Comparison between the Efficacy of Steroids and Acyclovir in the Management of Patients with Bells Palsy

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ABSTRACT

Introduction: Bell's palsy accounts for about 70% of all cases of peripheral facial palsy and the annual incidence is about 30/100 000 population with a peak incidence between the second and fourth decades of life. Two main types of pharmacological treatment have been used to improve outcomes from Bell's palsy: steroids and antivirals. Studies have produced somewhat conflicting results, however, and there is debate over the effectiveness of antivirals on top of steroids. Study aimed to assess the efficacy of steroid and acyclovir used alone and in combination in the treatment for Bells palsy patients.

Material and Methods: A prospective study was carried out at Indira Gandhi government general hospital for a period of one year. Bells palsy patients in the age group of 18 – 75 years with unilateral idiopathic facial nerve palsy presenting to the hospital with more than 72 hours after the onset of facial nerve palsy were included for the study. A total of 84 patients were included for the study.They were divided into four groups of 21 each. Group I patients received steroid alone, group II patients were given acyclovir alone, group III patients had both steroid and acyclovir and group IV patients received only placebo (multivitamins).

Results: After the intervention at the end of 6 months we found that majority of the patients had improved from grade III to grade I in group I (steroid only group) compared to other groups and it was followed by group III (acyclovir and steroid) and this difference was found to be statistically significant ($p<.05$), whereas patients in group IV (multivitamin placebo group) did not show any improvement in the grading of facial palsy. The parameters of the nerve conduction study, latency, amplitude, duration and area had shown a statistical significant improvement at the end of 6 months compared to the base line values particularly in group I (steroid only) and group III (steroid plus acyclovir) patients of Bells palsy.

Conclusion: Bell's Palsy treated with Steroids is significantly better than other treatment in restoration and improvement in facial function.

Keywords: Bells Palsy, Steroids, Acyclovir, House-Brackmann Scale and Nerve Conduction Study.

INTRODUCTION

The facial nerve plays a crucial role in emotional expression. Impairment of the facial muscles causes considerable functional, psychosocial and aesthetic disturbance to the affected individual. The aetiology of peripheral facial palsy can be infectious, which include herpes zoster, borreliosis (Lyme disease), meningitis, and infection of the middle ear.[1] When there is no identifiable cause of the palsy it is termed "idiopathic" or "Bell's palsy". Bell's palsy is an abrupt onset of unilateral weakness or paralysis of the face due to acute peripheral facial nerve dysfunction, with no readily identifiable cause, and with some recovery of function within 6 months.[2] Bell's palsy accounts for about 70% of all cases of peripheral facial palsy and the annual incidence is about 30/100 000 population with a peak incidence between the second and fourth decades of life. There is no difference in gender or side of the face, and no seasonal clustering. In most cases, the natural course of Bell's palsy is favourable but at least 30% of patients will have some sequelae and 4% have severe residual paresis, synkinesis and/or contracture.[3] Different facial nerve grading scales have been developed and among them the House-Brackmann scale (HBS) is the most commonly used grading system for facial nerve disorders, it has six grades, or scores, where I = normal function and VI = complete paralysis.[4]

Many patients with idiopathic facial nerve palsy recover without intervention; however, up to 30% have poor recovery of facial muscle control and experience facial disfigurement, psychological trauma, and facial pain.[5] Two main types of pharmacological treatment have been used to improve outcomes from Bell's palsy: steroids and antivirals.[6] The rationale for these treatments is based on the presumed pathophysiology of Bell's palsy, namely inflammation and viral infection. The neuronal inflammation associated with Bell's palsy is thought to be secondary to viral infection. Herpes simplex virus has been detected in the endoneurial fluid in patients with Bell's palsy.[7] On the basis of this evidence, some clinicians treat patients with antivirals, including aciclovir, famciclovir, and valaciclovir.[8] The benefits of antivirals alone are not clear, thus the role of combination therapy with steroids plus antivirals has been investigated for the treatment of Bell's palsy.[9-11] Studies have produced somewhat conflicting results, however, and there is debate over the effectiveness of antivirals on top of steroids.[12] The most recent guidelines from the American Academy of Neurology suggest that acyclovir combined with prednisone

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is "possibly effective" for Bell's palsy.[13] Despite a lack of clear evidence, many clinicians treat Bell's palsy with combination therapy. Two recent Cochrane reviews assessed the effectiveness of corticosteroids and antiviral agents in patients with Bell's palsy. The analysis of corticosteroid treatment pooled the results of four randomized, controlled trials with a total of 179 patients.[14] The review of antiviral treatment included three studies involving 246 patients.[8] Both reviews independently concluded that insufficient data exist to support the use of either or both therapies. In India very few studies had been conducted in assessing the efficacy of steroids and antivirals for treating Bells palsy and so the present study was undertaken to assess the efficacy of both steroids and antiviral drugs either used alone or in combination in the treatment for Bells palsy.

