ABSTRACT

Objectives: Corticosteroids have been used in the treatment of Bell’s palsy and several other postinfectious neurological conditions. We hypothesized that administration of a single dose of intravenous (IV) methylprednisolone might be an effective alternative to oral prednisolone.

Materials and Methods: In this open label, randomized trial, patients with acute Bell’s palsy were randomized into two groups. One group received single dose (500 mg) of IV methylprednisolone while the other group received 10 days of oral prednisone. Outcome was assessed at 1 and 3 months with House–Brackmann scale.

Results: At 3 months, 93 (79.48%) patients had completely recovered. IV methylprednisolone and oral prednisolone groups had similar recovery rates (80% vs. 78.33%, P > 0.05). Patients with Grade 2 and 3 recovered completely. In patients with Grade 6, the recovery rate was 20%. A better outcome was observed if corticosteroids were administered within 3 days of onset of palsy.

Conclusion: Intravenous methylprednisolone and oral prednisolone showed equivalent benefit in patients with acute Bell’s palsy.

KEY WORDS: Corticosteroids, facial nerve, methylprednisolone

Introduction

Bell’s palsy is the most common cause of acute facial nerve paralysis. Even though it is a benign and self-limiting disease, in many patients it can lead to significant physical, social and psychological morbidity.[1-4] A variety of treatment options has been tried with varying results. It has been postulated that Bell’s palsy occurs as an inflammatory reaction to viral infection. However, the role of antiviral drugs is controversial.[5-10] Corticosteroids, currently, remain the single most important treatment option.[11,12] Bell’s palsy, usually, occur rapidly, and any pharmacological intervention is difficult. Intravenous (IV) corticosteroids are of proven value in similar acute inflammatory neurological illness such as multiple sclerosis, acute disseminated encephalomyelitis and transverse myelitis. Hence, it is worthwhile to study the value of IV corticosteroids vis-à-vis oral corticosteroids. In this study, we compared the efficacy of a single dose of 500 mg of IV methylprednisolone with a 10 days oral prednisolone regime on recovery of patients with Bell’s palsy.

Materials and Methods

The study was designed as an open labeled, randomized controlled trial. The study was conducted between August 2011 and October 2013. Patients were enrolled from the outdoor services of the Department of Neurology, King George’s Medical University, Lucknow, India. Institutional Ethics Committee approved the study. Informed consent was taken from all the patients before inclusion in the study.

Inclusion Criteria

We recruited adult patients with unilateral acute facial palsy of no identifiable cause, within 1-week of onset.

Exclusion Criteria

Patients with any of the following conditions were excluded: pregnancy, diabetes, severe hypertension, renal or hepatic disease, gastric or duodenal ulcer, presence of acute otitis media or ipsilateral chronic otitis, recent head injury, psychiatric disease or any other condition where the use of corticosteroids was contraindicated.
Randomization and Treatment Allocation

The patients were divided into two groups, according to a pre-generated computerized randomization table. Patients in group 1 received a single dose of 500 mg of IV infusion of methylprednisolone while those in group 2 received oral prednisolone in a tapering dosage schedule (60 mg daily for initial 5 days, tapered by 10 mg daily over next 5 days).

Follow-up and Outcome Assessment

All patients were followed for a minimum of 3 months after inclusion, and the outcome analysis was done at 1-month and at 3 months. Cut-off at 1-month and 3 months were used to study the short-term recovery patterns, defined as recovery occurring in <4 months.[11] The primary outcome was assessed using the House–Brackmann grading system for facial nerve function, which assigns patients to 1 of 6 categories. Grade 1 indicates normal function, while Grade 6 indicates no facial function. Intermediate severity grades were defined as slight (Grade 2), moderate (Grade 3), moderately severe (Grade 4) and severe (Grade 5) depending upon the loss of tone, magnitude of weakness, and presence of synkinesis, contracture or hemifacial spasm.[13] Patients were also advised to communicate telephonically or report immediately in case of any serious adverse event. Possible adverse events were evaluated at each study visit. Assessment of the patients was carried out on the basis of grade of palsy as well as early (≤ 3 days) versus late (between 4 and 7 days) initiation of treatment regimes. Final outcome was measured in terms of complete recovery of the facial nerve function (Grade 1 of House–Brackmann grading system) at 3 months.

Statistical Analysis

The results were expressed as percentage and mean ± standard deviation. The Chi-square Fisher exact test, where ever applicable, was used to compare the dichotomous variables. The Chi-square for trend analysis was used to compare categorical variables. The unpaired t-test was used to compare continuous variables. P < 0.05 was considered as significant. All the analyses were carried out using SPSS version 16.0 (SPSS Inc., Chicago, IL).

Results

During the study period, we screened 151 patients with Bell’s palsy. Twenty-seven patients were excluded out of whom 14 patients had been initiated on corticosteroids, 9 on antiviral treatment, and 4 patients had a known contraindication to corticosteroids. Finally, 124 patients were enrolled in the study. At 3 months, 7 patients were lost to follow-up and 117 patients were subjected to outcome analysis [Figure 1]. All the baseline parameters under study were comparable between two groups [Table 1].

