Comparison of the efficacy of prednisolone versus prednisolone and acyclovir in the treatment of Bell's palsy

Alijan A. Ahangar, MD, Seydreza Hosseini, MD, Roshanak Saghebi, MD.

ABSTRACT

Objectives: To compare the efficacy of 2 regimens of prednisolone versus prednisolone and acyclovir in the treatment of Bell's palsy.

Methods: A retrospective study was performed on 496 Bell's palsy patients attending Yahyanejad Hospital, Babol, Iran from 1995 to 2004, divided in 2 groups. The first group was treated with regimen one (oral prednisolone), and the second group was treated with regimen 2 (oral prednisolone plus oral acyclovir) for 2 weeks. All cases were followed for 6 months.

Results: Two hundred and forty-eight cases (108 males, 140 females) were treated with regimen one, and 248 cases (113 males, 135 females), were treated with regimen 2. Both groups had a mean age of 20-39 years. At the end of therapy, the recovery rate with regimen 2 was 95.6% (237 patients), whereas regimen one showed a recovery rate of 91.2% (226 patients) (p=0.047).

Conclusion: This study showed acyclovir plus prednisolone to be more effective than prednisolone alone in the treatment of Bell's palsy.

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Bell's palsy, a peripheral facial nerve paresis, is the most common disorder of the facial nerve and one of the most common mononeuropathies. The frequency of Bell's palsy varies between 62-93% of all cases of facial nerve paresis,[1] with an incidence rate of between 14-25 cases per 100,000 population.[2] There are only minor differences in the frequency of Bell's palsy between males and females and also in various races.[3] Interestingly, there is a slightly higher incidence in the winter.[4] Bell's palsy may result in incomplete or complete paralysis of facial innervated muscles with some changes in the face, which can be very annoying for the patient.[5] Diagnosis is based on history, physical examination, and the results of laboratory tests.[6-9] Seventy-five percent of patients with Bell's palsy experience complete recovery approximately within 2-3 weeks. An additional 15% experience satisfactory improvement, but may have persistent facial asymmetry. Five to 10% of patients have poor recovery until 4 months after disease onset, with persistent neurological impairment and cosmetic problems.[10] Many patients with Bell's palsy will develop some complications such as synkinesis, crocodile tears and 'sweating' of the ear while eating.[11] All of these complications are due to incomplete improvement of Bell's palsy, and these complications, and especially cosmetic problems of the face, emphasize the importance of an early and

From the Department of Neurology (Ahangar), Yahyanejad Hospital, the Department of Social Sciences (Hosseini), and the Department of Social Medicine (Saghebi), Education Development Center, Babol Medical Sciences University, Babol, *Iran*.

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Address correspondence and reprint request to: Dr. Alijan A. Ahangar, Department of Neurology, Yahyanejad Hospital, Babol Medical Sciences University, 471466855, Babol, *Iran*. Tel. +98 11122225035. Fax. +98 1112290141. E-mail: alijanahmadiahangar@yahoo.com

effective treatment of the patient with Bell's palsy.[12] Several studies in recent years considered herpes simplex virus type 1 (HSV-1) as a probable cause of Bell's palsy,[13-19] and suggest anti-viral therapy such as acyclovir alone or along with corticosteroids, which is a classic treatment of the disorder.[20-24] However, in some recent studies the viral etiology has not been confirmed, and so, the etiology of Bell's palsy remains a mystery.[25,26] The current study was conducted to compare 2 therapeutic regimens: prednisolone alone and prednisolone plus acyclovir in the treatment of Bell's palsy.

