ORIGINAL ARTICLE

Early Treatment with Prednisolone or Acyclovir in Bell's Palsy

Frank M. Sullivan, Ph.D., Iain R.C. Swan, M.D., Peter T. Donnan, Ph.D., Jillian M. Morrison, Ph.D., Blair H. Smith, M.D., Brian McKinstry, M.D., Richard J. Davenport, D.M., Luke D. Vale, Ph.D., Janet E. Clarkson, Ph.D., Victoria Hammersley, B.Sc., Sima Hayavi, Ph.D., Anne McAteer, M.Sc., Ken Stewart, M.D., and Fergus Daly, Ph.D.

ABSTRACT

BACKGROUND

Corticosteroids and antiviral agents are widely used to treat the early stages of idiopathic facial paralysis (i.e., Bell's palsy), but their effectiveness is uncertain.

METHODS

We conducted a double-blind, placebo-controlled, randomized, factorial trial involving patients with Bell's palsy who were recruited within 72 hours after the onset of symptoms. Patients were randomly assigned to receive 10 days of treatment with prednisolone, acyclovir, both agents, or placebo. The primary outcome was recovery of facial function, as rated on the House–Brackmann scale. Secondary outcomes included quality of life, appearance, and pain.

RESULTS

Final outcomes were assessed for 496 of 551 patients who underwent randomization. At 3 months, the proportions of patients who had recovered facial function were 83.0% in the prednisolone group as compared with 63.6% among patients who did not receive prednisolone ($P<0.001$) and 71.2% in the acyclovir group as compared with 75.7% among patients who did not receive acyclovir (adjusted $P=0.50$). After 9 months, these proportions were 94.4% for prednisolone and 81.6% for no prednisolone ($P<0.001$) and 85.4% for acyclovir and 90.8% for no acyclovir (adjusted $P=0.10$). For patients treated with both drugs, the proportions were 79.7% at 3 months ($P<0.001$) and 92.7% at 9 months ($P<0.001$). There were no clinically significant differences between the treatment groups in secondary outcomes. There were no serious adverse events in any group.

CONCLUSIONS

In patients with Bell's palsy, early treatment with prednisolone significantly improves the chances of complete recovery at 3 and 9 months. There is no evidence of a benefit of acyclovir given alone or an additional benefit of acyclovir in combination with prednisolone. (Current Controlled Trials number, ISRCTN71548196.)

From the Scottish School of Primary Care (F.M.S.), Community Health Sciences (P.T.D., F.D.), and Dental Health Services Research Unit (J.E.C.), University of Dundee, Dundee; the Department of Otolaryngology (I.R.C.S.) and the Division of Community Based Sciences (J.M.M., S.H.), University of Glasgow, Glasgow; the Department of General Practice and Primary Care (B.H.S., A.M.) and the Health Economics Research Unit (L.D.V.), University of Aberdeen, Aberdeen; Community Health Sciences (B.M., V.H.) and the Department of Clinical Neurosciences (R.J.D.), University of Edinburgh, Edinburgh; and St. John's Hospital, National Health Service Lothian, Livingston (K.S.) — all in the United Kingdom. Address reprint requests to Dr. Sullivan at the Scottish School of Primary Care, Mackenzie Bldg., University of Dundee, Kirsty Semple Way, Dundee DD2 4BF, United Kingdom, or at f.m.sullivan@chs.dundee.ac.uk.

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Bell's palsy is acute, idiopathic, unilateral paralysis of the facial nerve.[1] Vascular, inflammatory, and viral causes have been suggested from paired serologic analyses and studies of the cerebral ganglia, suggesting an association between herpes infection and the onset of facial paralysis.[2-4] Epidemiologic studies show that 11 to 40 persons per 100,000 are affected each year, most commonly between the ages of 30 and 45 years.[5] Although most patients recover well, up to 30% of patients have a poor recovery, with continuing facial disfigurement, psychological difficulties, and facial pain.[6,7] Treatment remains controversial and variable.[8] Prednisolone and acyclovir are commonly prescribed separately and in combination, although evidence of their effectiveness is weak.[9,10]

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.[11] The review of antiviral treatment included three studies involving 246 patients.[12] Both reviews independently concluded that insufficient data exist to support the use of either or both therapies.

