

BELL'S PALSY MANAGEMENT: ACYCLOVIR IN COMBINATION WITH PREDNISOLONE VERSUS PREDNISOLONE ALONE – A COMPARATIVE STUDY

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ABSTRACT

Background: Bell's palsy is an idiopathic facial nerve palsy of sudden onset. There are controversies regarding its optimal treatment. The objective of this study was to find out whether prednisolone and acyclovir given in combination is superior to prednisolone alone. **Methods:** This hospital-based comparative study was carried out in Neurology Unit, Postgraduate Medical Institute, Lady Reading Hospital Peshawar, from January 2009 to September 2011. A total of 415 patients with Bell's palsy, aged ≥ 7 years were randomly assigned to two groups. Group A received prednisolone and acyclovir in combination while Group B received prednisolone alone. Data were analyzed using SPSS version 15.0. **Results:** Out of 415 patients, 185(44.58%) were males and 230(55.42%) females. Mean age was 38.52 ± 11.42 years. Group A had 209 patients and Group B 206. They were followed for 4 months. Group A had 94.7% recovery rate while Group B had 87.3% ($p < 0.05$). **Conclusion:** Acyclovir and prednisolone in combination is more beneficial than prednisolone alone in the treatment of Bell's palsy.

KEY WORDS: Bell's palsy, Prednisolone, Acyclovir.

INTRODUCTION

Bell's palsy is defined as an idiopathic facial nerve palsy of sudden onset.¹ Its annual incidence is approximately 20 per 100,000. The median age is 40 but the disease can occur at any age. Men and women are equally affected, and there is no predilection for either side of the face.²

The most alarming symptom of Bells palsy is unilateral facial weakness. Denervation of the orbicularis oculi muscle results in the inability of the patient to close the eye lids effectively, while denervation of the risorius muscle results in the limited retraction of the angle of mouth. Less common symptoms include hyperacusis, decreased production of tears, altered taste, and numbness or pain around the ear of the affected site.³

The location of injury is peripheral to the nerve nucleus. The injury is thought to occur near, or at, the geniculate ganglion. If the lesion is proximal to the geniculation ganglion, the motor paralysis is accompanied by gustatory and autonomic abnormalities, while lesion between the geniculate ganglion and the origin of chorda tympani produces same effects, except that lacrimation is spared. If the lesion is at the stylomastoid foramen it may result in facial paralysis only.⁴

About 70 to 80% of untreated patients recover without significant long term facial weak-

ness and other sequel, thus the prognosis is otherwise also favorable, but the goal of treatment is to further improve the rate of a normal or near-normal outcome.³

Treatment of Bell's palsy remains controversial and variable. Two main types of pharmacological treatment have been used to improve outcomes from Bell's palsy: steroids alone or in combination with antivirals. The rationale for these treatments is based on the presumed patho-physiology of Bell's palsy, namely inflammation and viral infection.⁵

Enhancement of the facial nerve on magnetic resonance imaging has been observed in Bell's palsy, suggesting that inflammation is in part responsible for the associated paralysis.⁶ As a consequence, steroids have been used to treat Bell's palsy and have been shown to significantly improve outcomes compared with placebo.⁷

In 1972, McCormick first suggested that herpes simplex virus (HSV) is responsible for idiopathic facial palsy. This was based on the analogy that HSV was found in the cold sores, and he hypothesized that HSV may remain latent at the geniculate ganglia. Since then autopsy studies have shown HSV in the geniculate ganglion of patients with Bell's palsy.⁸ On the basis of this evidence,

some clinicians treat patients with anti-virals, including aciclovir, famciclovir, and valaci-clovir.

The role of combination therapy with steroids plus anti-virals has been investigated for the treatment of Bell's palsy. Studies have produced somewhat conflicting results and there is still controversy about the effectiveness of anti-virals on top of steroids.⁹⁻¹³

Despite lack of clear evidence, many clinicians treat Bell's palsy with combined therapy i.e. steroids plus antivirals. The aim of this study was to find out whether prednisolone plus acyclovir given in combination is superior to prednisolone given alone in patients with Bell's palsy.