Study aimed to assess the efficacy of steroid and acyclovir used alone and in combination in the treatment for Bells palsy patients.

MATERIAL AND METHODS

A prospective study was carried out at Indira Gandhi government general hospital for a period of one year. The study was started after getting the clearance from the institutional ethical committee. Bells palsy patients in the age group of 18 – 75 years with unilateral idiopathic facial nerve palsy presenting to the hospital with more than 72 hours after the onset of facial nerve palsy were included for the study. Patients presenting with co-morbid conditions like with diabetes, tuberculosis, serious heart diseases, glaucoma, hepatic disease, neurological diseases, and renal diseases, pregnant and lactating mothers, patients already on antivirals and systemic steroids medications, patients with history of acute or chronic otitis media, patients with history of trauma and immunodeficiency disorders and fertile females planning for pregnancy were excluded from the study. A total of 84 patients were included for the study according to the inclusion and exclusion criteria. Informed consent was obtained from all the patients involved in the study.

All the 84 patients were divided into four groups of 21 patients in each group. Group I patients were given only steroid (prednisolone 60 mg/day for a week then tapered over 10 days), Group II patients received acyclovir alone (800 mg/day for 5 days), Group III patients were administered with both steroid and acyclovir (Prednisolone 60 mg/day for a week then tapered over 10 days and Acyclovir 800 mg/day for 5 days) and Group IV patients were given only a placebo (multivitamins). After initial clinical assessment patients were subjected to routine hematological and biochemical examination. Nerve conduction study was done using RMS EMG EP MARK –II under standard conditions. Nerve conduction velocity and CMAP amplitude and the amplitude difference between the two sides were studied. All nerve conduction studies were done bilaterally. The normal unaffected side is kept as a control and affected side latency and CMAP amplitude difference is calculated at the time of admission and after 6 months of follow up. The House-Brackmann scale (HBS) grading system was used to assess the severity of the facial nerve disorder, it has six grades where grade I indicates normal function and grade VI indicates complete paralysis.

The efficacy of the interventions was measured in terms of improvement in the nerve conduction studies 6 months after intervention in comparison with the baseline value and similarly the change in the grade of the House-Brackmann scale (HBS) was also monitored.

STATISTICAL ANALYSIS

All data were entered and analysed using SPSS version 21. The quantitative variables between any two groups were compared using parametric (T–independent test) and non-parametric tests (Mann Whitney U test), wherever appropriate and similarly Analysis of variance (ANOVA) or the equivalent test in non-parametric methods namely Kuruskal Wallis tests were also used, considering $p<.05$ as statistically significant.

RESULTS

Table 1 shows the age and gender wise distribution of the study subjects involved in all the four groups. It is seen from the table that male were more in number than the females in all the four groups but the proportion is almost equal in all the groups. Majority of the patients were in the age group between 30 and 40 years with the mean age varying between 33 and 37 years and no significant difference was observed in the age group and the gender between the four groups. The mean duration of the onset of facial nerve palsy and the patient reporting to our hospital was four days on an average in all the four groups and with respect to the side of the involvement we found almost equal distribution in both right sided and left sided facial nerve palsy in all the groups (table 2). The degree of facial nerve weakness was graded using House Brackman grading system in which the grades ranges from I to VI based on the gross features of facial nerve involvement, at rest features, motion of the forehead, eye and mouth. In our study majority of the study subjects in all the four groups had grade III facial nerve palsy followed by grade II palsy none of the patients had grade VI facial palsy (complete paralysis) and no statistical significant difference was observed between the groups with respect to the grading of facial palsy (table 3). After the intervention at the end of 6 months we found that majority of the patients had improved from grade III to grade I in group I (steroid only group) compared to other groups and it was followed by group III (acyclovir and steroid) and this difference was found to be statistically significant ($p<.05$), whereas patients in group IV (multivitamin placebo group) did not show any improvement in the grading of facial palsy as majority of the patients were still with grade II or grade III facial palsy (table 4). Nerve conduction study was performed for all patients initially at the time of admission and later after intervention at the end of 6 months. Latency, amplitude, duration, velocity and area were the parameters measured in the nerve conduction test. Among these parameters the latency, amplitude, duration and area were the parameters which showed a statistical