Given this lack of evidence, the Health Technology Assessment Program of the National Institute for Health Research commissioned an independent academic group to determine whether prednisolone or acyclovir used early in the course of Bell's palsy improves the chances of recovery.[13]

METHODS

PATIENTS

We established receiving centers at 17 hospitals throughout Scotland, to which potential patients with Bell's palsy were referred. Eligible patients with a confirmed diagnosis who consented to join the study were randomly assigned to study groups and were followed for 9 months. Complete details of the study design and the analysis plan have been published previously.[14] The complete study protocol appears in the Supplementary Appendix, available with the full text of this article at www.nejm.org.

We recruited adults 16 years of age or older with unilateral facial-nerve weakness of no identifiable cause who presented to primary care or the emergency department and could be referred to a collaborating otorhinolaryngologist within 72 hours after the onset of symptoms. Exclusion criteria were pregnancy, breast-feeding, uncontrolled diabetes (glycated hemoglobin level, >8%), peptic ulcer disease, suppurative otitis media, herpes zoster, multiple sclerosis, systemic infection, sarcoidosis and other rare conditions, and an inability to provide informed consent.

All patients provided written informed consent after the aims and methods of the study had been described to them and after they had received an information sheet. The study was approved by the Multicenter Research Ethics Committee for Scotland and was conducted in accordance with the provisions of the Declaration of Helsinki and Good Clinical Practice guidelines. Drugs (including placebo) were purchased from Tayside Pharmaceuticals, an organization that manufactures special medicines for the National Health Service in Scotland and for commercial customers.

STUDY DESIGN

From June 2004 to June 2006, we conducted a two-by-two factorial study across the whole of mainland Scotland (total population, 5.1 million), with referrals mainly from primary care to 17 hospitals serving 88% of the country's total population. Follow-up was continued until March 2007, when the last patients to be recruited underwent their 9-month assessments. Patients were recruited through their family doctors, emergency departments, the national 24-hour medical telephone consultancy service, and dentists' offices. Patients, recruiters, study visitors, and outcome assessors were all unaware of study-group assignments.

As soon as the senior otorhinolaryngologist who had been trained in the study procedures at the trial site confirmed a patient's eligibility to participate and consent was obtained, the patient was randomly assigned to a study group by an independent, secure, automated telephone-randomization service provided by the University of Aberdeen's Health Services Research Unit.[15] Randomization was performed with the use of a permuted-block technique, with block sizes of four or eight and no stratification. Patients were instructed to take the first dose of the study drug before leaving the hospital and the remaining doses at home during the next 10 days.

Patients underwent randomization twice, which resulted in four study groups that each received two preparations: prednisolone (at a dose of 25 mg

twice daily) and placebo (lactose), acyclovir (400 mg five times daily) and placebo, prednisolone and acyclovir, and two placebo capsules. Tayside Pharmaceuticals managed the preparation of active and placebo ingredients in cellulose capsules and the drug bottling, labeling, and distribution to clinical sites. Only Tayside Pharmaceuticals and the 17 hospital pharmacies had access to the codes. Thus, each patient received two bottles of odorless capsules with an identical appearance.

Within 3 to 5 days after randomization, a researcher visited patients at home or, if preferred, at a doctor's office to complete a baseline assessment. Repeat visits to assess recovery occurred at 3 months. If recovery was incomplete (which was defined as grade 2 or more on the House–Brackmann scale) at this visit, the visit was repeated at 9 months. Researchers analyzed clinical records for 15% of patients to validate primary care and hospital-consultation data, toxic effects, and coexisting illnesses after the final visit. An independent data and safety monitoring committee performed a review 14 months after recruitment began.

