that the addition of acyclovir to treatment had no effect on the recovery period (p=0.77). However, in severe

cases, the combination therapy seemed to be more beneficial than single-steroid therapy (p=0.02) (Table 3).

MRI of the brain and temporal bone was performed on 20 (25%) patients in order to identify the reason for the absence of full recovery. Arachnoid cyst was determined in two patients and periventricular gliosis in one. Abnormal results were not associated with peripheral facial paralysis.

Discussion

In this study, we determined the clinical profiles of patients with childhood Bell's palsy and investigated whether an acyclovir and prednisolone combination was superior to prednisolone monotherapy. In agreement with our research, several previous studies of children and adults observed no difference in male to female ratios. Consistent with other studies, paralysis was more

Table 2. Demographic and clinic features in terms of disease severity

	Mild (Grade 2, 3)	Severe (Grade 4, 5, 6)	Total n (%)	p value
Sex				
Male, n (%)	10 (12.5)	21 (26.3)	31 (38.7)	0.58
Female, n (%)	19 (23.7)	30 (37.5)	49 (61.3)	
Mean age (years) (± SD)	10.2 (±1.8)	8.8 (±2.1)	9.5 (±2.4)	0.62
Affected side				
Right, n (%)	12 (15)	24 (30)	36 (45)	0.08
Left, n (%)	17 (21.2)	27 (33.8)	44 (55)	
Time since consultation, (day) (mean)	4.7 (±1.8)	2.3 (±1.1)	3.5 (±1.7)	0.047
Family history, n (%)	2 (2.5)	5 (6.2)	7 (8.7)	0.78
Recurrence, n (%)	2 (2.5)	1 (1.2)	3 (3.7)	0.76
Season				
Winter, n (%)	9 (11.2)	22 (27.5)	31 (38.7)	0.81
Spring, n (%)	2 (2.5)	7 (8.7)	9 (11.2)	
Summer, n (%)	1 (1.2)	7 (8.7)	8 (10)	
Fall, n (%)	17 (21.2)	15 (18.7)	32 (40)	
Complete recovery by the				
15th day, n (%)	17 (21.2)	5 (6.2)	22 (27.5)	0.01*
1st month, n (%)	11 (13.7)	27 (33.7)	38 (47.5)	
3rd month, n (%)	1 (1.2)	18 (22.6)	19 (23.8)	
6th month, n (%)	-	1 (1.2)	1 (1.2)	
Neuroimaging (n=20)				
Normal, n (%)	-	17 (85)	17 (85)	-
Abnormal, n (%)	-	3 (15)	3 (15)	
Physiotherapy				
Home exercise, n (%)	28 (35)	32 (40)	60 (75)	0.08
Electric stim + Home exercise, n (%)	1 (1.2)	19 (23.8)	20 (25)	

*SD: Standard deviation

Table 3. Comparison of prednisolone and acyclovir combination versus prednisolone therapy alone

	Prednisolone, n (%)	Prednisolone + Acyclovir, n (%)	p value
Sex			
Male	18 (22.6)	12 (15)	0.89
Female	28 (35)	22 (27.4)	
Mean age (years) (± SD)	9.2 (± 1.8)	10.2 (±2.1)	0.08
HBFNGS			
Mild	24 (30)	5 (6.3)	0.09
Severe	22 (27.4)	29 (36.3)	
Complete recovery in the 1st month	32 (40)	28 (35)	0.77
Complete recovery in the 1st month in severe cases	8/22	23/29	0.02

HBFNGS: House-Brackman Facial Nerve Grading scale, SD: Standard deviation

common in winter and fall, when the incidence of viral infections is greater (10,11). Although Bell's palsy is described as "idiopathic", studies have shown that herpes simplex virus type 1 and varicella zoster virus at both primary infection and during reactivation are capable of causing peripheral facial paralysis (12,13,14). The spread and reproduction of neurotropic activated viruses has been proved using polymerase chain reaction DNA analysis (15). The demonstration of an association between inactivated intranasal influenza vaccine and facial paralysis in case-controlled studies led to this vaccine being removed from use in Switzerland (16). Various viral agents, such as Echovirus and Epstein-Barr virus, have been identified in facial paralyses (2). All these studies have involved adult patients, and there are insufficient studies of viral etiology in Bell's palsy in childhood.