After 1-month of treatment, 31 (54.38%) patients from group 1 and 23 (38.33%) from group 2 recovered completely; a total of 54 (46.16%) patients thus recovered completely. The patients treated with IV methylprednisolone and oral prednisolone, both, showed improvement in the symptoms. The results were however statistically nonsignificant when compared between the two groups.

After 3 months of treatment, 46 (80.7%) patients from group 1 and 47 (38.33%) from group 2 recovered completely; a total of 93 (79.48%) patients recovered completely. No statistically

Figure 1: Flow chart of the study
significant differences were observed between the two treatment group.

**Sub Group Analysis**

**According to grade of palsy**

After 1-month, patients with facial palsy (Grade 2 and 3) showed early and complete recovery. All patients of Grade 2 and 3 recovered completely while only 53% and 32.2% patients in Grade 4 and Grade 5, respectively, showed complete recovery. No meaningful recovery was observed in patients with Grade 6 Bell’s palsy.

After 3 months, trends of recovery almost converged in terms of the difference in the two groups. In Grade 6, only 1 (20%) patient from group 1 showed complete recovery [Table 2].

**According to the initiation of treatment**

The patients were also analyzed according to early (≤3 days) versus late (between 4 and 7 days) initiation of treatment based upon their time of arrival for the treatment. In the methylprednisolone group, at 1-month, 58.33% patients (early group) and 47.61% patients (late group) had complete recovery. At 3 months, 83.33% and 76.19% patients in the two respective group had complete recovery.

In oral prednisolone group, at 1-month, 40% patients (early group) and 34.78% patients (late group) had complete recovery, while at 3 months 81% and 73.91% patients, respectively, had complete recovery. A trend toward better recovery with early institution of treatment (IV or oral) was observed where IV methylprednisolone was found to be better than oral prednisolone, but the difference was not statistically significant.

**Adverse events**

None of the patients in either treatment groups reported any adverse event during the study period.

**Discussion**

This study evaluated the efficacy of a single dose IV methylprednisolone versus oral prednisolone. We observed that a single dose administration of IV methylprednisolone is as effective as 10 days treatment with oral prednisolone in patients with acute Bell’s palsy. Treatment options for patients of Bell’s palsy are aimed to facilitate functional recovery. Treatment options include corticosteroids and antiviral drugs, alone or in combination. Even without treatment, a large number of patients (approximately 70%) recover completely within 6 months and approximately 30% of patients may not recover completely.[14,15] We noted that approximately 80% patients recovered completely at 3 months of treatment with either IV methylprednisolone or oral prednisolone. Intravenous methylprednisolone resulted in nonsignificantly better functional recovery rate especially at 1-month when assessed against oral prednisolone and in terms of early institution of treatment (≤3 days). Combined treatment with a corticosteroid and an antiviral agent has been shown to be more effective in treating severe to complete Bell’s palsy than corticosteroid treatment alone.[16] Physical therapy appears to be effective only in the more severe Bell’s palsy, whereas less severe Bell’s palsy might result in complete spontaneous recovery, regardless of physical therapy.[17]

We showed that grade of Bell’s palsy (severity) is the most important prognostic determinant for recovery. Our results are similar to those reported by Sullivan et al. who found that patients with facial palsy of lower grades had a better outcome.[18] Grade 6 patients infrequently had complete recovery. In patients with Bell’s palsy, early treatment with prednisolone significantly improves the chances of complete recovery at 3 and 9 months. Consistent with these findings, our results also suggested that treatment of Bell’s palsy should be commenced promptly.

In majority number of patients, facial nerve spontaneously and completely recovers. The limitation of our study was the non-inclusion of a control group owing to an ethical concern of depriving patients of a recommended form of treatment.[11,12] The study was targeted to look for short-term recovery patterns; an extension to 6 months would have provided more details of patients with incomplete recovery or those in the process of recuperation.

A multicentric double-blind study, with a longer follow-up, may be done to study the efficacy of the two corticosteroids. A 5 days regimen of IV methylprednisolone, for severe Bell’s palsy, also needs to be investigated.

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**Table 1:**

Baseline demographic and clinical characteristics of patients with Bell’s palsy

| Variable                        | IV MPS (n=57) | Oral prednisolone (n=60) | Both group (n=117) |
|---------------------------------|---------------|--------------------------|--------------------|
| Mean age (years)                | 36.22±10.75   | 38.93±11.86              | 37.61±11.36        |
| Gender                          |               |                          |                    |
| Male                            | 31            | 35                       | 66                 |
| Female                          | 26            | 25                       | 51                 |
| Affected side                   |               |                          |                    |
| Right                           | 31            | 32                       | 63                 |
| Left                            | 26            | 28                       | 54                 |
| Duration of illness             |               |                          |                    |
| Mean (days)                     | 4.21±2.62     | 4.16±2.61                | 4.18±2.60          |
| Within 3 days                   | 36            | 37                       | 73                 |
| After 3 days                    | 21            | 23                       | 44                 |
| Grade of palsy (mean)           | 4.10±1.20     | 4.0±1.16                 | 4.05±1.18          |