OUTCOME MEASUREMENTS

The primary outcome measure was the House–Brackmann grading system for facial-nerve function (see the Supplementary Appendix),[16] an easily administered, widely used clinical system for grading recovery from facial-nerve paralysis caused by damage to lower motor neurons. The scoring system assigns patients to one of six categories on the basis of the degree of facial-nerve function, with grade 1 indicating normal function. The primary outcome was assessed by documenting the facial appearance of patients in digital photographic images in four standard poses: at rest, with a forced smile, with raised eyebrows, and with eyes tightly closed. (Images of a patient at enrollment are available in the Supplementary Appendix.) The photographs were assessed and graded independently by a panel of three experts — an otorhinolaryngologist, a neurologist, and a plastic surgeon — who were unaware of study-group assignments and the stage of assessment. Ninety-two percent of the panel members' assessments differed by no more than one House–Brackmann grade. Discrepancies of more than one grade were reassessed. The median of the three grades provided a final determination.

Secondary outcomes were health-related quality of life, as measured with the Health Utilities Index Mark 3; facial appearance, as measured with the Derriford Appearance Scale 59; and pain, as measured with the Brief Pain Inventory. The Health Utilities Index Mark 3 provides a system for the classification of health-related quality of life status in eight dimensions: vision, hearing, speech, ambulation, dexterity, emotion, cognition, and pain, with five or six levels of severity per dimension. A preference-based scoring system is used, and responses are commonly converted into a single score ranging from −0.36 to 1.00, with 1 indicating full health; a negative score indicates a quality of life that is considered by the patient to be worse than death. The questionnaire is designed for use in clinical practice and research, health policy evaluation, and general population surveys.[17] The Derriford Appearance Scale contains 59 questions covering aspects of self-consciousness and confidence, with scores ranging from 8 to 262 and higher scores indicating a greater severity of distress and dysfunction.[18] The Brief Pain Inventory measures both the severity of pain and the extent to which pain interferes with normal activities; scores range from 0 to 110, with higher scores indicating greater severity.[19]

ADVERSE EVENTS

Adverse events were reviewed at each study visit. Compliance with the drug regimen was reviewed at the first visit and during telephone calls on day 7 after randomization and within a week after the final day of the study (10 days after randomization). Patients were instructed to return pill containers and any unused capsules in the container to the study center at the University of Dundee.

STATISTICAL ANALYSIS

All analyses were based on the intention-to-treat principle, and specific comparisons were prespecified in the protocol. We initially tested the data for any interaction among study groups. If the results were not significant, we compared the primary outcome measure of complete recovery (grade 1 on the House–Brackmann scale) at 3 months and 9 months between patients who did and those who did not receive prednisolone, using a two-sided Fisher's exact test. We repeated this procedure for acyclovir. In addition, we then compared prednisolone with placebo, acyclovir with placebo, and the combination of the two drugs with placebo. Prespecified secondary analyses compared scores on quality of life, facial appearance, and pain with the use of