Age group	Group I (steroid only)		Group II (acyclovir only)		Group III (steroid plus acyclovir)		Group IV (placebo)	
	Male	Female	Male	Female	Male	Female	Male	Female
20 – 25	0	0	0	0	1 (7%)	0	1 (6.2%)	0
26 – 30	1 (6.6%)	0	2 (11.7%)	0	1 (7%)	1 (14.2%)	2 (12.5%)	1 (20%)
31 – 35	6 (40%)	2 (33.3%)	7 (41.1%)	2 (50%)	5 (35.7%)	3 (42.8%)	4 (25%)	1 (20%)
36 – 40	5 (33.3%)	2 (33.3%)	4 (23.5%)	1 (25%)	4 (28.5%)	1 (14.2%)	6 (37.5%)	2 (40%)
41 – 45	2 (13.3%)	0	2 (11.7%)	1 (25%)	0	0	2 (12.5%)	0
46 – 50	1 (6.6%)	1 (16.6%)	1 (5.8%)	0	2 (14.2%)	1 (14.2%)	1 (6.2%)	1 (20%)
>50	0	1 (16.6%)	1 (5.8%)	0	1 (7%)	1 (14.2%)	0	0
Total	15 (100%)	6 (100%)	17 (100%)	4 (100%)	14 (100%)	7 (100%)	16 (100%)	5 (100%)
Mean ± SD	33.3 ± 3.4		35.1 ± 3.6		38.4 ± 4.1		37.5 ± 3.8	
P value	0.284							
P value derived by applying ANOVA								

Table-1: Age and gender wise distribution of the study subjects

Variables	Group I (n=21)	Group II (n=21)	Group III (n=21)	Group IV (n=21)
Mean duration of onset (in days) (mean ± SD)	4.2 ± 0.5	3.8 ± 0.5	4.4 ± 0.4	4.3 ± 0.2
Right sided palsy	11 (52.3%)	8 (38%)	12 (57%)	12 (57%)
Left sided palsy	10 (47.7%)	13 (62%)	9 (43%)	9 (43%)

Table-2: Distribution of the study subjects based on the mean duration of onset and the side involvement of the facial nerve palsy

House brackman grading	Group I (n=21)	Group II (n=21)	Group III (n=21)	Group IV (n=21)	P value
Grade I	2 (9.5%)	1 (4.7%)	0	2 (9.5%)	0.653
Grade II	5 (23.8%)	6 (28.5%)	5 (23.8%)	4 919%)	
Grade III	6 (28.5%)	7 (33.3%)	7 (33.3%)	5 (23.8%)	
Grade IV	4 (19%)	3 (14.2%)	5 (23.8%)	7 (33.3%)	
Grade V	4 (19%)	4 (19%)	4 (19%)	3 (14.2%)	
P value derived by applying Kruskal Wallis test					

Table-3: Distribution of study subjects based on House Brackman facial nerve grading system at the time of admission

House brackman grading	Group I (n=21)	Group II (n=21)	Group III (n=21)	Group IV (n=21)	P value
Grade I	16 (76.1%)	9 (42.8%)	13 (61.9%)	3 (14.2%)	<.001
Grade II	4 (19%)	5 (23.8%)	5 (23.8%)	5 (23.8%)	
Grade III	1 (4.7%)	6 (28.5%)	3 (14.2%)	5 (23.8%)	
Grade IV	0	1 (4.7%)	0	6 (28.5%)	
Grade V	0	0	0	2 (9.5%)	
P value derived by applying Kruskal Wallis test					

Table-4: Distribution of study subjects based on House Brackman facial nerve grading system at the end of 6 months after intervention

Nerve conduction study		Group I (n=21)	Group II (n=21)	Group III (n=21)	Group IV (n=21)
Latency (ms)	Baseline value	9.26 ± 0.81	9.41 ± 1.1	9.33 ± 0.93	9.89 ± 0.68
	6 months after intervention	9.81 ± 1.08	9.53 ± 0.81	9.92 ± 0.74	9.94 ± 0.84
	P value	0.016	0.081	0.021	0.714
Amplitude (mV)	Baseline value	1.71 ± 0.58	1.74 ± 0.74	1.68 ± 0.51	1.72 ± 0.33
	6 months after intervention	1.98 ± 0.42	1.80 ± 0.36	1.93 ± 0.41	1.79 ± 0.36
	P value	0.010	0.071	0.026	0.638
Duration (ms)	Baseline value	7.62 ± 1.86	7.71 ± 2.1	8.18 ± 1.92	7.46 ± 1.65
	6 months after intervention	7.20 ± 1.78	7.59 ± 1.9	7.62 ± 1.98	7.38 ± 1.74
	P value	0.016	0.078	0.010	0.515
Velocity (m/s)	Baseline value	29.6 ± 4.8	31.2 ± 5.6	30.1 ± 4.9	28.9 ± 5.2
	6 months after intervention	44.3 ± 5.4	39.6 ± 4.57	45.4 ± 5.02	34.3 ± 4.98
	P value	<.001	<.001	<.001	0.074
Area (mVms)	Baseline value	3.63 ± 0.87	3.51 ± 0.54	3.48 ± 0.92	3.58 ± 0.81
	6 months after intervention	4.02 ± 0.98	3.74 ± 1.01	3.86 ± 0.89	3.73 ± 0.91
	P value	<.001	0.081	0.021	0.148
P value derived by applying ANOVA					

Table-5: Comparison of nerve conduction test values before and after intervention among the study subjects

significant improvement at the end of 6 months compared to the base line values particularly in group I (steroid only) and group III (steroid plus acyclovir). The nerve velocity had shown a significant improvement in group I, II and III, whereas none of the parameters had shown any improvement among group IV subjects (table 5).