MATERIAL AND METHODS

This was a hospital based comparative study. The study was carried out in neurology unit Post graduate Medical Institute Lady Reading Hospital, Peshawar from January 2010 to September 2011. Hospital ethical committee had approved this study. After obtaining an informed consent, a total of 468 patients with Bell's palsy (with unilateral facial-nerve weakness of no identifiable cause), aged 7 years and above were included. Randomization was done by simple lottery method into two groups i.e. Group A and B. Group A received prednisolone and acyclovir while Group B received prednisolone alone. Treatment was initiated within 72 hours of facial paralysis. In both the groups prednisolone was given for a period of 7 days with tapering thereafter to zero over the next 3 days (in children prednisolone was used in a dose of 1 mg /kg body weight), while acyclovir was given in dose of 400 mg five times per day for 5 days. All patients were reviewed at 3, 6 and 16 weeks interval to monitor their House-Brackman scale.

The facial appearance of patients was assessed in four standard poses: at rest, with a forced smile, with raised eyebrows, and with eyes tightly closed. The House-Brackmann grading scale¹⁴ was used for recording the initial presentation of patients with Bell's palsy (baseline assessment) and their outcome /recovery on follow-up visits. This scoring system assigns patients to one of six categories on the basis of the degree of facial-nerve function. A House-Brackmann grade of at least 2 was defined as facial muscle recovery. (Table 1)

Out of the 468 patients, 415 patients came for regular follow-up. Group A comprised of 209 patients while Group B comprised of 206 patients. Patients who were lost to follow-up were excluded in order to ensure consistent analysis. Facial palsy due to secondary causes like suppurative otitis media, multiple sclerosis, systemic infection, sar-

Table 1: House-Brackman scale.

Grade I	Normal symmetrical function
Grade II	Slight weakness noticeable only on close inspection Complete eye closure with minimal effort Slight asymmetry of smile with maximal effort Synkinesis barely noticeable, contracture, or spasm absent
Grade III	Obvious weakness, but not disfiguring May not be able to lift eyebrow Complete eye closure and strong but asymmetrical mouth movement Obvious, but not disfiguring synkinesis, mass movement or spasm
Grade IV	Obvious disfiguring weakness Inability to lift brow Incomplete eye closure and asymmetry of mouth with maximal effort Severe synkinesis, mass movement, spasm
Grade V	Motion barely perceptible Incomplete eye closure, slight movement corner mouth Synkinesis, contracture, and spasm usually absent
Grade VI	No movement, loss of tone, no synkinesis, contracture, or spasm

coidosis, Lyme's disease and uncontrolled diabetes etc. were not included in the study. Also patients with Bell's palsy in whom duration of symptoms were more than 72 hours were also excluded from the study. Clinical examination was carried in all patients and relevant investigations were performed where in doubt regarding the diagnosis to exclude secondary causes.

Confounding variables were controlled by matching characteristic of the two groups such as age and gender. Data were analyzed using SPSS version 15.0. Mean ± standard deviation (SD) was calculated for numerical variables like age. Qualitative variables such as gender and House-Brackmann grade were presented in frequency and percentages. Chi-square test was applied to calculate statistical difference between patients with Bell's palsy who received prednisolone plus acyclovir in combination and those who received prednisolone alone. P value was generated and

less than 0.05 was considered significant. Data were presented in Tables.

RESULTS

Initially 468 patients were enrolled in this study, but 415 patients came for regular follow-up. Patients lost to follow-up were excluded. Out of 415 patients included in the study, 185 (44.58%) were males and 230 (55.42%) females and, with male to female ratio of 1:1.24. They were divided into two groups. Group A comprised of 209 while Group B 206 patients. Gender distribution in both the groups is shown in Table 2. Age of the patients ranged from 7 to 68 years with a mean age of 38.52±11.42 years. Age distribution in both the groups is shown in Table 3.

Mean House-Brackman grade before initiation of treatment was 4.6. The overall rate of recovery (improvement to House-Brackman grade 2 after treatment) in Group A patients was 198

Table 2: Gender distribution of patients with Bell's palsy (n=415).