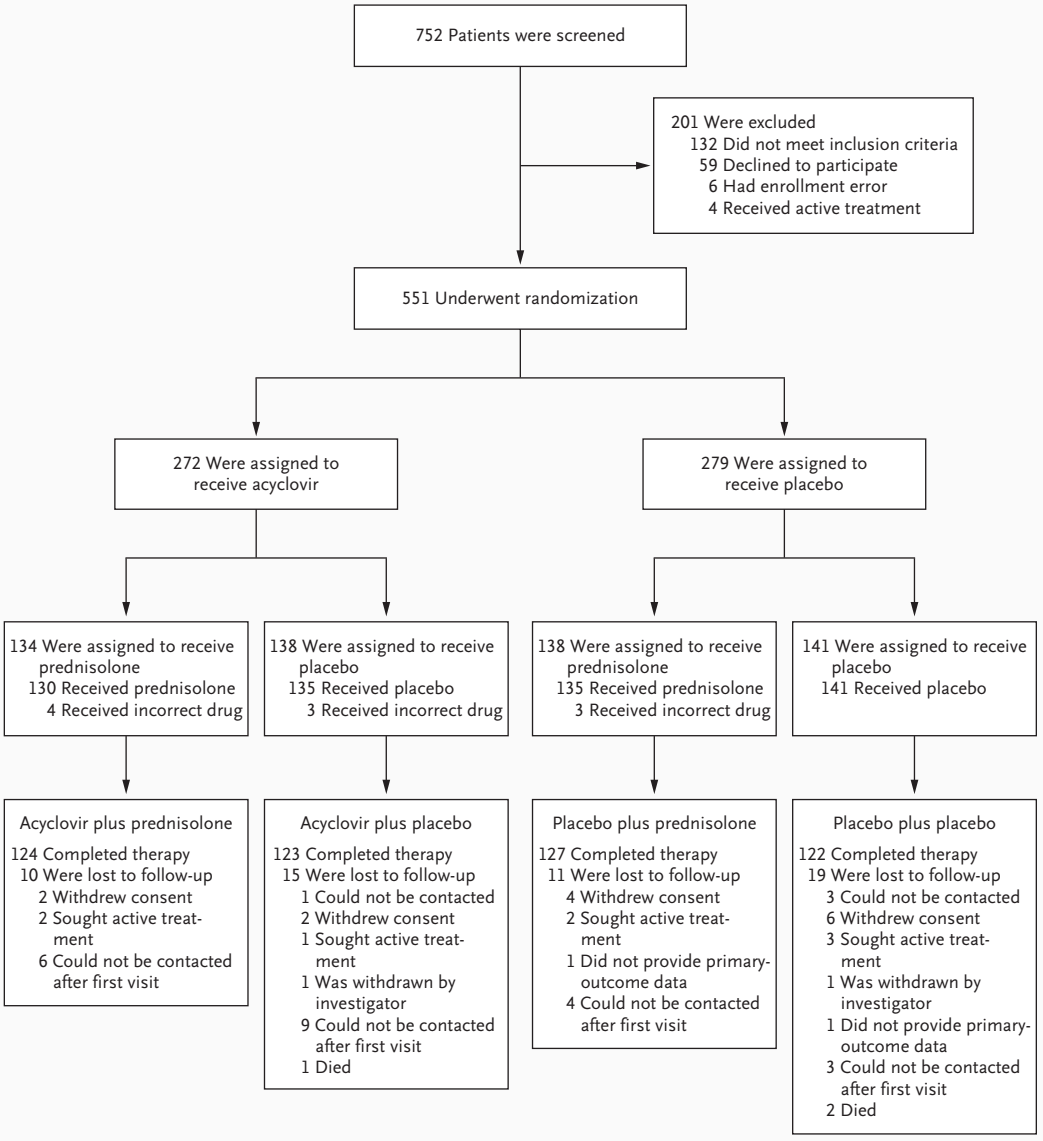

Figure 1. Enrollment and Outcomes.

t-tests or Mann–Whitney tests in cases in which the data were not normally distributed. Then we used logistic regression to adjust the analysis for all baseline characteristics that we measured: age, sex, the time from the onset of symptoms to the initiation of treatment, scores on the House–Brackmann scale, and scores for quality of life, appearance, and pain. The significance of baseline factors was assessed with the use of Wald tests, with a P value of less than 0.05 considered to indicate statistical significance.

The results were also assessed for sensitivity to dropout, assuming that the dropouts were missing at random. A propensity score for dropout at 9 months was estimated with the use of logistic regression, and a further analysis was carried out to weight results according to the reciprocal of the probability of remaining in the study.[20]

The relevant Cochrane reviews suggested that 32 to 37% of patients with Bell's palsy have incomplete recovery without treatment and that this percentage can be reduced to 22% with effective treatment. A between-group difference in the complete-recovery rate of at least 10 to 12 percentage

points was considered to be clinically meaningful. The randomization of 236 patients per treatment (a total of 472 patients) provided a power of 80% to detect such a difference. Since the study design was factorial, the power was the same for each pairwise comparison of treatments (assuming there was no interaction between treatments).