Methods. A retrospective study was performed on the data collected from 496 patients with Bell's palsy attending the Neurology Department of Yahyanejad Hospital, Babol Medical University, Iran, from 1995 to 2004. Patients were treated for 2 periods of time with 2 different drug regimens. In recent years, the regimen of choice for Bell's palsy in our department has changed from prednisolone[10,23,27] to the combined therapy of prednisolone and acyclovir.[2,12,24] Two hundred and forty-eight consecutive Bell's palsy patients (from 2000 to 2004) were treated with prednisolone plus acyclovir and were compared with the same number of patients, as the control group, referred in previous years (from 1995 to 2000) and treated with prednisolone alone. The recovery rates of these 2 therapeutic regimens were compared with each other. The criteria for the diagnosis of Bell's palsy in this study were: acute onset of the facial muscle weakness, incomplete or none eye closure and nasolabial fold flattening on the affected side. The Bell's palsy was diagnosed by a neurologist and assessed (if necessary) by para clinics and neuroimaging procedures to rule out other causes of facial paresis. As all of the consecutively referred patients with different severities of facial paresis were included in this study, the initial severity of the Bell's palsy in these 2 groups was the same. Exclusion criteria included a history of uncontrolled hypertension, severe diabetes mellitus, peptic ulcer, or cases referred after the fourth day of initiation of the disorder. Therefore, peripheral facial paresis cases, after ruling out any known etiology, were included in this study. The dosage of prednisolone was 1 mg/kg in the first week and tapered over 2 weeks. Acyclovir was administered 1500 -2000 mg daily for 10 days.[14] The patients were reviewed at the end of the second week, and in cases of any failure in improvement of the facial paresis, they were reviewed again at the end of the first, third, and sixth months. The course of facial paresis improvement of the patients was recorded in their hospital sheets whenever they were reviewed. The facial paresis improvement clinical criteria were eye-closure ability, lip-opening, showing teeth and nasolabial symmetry, which altogether were considered as complete recovery,[7] equivalent to grade one in House and Brackman classification[28] and to grades of more than 36 in Yanagihara classification of facial paresis.[29]

The data were analyzed by SPSS and for comparison of the efficacy of both regimens of therapy, Mann Whitney and Fisher's exact tests were used. *P*-values less than 0.05 were considered significant.

Table 1 - Frequency of Bell's palsy patients according to the age and gender in group 1 (treated with prednisolone) and group 2 (treated with prednisolone and acyclovir).

Age group (years)	Group I		Group II	
	Male	Female	Male	Female
<20	10	18	12	15
20-39	45	52	41	50
40-59	34	40	36	38
60-79	19	30	24	32
Total	**108 (44%)**	**140 (56%)**	**113 (46%)**	**135 (54%)**

Results. The frequency of Bell's palsy according to the age and gender of each group is show in **Table 1**, illustrating more females than males in each group, with most patients in the 20-39 years age group. At the end of 6 months, 226 (91.2%) of the prednisolone group and 237 (95.6%) of prednisolone plus acyclovir group had complete recovery ($p = 0.047$) (**Table 2**). **Table 3** shows the comparison of each group's improvement, with the maximum time of recovery in both groups at the end of week 2. There was no statistically significant difference in the mean time of recovery between both groups ($p>0.05$). Although the frequency of the disorder in females was higher than males in both groups, the recovery rates were the same.

Discussion. In this study, in the patients treated with acyclovir and prednisolone, the recovery rate was 95.6%, whereas in the prednisolone treated group it was found to be 91.2% ($p=0.047$), revealing the efficacy of acyclovir in the treatment of Bells palsy. Although for many years, corticosteroids had been used in the treatment of Bell's palsy,[17,27] in recent years, due to its probable viral etiology, antiviral therapies such as acyclovir have also been administered. Some reports support the idea of a viral etiology of Bell's palsy, such as Murakami et al[8] who studied a group of

Table 2 - Recovery rates of Bell's palsy patients treated with prednisolone (group 1) and prednisolone plus acyclovir (group 2).

No. of patients			Recovery rate										Unrecovery rate	
			2nd week		1st month		3rd month		6th month		Total			
Gender	**P**	**P+A**	**P**	**P+A**	**P**	**P+A**	**P**	**P+A**	**P**	**P+A**	**P**	**P+A**	**P**	**P+A**
							No. (%)							
Female	140 (56)	135 (54)	90 (36.3)	92 (37.1)	28 (11.3)	27 (1.9)	7 (2.9)	6 (4)	4 (1.6)	5 (2)	**129 (52)**	**130 (52.4)**	11 (4.4)	5 (2)
Male	108 (44)	113 (46)	65 (26.3)	69 (27.9)	24 (9.6)	30 (12.1)	5 (2)	6 (5)	3 (1.2)	2 (0.8)	**97 (39.2)**	**107 (43.2)**	11 (4.4)	6 (2.4)
Total	**248 (100)**	**248 (100)**	**155 (62.6)**	**161 (65)**	**52 (20.9)**	**57 (23)**	**12 (4.9)**	**12 (4.8)**	**7 (2.8)**	**7 (2.8)**	**226 (91.2)**	**237 (95.6)**	22 (8.8)	11 (4.4)

P - prednisolone, P+A - prednisolone plus acyclovir

Table 3 - Comparison of the recovery rate of Bell's palsy patients in group 1 (treated with prednisolone) and group 2 (treated with prednisolone plus acyclovir) at different times.