Group	Gender		Total
	Male	Female	
A	92 (44.02%)	117 (55.98%)	209
B	93 (45.15%)	113 (54.85%)	206
Total	185 (44.58%)	230 (55.42%)	415

Table 3: Age distribution of patients with Bell's palsy

Group	Number of patients	Age groups		
		7-25 years	26-49 years	>50 years
A	209	64 (30.62%)	111 (53.11%)	34 (16.27%)
B	206	60 (29.13%)	122 (59.22%)	24 (11.65%)

(94.7%) while that in Group B was 180 (87.3%) i.e. (p<0.05), Odds ratio 1.16 (95% Confidence interval 0.84-1.52).

DISCUSSION

Increasing evidence implies that Bells palsy is caused by the latent Herpes Simplex virus being reactivated from the cranial nerve ganglion, reactivation of this presumably causes inflammation of the facial nerve.^{5,8,15} Murakami et al found that 11 patients of the 14 turned out to have posi-

tive PCR for Herpes Simplex virus in the endoneural fluid of patients with Bell's palsy.¹⁶

This led to the trials of anti-viral therapy in Bell's palsy patients.^{5,7} Compared with placebo, these trials found no benefit for antiviral therapy alone. However, the data are conflicting with regard to the possibility of additional benefit when antiviral agents are administered with glucocorticoids.¹⁷⁻¹⁹

In the present study prednisolone plus acyclovir given in combination in Bell's palsy patients had a 94.7% recovery while prednisolone given alone had a 87.3% recovery, i.e. p value <0.05, Odds ratio 1.18 (95% Confidence interval 0.78-1.56).

In a meta-analysis involving 18 trials and 2786 patients, treatment with glucocorticoids alone was associated with a reduced risk of unfavorable recovery (relative risk [RR] 0.69, 95% CI 0.55-0.87), whereas treatment with antiviral agents alone was not (RR 1.14, 95% CI 0.80-1.62).⁹

In pooled data from eight trials, the same meta-analysis found a trend towards a reduced risk of unfavorable recovery for combined antiviral and glucocorticoid treatment compared with glucocorticoid treatment alone, but the outcome just missed statistical significance (RR 0.75, 95% CI 0.56-1.0).⁹

In a second meta-analysis of six trials and 1145 patients, there was no significant benefit of combined antiviral and glucocorticoid treatment for achieving at least partial facial muscle recovery (odds ratio 1.5, 95% CI 0.83-2.69).¹⁰

The divergent results of these two meta-analyses may be due to differences in Methodologies used. Secondly, investigators studying Bell's palsy rarely perform thorough molecular diagnostic testing for viral etiologies. Varicella zoster virus, has been reported to be associated with 8% to 28% of Bell's palsy cases.²⁰ This virus is less sensitive to anti-virals and the doses used in treatment trials are generally not high enough to treat a Varicella zoster virus infection. Thus, if patients with this type of infection were included in the trials, the potential benefit of anti-viral therapy may be diluted (as may be the case for the Sullivan et al and Engstrom et al studies).^{7,17}

In our study the mean House-Brackman grade before initiation of treatment was 4.6. In the Sullivan et al study⁷ (which showed no benefit of adding aciclovir to steroids) the mean House-Brackmann grade was 3.6, whereas the mean score was 4.3 in the Hato et al study, which reported a significant benefit of adding valaciclovir (97 versus 90 percent).²¹

Minnerop et al performed a sub-group analysis of patients who presented with severe facial muscle paralysis (House-Brackmann grade of 5 or 6) and found significantly better facial muscle recovery in patients who received famciclovir plus steroids than in those on steroids alone (72% v 47%, respectively).²² These data suggest that antiviral therapy may benefit in particular those patients with more severe facial paralysis at presentation.

Numthavaj P et al suggested that the current practice of treating Bell's palsy with anti-viral therapy plus corticosteroid may lead to slightly higher recovery rates compared to treating with prednisone alone.²³

Thaera GM et al showed that corticosteroids effectively reduce the risk of an unfavorable outcome in Bell's palsy. Antiviral agents, when administered concurrently with corticosteroids, may result in additional benefit.²⁴

CONCLUSION

Acyclovir and prednisolone given in combination is more beneficial than prednisolone given alone.

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