RESULTS

STUDY POPULATION

Of 752 patients who were referred for participation in the study, 132 were found to be ineligible; of the remaining 620 patients, 551 (88.9%) underwent randomization. Of these patients, 415 had been referred by their family doctor (75.3%) and 41 by an emergency department (7.4%). Since 55 patients dropped out of the study before a final determination of the House–Brackmann grade, a final outcome was available for 496 patients (90.0%) (Fig. 1).

The patients were equally divided between men and women, the mean (±SD) age was 44.0±16.4 years, and the degree of initial facial paralysis was moderate to severe (Table 1). After the onset of symptoms, most patients (53.8%) initiated treatment within 24 hours, 32.1% within 48 hours, and 14.1% within 72 hours. A total of 426 patients (86%) returned pill containers; of these patients, 383 (90%) returned empty containers, indicating complete compliance, 32 (8%) returned doses for 5 days or less, and 11 patients (3%) returned doses for 6 days or more.

There was no significant interaction between prednisolone and acyclovir at either 3 months or 9 months (P=0.32 and P=0.72, respectively). Table 2 presents the adjusted outcome data for the 496 patients who completed the study. Of these patients, 357 had recovered by 3 months and did not require a further visit. Of the remainder, 80 had recovered at 9 months, leaving 59 with a residual facial-nerve deficit.

At 3 months, rates of complete recovery differed significantly between the prednisolone comparison groups: 83.0% for patients who received prednisolone and 63.6% for those who did not,

Table 1. Baseline Characteristics of the Patients.*

Characteristic	Prednisolone (N=251)	No Prednisolone (N=245)	Acyclovir (N=247)	No Acyclovir (N=249)	Total (N=496)
Sex — no. (%)					
Male	135 (53.8)	118 (48.2)	119 (48.2)	134 (53.8)	253 (51.0)
Female	116 (46.2)	127 (51.8)	128 (51.8)	115 (46.2)	243 (49.0)
Age — yr	43.2±16.2	44.9±16.6	45.0±16.6	43.0±16.1	44.0±16.4
Score on House–Brackmann scale†	3.5±1.2	3.8±1.3	3.6±1.3	3.7±1.2	3.6±1.3
Score on Health Utilities Index Mark 3‡	0.80±0.22	0.78±0.21	0.79±0.21	0.78±0.22	0.79±0.22
Score on Derriford Appearance Scale 59§	71±37	75±41	72±39	74±38	73±39
Score on Brief Pain Inventory¶	10±18	16±21	12±18	14±21	13±20
Time between onset of symptoms and start of treatment — no. (%)					
Within 24 hr	120 (47.8)	147 (60.0)	137 (55.5)	130 (52.2)	267 (53.8)
>24 to ≤48 hr	95 (37.8)	64 (26.1)	75 (30.4)	84 (33.7)	159 (32.1)
>48 to ≤72 hr	25 (10.0)	18 (7.3)	25 (10.1)	18 (7.2)	43 (8.7)
Unknown (but ≤72 hr)	11 (4.4)	16 (6.5)	10 (4.0)	17 (6.8)	27 (5.4)

* Plus–minus values are means ±SD. The subcategories listed in the four columns match the analysis presented in Table 2 rather than that of the study groups discussed in the text and represented in the figures. Data for the four study groups are available in the Supplementary Appendix. Percentages may not total 100 because of rounding.

† Data are missing for 12 patients on the House–Brackmann scale, which ranges from 1 to 6, with higher grades indicating worse facial paralysis.

‡ Data are missing for 13 patients on the Health Utilities Index Mark 3, which ranges from –0.36 to 1.00 (as assessed by the patient), with 1 indicating full health; negative scores indicate a quality of life that is considered worse than death.

§ Data are missing for 13 patients on the Derriford Appearance Scale 59, which ranges from 8 to 262, with higher scores indicating more distress and dysfunction.

¶ Data are missing for 7 patients on the Brief Pain Inventory, which ranges from 0 to 110, with higher scores indicating greater severity.