**Table 2:**

Outcome assessment (complete recovery to grade 1) at 1-month and 3 months between the two groups in different grades

| Grades/ follow-up | Group 1 (n=57) (%) | Group 2 (n=60) (%) | OR (95% CI) P |
|-------------------|---------------------|---------------------|---------------|
| Grade 2 and 3     | n=14                | n=16                |               |
| 1-month           | 14 (100)            | 16 (100)            | NA            |
| 3 months          | 14 (100)            | 16 (100)            | NA            |
| Grade 4           | n=26                | n=22                |               |
| 1-month           | 13 (50)             | 5 (23)              | 3.14 (0.75-13.67) 0.07 |
| 3 months          | 22 (84)             | 18 (81)             | 1.22 (0.21-7.01) 0.79 |
| Grade 5           | n=12                | n=18                |               |
| 1-month           | 4 (33)              | 2 (11)              | 4.00 (0.46-41.23) 0.13 |
| 3 months          | 9 (75)              | 13 (72)             | 1.15 (0.17-8.29) 0.86 |
| Grade 6           | n=5                 | n=4                 |               |
| 1-month           | 0 (0.0)             | 0 (0.0)             | NA            |
| 3 months          | 1 (20)              | 0 (0.0)             | NA            |

CI=Confidence interval, n=Number of patients, NA=Not applicable, OR=Odds ratio
### CONSORT 2010 checklist for clinical trials

| Section/Topic                  | Item No | Checklist Item                                                                 | Reported on page No |
|-------------------------------|---------|---------------------------------------------------------------------------------|---------------------|
| Title and abstract            | 1a      | Identification as a randomised trial in the title                               | 1                   |
|                               | 1b      | Structured summary of trial design, methods, results and conclusions (for specific guidance see CONSORT for abstracts [21,31]) | 1                   |
| Introduction                  |         |                                                                                 |                     |
| Background and objectives     | 2a      | Scientific background and explanation of rationale                              | 2                   |
|                               | 2b      | Specific objectives or hypotheses                                              | 2                   |
| Methods                       |         |                                                                                 |                     |
| Trial design                  | 3a      | Description of trial design (such as parallel, factorial) including allocation ratio | 2                   |
|                               | 3b      | Important charges to methods after trial commencement (such as eligibility criteria), with reasons | 2                   |
| Participations                | 4a      | Eligibility criteria for participants                                           | 2                   |
|                               | 4b      | Settings and locations where the data were collected                            | 2                   |
| Interventions                 | 5       | The interventions for each group with sufficient details to allow replication, including how and when they were actually administered | 2                   |
| Outcomes                      | 6a      | Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed | 2-3                 |
|                               | 6b      | Any changes to trial outcomes after the trial commenced, with reasons           | NA                  |
| Sample size                   | 7a      | How sample size was determined                                                  | 3                   |
|                               | 7b      | When applicable, explanation of any interim analyses and stopping guidelines    | NA                  |
| Randomisation                 |         |                                                                                 |                     |
| Sequence generation           | 8a      | Method used to generate the random allocation sequence                           | 2                   |
|                               | 8b      | Type of randomization, details of any restriction (such as blocking and block size) | 2                   |
| Allocation concealment        | 9       | Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned | NA                 |
| Implementation                | 10      | Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions | NA                 |
| Blinding                      | 11a     | If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how | NA                 |
|                               | 11b     | If relevant, description of the similarity of interventions                    | NA                 |
| Statistical methods           | 12a     | Statistical methods used to compare groups for primary and secondary outcomes   | 3                   |
|                               | 12b     | Methods for additional analyses, such as subgroup analyses and adjusted analyses | 3                   |
| Results                       |         |                                                                                 |                     |
| Participant flow (a diagram is strongly recommended) | 13a | For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analyzed for primary outcome | 3 and figure-1 |
|                               | 13b | For each group, losses and exclusions after randomization, together with reasons | 3                   |
| Recruitment                   | 14a     | Dates defining the periods of recruitment and follow-up                         | 2-3                 |
|                               | 14b | Why the trial ended or was stopped                                              | NA                 |
| Baseline data                 | 15      | A table showing baseline demographic and clinical characteristics for each group | Table 1            |
| Number analysed               | 16      | For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups | Figure-1          |
| Outcomes and estimation       | 17a     | For each primary and secondary outcomes, results for each group, and the estimated effect size and its precision (such as 95% confidence interval) | 3                   |
|                               | 17b     | For binary outcomes, presentation of both absolute and relative effect sizes in recommended | NA                 |
| Ancillary analyses            | 18      | Results of any other analyses perform, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory | NA                 |
| Harms                         | 19      | All important harms or unintended effects in each group (for specific guidance see CONSORT for harms [28]) | 3                   |
| Discussion                    |         |                                                                                 |                     |
| Limitations                   | 20      | Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses | 4                   |
| Generalizability              | 21      | Generalizability (external validity, applicability) of trial findings           | 4                   |
| Interpretation                | 22      | Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence | 4                   |

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Conclusion

Single dose of 500 mg of IV methylprednisolone may be an equally efficacious alternative to a 10 days course of oral prednisolone. Early institution of treatment should be attempted for optimum results.

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