DISCUSSION

The present study aimed to determine the most efficient treatment for bells palsy by doing a comparative study where the patients were divided into four groups, group I treated with steroids alone, group II treated with an antiviral drug acyclovir alone, group III patients treated with a combination therapy of steroid and acyclovir and the group IV patients were given multivitamin tablets as placebo. Most of the demographic parameters and the clinical parameters were comparable between all the four groups. The severity of Bell's Palsy was assessed using House Brackhmann Facial Grading Scale and the degree of nerve damage was measured using Nerve Conduction Study. All patients were given eye care, disease education, physiotherapy and facial exercises and they were observed for 6 months. Patients treated with steroids showed significant improvement in Grades of facial recovery when compared to other group patients. In comparison to our study most of the previous studies had also used the House Brackhmann scale for assessing the facial nerve functions. Scandinavian Bell's palsy study (SBPS) has so far been the largest randomised, double-blind, placebo-controlled multi-centre trial assessing corticosteroid and antiviral treatment for Bell's palsy.[15] Patients who received prednisolone had a shorter time to complete recovery of facial function and a more favourable outcome at 12 months compared with patients not receiving prednisolone. Synkinesis was also less common in prednisolone-treated patients. Valaciclovir alone was not proved to be effective, and did not give any additive effect to prednisolone.[15]

A Scottish trial of 551 patients randomly assigned within 72 hours of onset to 10 days of 25 mg prednisolone twice daily and placebo, aciclovir 400 mg five times daily and placebo, both prednisolone and aciclovir or placebo, reported similar results. The investigators of the study concluded that early treatment with prednisolone 50 significantly improved the chances of complete recovery at 3 and 9 months. There was no benefit from aciclovir.[16] The nerve damage in Bell's palsy is consistent with oedema and inflammation of the nerve in the Fallopian canal.[17,18] Early administration of anti-inflammatory corticosteroids may reduce oedema and subsequent spreading of conduction block or axonotmesis.[19] The effect of early prednisolone treatment in Bell's palsy is in accordance with the reported effect of corticosteroids in vestibular neuritis, a disease which may have the same pathogenesis as Bell's palsy.[20,21]

Prednisolone plus valaciclovir was not more effective than prednisolone alone. This result is in accordance with previous findings involving valaciclovir and aciclovir plus corticosteroids.[16,22] Nevertheless, an additional effect of aciclovi or valaciclovir on corticosteroid treatment has been reported.[23]

Minnerop et al performed a subgroup 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, achieved normal function).[24] However, only 18 and 17 patients respectively were included in this analysis. These data suggest that antiviral therapy may benefit in particular those patients with more severe facial paralysis at presentation. On the other hand, one of the most recently published trials, by Engstrom et al,is in opposition to this argument. Patients in this trial had a median House-Brackmann grade of 4 at presentation, which is very similar to the level of palsy observed by Hato et al, and the authors convincingly showed no benefit of adding valaciclovir to steroids alone.[15,23]

A recent Cochrane review conduted by Jeremy M. etal by including three types of antivirals namely acyclovir, valacyclovir, and famciclovir and a sensitivity analysis had revealed a larger magnitude of effect when trials using acyclovir were excluded (risk ratio 0.65;
95% confidence interval 0.36 to 1.16),[25] which was consistent with a recent study by Kim et al that suggested famciclovir improves facial nerve recovery compared with acyclovir in patients with severe Bell's palsy. Caution should be taken when prescribing antivirals to patients with renal failure because creatinine clearance will affect the dosing regimen.[26]

One of the major limitation of the present study was usage of House- Brackmann scale in grading the facial nerve palsy as the scale has been criticized for insufficient sensitivity to change and difficulty in assigning grades because patients may have contrasting degrees of function in different parts of the face.[27,28] Alternative scales, such as the Sydney and Sunnybrook facial grading systems, are available but are more difficult to use in clinical practice.[29]

CONCLUSION

Bell's Palsy treated with Steroids is significantly better than other treatment in restoration and improvement in facial function. The benefit of antiviral therapy combined with steroids for patients with severe facial muscle paralysis at presentation who do not have Varicella zoster virus reactivation is, however, an ongoing question. Future prospective double blind studies that use modern diagnostics, such as polymerase chain reaction, for the detection of Herpes virus reactivation are needed to resolve this issue.

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