Even if no infectious agent is determined in laboratory and clinical examinations, Bell's palsy is an inflammatory event, and this inflammation must be suppressed in treatment (6). The basic aim of treatment is to achieve complete recovery without sequelae, contracture or synkinesis. Prednisolone is regarded as the classic therapeutic option. This is administered by the oral route at 1-2 mg/kg/day. No difference has been reported between doses of 1 or 2 mg/kg/day in terms of achieving clinical improvement (17). We think that the use of oral prednisolone at 1 mg/kg/day is effective in almost all of our patients. However, uncertainty still prevails concerning the use of acyclovir in Bell's palsy. In the first of two randomized controlled studies comparing an antiviral and prednisolone combination with prednisolone therapy alone in Bell's palsy, 210 adult patients were treated with valacyclovir and prednisolone, and 230 with prednisolone and placebo. In another study, 127 patients received prednisolone only, and 124 received a prednisolone and acyclovir combination. Neither study observed any superiority of combination therapy over prednisolone monotherapy (18,19). However, another recent retrospective study involving 1342 patients with adult Bell's palsy reported that the addition of acyclovir to prednisolone had no positive effect on facial paralysis improvement (20).

The Bell's palsy guideline published by the American Academy of Otolaryngology-Head and Neck Surgery Foundation in 2013 did not recommend single antiviral therapy, and made no comment regarding whether a steroid and antiviral combination might be recommended, reporting only that extensive studies were required (21). As shown by these studies reporting inconsistent results, the uncertainly over acyclovir therapy in Bell's palsy still persists. There have been no randomized controlled studies performed in childhood, and retrospective studies are few in number and have involved limited patient groups. There was no significant difference in recovery times between the group receiving combination therapy and the patients receiving prednisolone monotherapy in the present study (p=0.77). In a study involving a limited number of pediatric patients, Khajeh et al. (22) showed that an acyclovir-prednisolone combination accelerated recovery, particularly in severe-type Bell's palsy, consistent with our own study. Kawaguchi observed reactivation of HSV-1 or VZV in 34% of adult patients with Bell's palsy. The effect of combination therapy with prednisolone and valacyclovir on recovery was not significantly higher compared with prednisolone alone (23).

Recurring Bell's palsy is rare in childhood, and it is essential to investigate secondary causes that may be responsible. Several secondary causes have been described in the literature, including tumors of the central nervous system, hypertension, Lyme disease, acute lymphoblastic leukemia, Ramsay Hunt syndrome, vasculitis, and facial nerve meningioma (24,25,26,27). In our study, otitis media was determined in four patients, hypertension in one, and pontine glioma in one. It was clear in the full physical examination that facial paralysis in these patients was not idiopathic but was associated with secondary causes. Fever and purulent discharge from the ear were present in the patients with otitis, and nervus abducens paralysis and altered consciousness were present in the patient with pontine glioma. Hypertension is a common and frequently significant differential diagnosis in patients with facial paralysis. It is particularly important in terms of being capable of diagnosis in the outpatient clinic, of diagnosis being rapid and inexpensive, and of prevention of morbidities that may occur when the condition is detected. Patients with facial paralysis secondary to hypertension have been reported in the literature, and also in one of our own cases (28). Although rare, Guillain-Barré syndrome should also be considered in the differential diagnosis of patients with pediatric facial paralysis (29).

The recovery process in Bell's palsy is closely linked to facial motor dysfunction at initial presentation. The lower the HBFNGS, the faster the recovery. Patients with incomplete facial paralysis may have better prognosis than those with full paralysis (2). Similarly, in the present study, and in line with the previous literature, complete recovery was not observed in only one of the 29 patients with mild Bell's palsy at the one-month follow-up, while complete recovery was not achieved in 20 of the 51 patients with severe paralysis (p=0.01).

Physiotherapy and assistant techniques occupy an important place alongside medical treatment in accelerating the recovery process in Bell's palsy (10). Home exercises are the most commonly employed rehabilitation method, and these were recommended to all our patients. ES is recommended in cases in which the recovery process is delayed despite medical treatment (10). ES was performed on 20 patients in whom complete recovery was not achieved in the first month in our case series. Residual paralysis persisted at six months in only one patient who received ES.

Bell's palsy can be diagnosed with complete neurological examination, and neuroimaging techniques are frequently not necessary. However, intracranial pathologies must be considered in facial paralyses that recur, are refractory to treatment, and especially in those accompanying other neurologic pathologies (30). MRI of the brain was performed on 20 patients in whom complete recovery was not observed in the first month in our case series, and no pathology capable of accounting for facial paralysis was determined in any. In addition, prospective studies have shown no improvement in facial pain in patient groups receiving combination therapy compared with patients using prednisolone only (31).

There are a number of limitations to this study. These include its retrospective nature and the enrolment of patients of different ages and with a variety of disease stages. However, our case number was higher than in similar studies from Turkey and worldwide, and this can be considered a particular strength of the study.

Conclusion

Bell's palsy frequently resolves entirely in childhood, and an acyclovir plus prednisolone combination is not superior to prednisolone alone. However, combination therapy seems more beneficial than single-steroid therapy in severe cases.

Ethics

Ethics Committee Approval: Retrospective study.

Informed Consent: The patient informed consent is not received as it is retrospective study.

Peer-review: Externally peer-reviewed.

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