Treated groups	Accumulative recovery rate No. (%)			
	2nd week	1st month	3rd month	6th month
Prednisolone	155 (62.6)	207 (83.5)	219 (88.3)	226 (91.1)
Prednisolone plus acyclovir	161 (65.0)	218 (87.9)	230 (92.7)	237 (95.6)
P-value	0.575	0.158	0.092	0.047

14 patients with Bell palsy, 9 patients with Ramsay-Hunt syndrome, and 12 controls. Viral genomes of HSV-1, varicella-zoster virus, and Epstein-Barr virus were analyzed in samples of facial nerve endoneurial fluid and posterior auricular muscle, using polymerase chain reaction (PCR). In their study, the HSV-1 genomes were detected in 11 of 14 patients (79%) with Bell palsy, but not in patients with Ramsay-Hunt syndrome or in the controls. In another study performed by Pitkaranta et al,[15] human herpes virus 6 DNA was detected by PCR in the tear fluid of 7 (35%) of 20 patients with Bell's palsy and in 1 (5%) of 20 healthy controls.

In many clinical trials, the combination therapy of prednisolone and acyclovir was compared with prednisolone alone in the treatment of Bell's palsy. Some reports show an increased recovery rate of Bell's palsy, with acyclovir and prednisolone combination therapy in comparison with prednisolone treatment alone. In the study by Hato et al,[30] 94 patients were treated with prednisolone (40-60 mg/day) and acyclovir (2000 mg/day), and 386 patients with prednisolone alone (40-60 mg/day). The recovery rate was significantly higher in the prednisolone and acyclovir treated group (95.7% versus 88.6%). These findings have also been reported by several other studies.[7,14,21,24] In contrast, in the study by Furuta et al,[13] no statistically significant difference was found in recovery rates between the combined regimen of prednisolone and acyclovir and the regimen of prednisolone, in the treatment of Bell's palsy. Controversially, other studies also support the idea that acyclovir is not beneficial in the treatment of Bell's palsy.[1,25,31] In our study, the group treated with prednisolone and acyclovir showed a statistically significant improved recovery rate compared with the group treated with prednisolone alone, supporting the efficacy of acyclovir treatment.

As considered in this study, acyclovir must be used in the early stages of the disease, as it is a nucleopeptide analogue that prevents virus replication by interfering with DNA polymerase enzyme.[30] As acyclovir is not a viricidal agent, if it is prescribed late and after virus replication, it will not be able to cure the patient. In Hato et al's study[14] on the combined therapy of prednisolone and acyclovir, and further study on a comparison of this combination therapy and prednisolone,[30] the recovery rate of combined therapy, if used in the first 3 days was 100%, and if used after this time period, was around 80%. Therefore, as shown in our study concerning significant recovery rate discrepancy between the 2 groups, it is recommended to administer acyclovir accompanied by prednisolone in the early onset of facial paresis in Bell's palsy to increase the complete recovery rate.

The complete recovery of facial paresis is very important for cosmetic problems especially in females who are sometimes more involved in this disorder (as in this study). Incomplete recovery of facial paresis can lead to facial deformity and result in a droopy appearance of the face, especially during speaking

and laughing, which can effect self-esteem. Certainly, complete recovery of facial paresis in Bell's palsy may lead to a decrease in other complications, such as facial hemispasms and synkinesis.

In summary, the appropriate treatment of Bell's palsy, which is the most common disorder of the facial nerve and, in severe cases, may lead to incomplete recovery and complications, is necessary. Based on the results of this study, and due to the high probability of its viral etiology, we recommend the use of a combined therapy of acyclovir and prednisolone to increase the recovery rate,[8,10,12] and decrease the complications of Bell's palsy.

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