Table 2. Primary and Secondary Outcomes at 3 Months and 9 Months.*

Variable	Prednisolone (N=251)	No Prednisolone (N=245)	Adjusted Odds Ratio (95% CI)	P Value	Acyclovir (N=247)	No Acyclovir (N=249)	Adjusted Odds Ratio (95% CI)	P Value
	No./Total No. (%)				No./Total No. (%)			
Primary outcome measure†								
Grade 1 on House–Brackmann scale‡								
At 3 mo	205/247 (83.0)	152/239 (63.6)	2.44 (1.55–3.84)	<0.001	173/243 (71.2)	184/243 (75.7)	0.86 (0.55–1.34)	0.50
At 9 mo	237/251 (94.4)	200/245 (81.6)	3.32 (1.72–6.44)	<0.001	211/247 (85.4)	226/249 (90.8)	0.61 (0.33–1.11)	0.10
	Unadjusted Mean		Adjusted Beta§		Unadjusted Mean		Adjusted Beta§	
Secondary outcome measures¶								
Score on Health Utilities Index Mark 3‖								
At 3 mo	0.91±0.17	0.91±0.13	−0.01±0.01	0.40	0.90±0.16	0.92±0.14	−0.01±0.01	0.32
At 9 mo	0.84±0.26	0.88±0.16	−0.06±0.03	0.04	0.86±0.21	0.88±0.19	−0.02±0.03	0.38
Score on Brief Pain Inventory**								
At 3 mo	1.51±6.41	2.04±8.14	−0.12±0.67	0.85	1.83±7.00	1.72±7.62	0.13±0.66	0.84
At 9 mo	1.36±5.29	1.83±6.37	−0.08±1.02	0.94	1.61±5.87	1.72±6.19	0.05±0.96	0.96
Score on Derriford Appearance Scale 59††								
At 3 mo	42.4±32.3	43.2±33.4	1.72±2.88	0.55	44.2±35.0	41.4±30.4	3.08±2.85	0.28
At 9 mo	40.0±36.1	49.9±35.5	−2.40±5.71	0.67	49.4±35.2	43.2±36.6	8.53±5.36	0.11

* Plus–minus values are means ±SD, unless otherwise indicated. Odds ratios are for complete recovery of facial-nerve function.
† For the primary outcome measure, odds ratios and P values have been adjusted for age, sex, the baseline score on the House–Brackmann scale, the receipt or nonreceipt of acyclovir and prednisolone, and the interval between the onset of symptoms and the initiation of a study drug.
‡ The House–Brackmann scale ranges from 1 to 6, with higher grades indicating worse facial paralysis.
§ Beta regression coefficients were calculated by adjusted multiple regression analysis. Plus–minus values in this category are means ±SE.
¶ For the secondary outcome measures, odds ratios and P values have been adjusted for baseline measurement of age, sex, score on the House–Brackmann scale, the receipt or nonreceipt of acyclovir and prednisolone, and the time from the onset of symptoms to the initiation of treatment.
‖ Scores on the Health Utilities Index Mark 3 range from −0.36 to 1.00 (as assessed by the patient), with 1 indicating full health; negative scores indicate a quality of life that is considered worse than death.
** Scores on the Brief Pain Inventory range from 0 to 110, with higher scores indicating greater severity.
†† Scores on the Derriford Appearance Scale 59 range from 8 to 262, with higher scores indicating more distress and dysfunction.

a difference of 19.4 percentage points (95% confidence interval [CI], 11.7 to 27.1; P<0.001). There was no significant difference between the complete-recovery rates in the acyclovir comparison groups: 71.2% for patients who received acyclovir and 75.7% for those who did not, a difference of 4.5 percentage points (95% CI, −12.4 to 3.3; unadjusted P=0.30; adjusted P=0.50). At 9 months, the rates of complete recovery were 94.4% for patients who received prednisolone and 81.6% for those who did not, a difference of 12.8 percentage points (95% CI, 7.2 to 18.4; P<0.001) and 85.4% for patients who received acyclovir and 90.8% for those who did not, a difference of 5.4 percentage points (95% CI, −11.0 to 0.3; unadjusted P=0.07; adjusted P=0.10). When the analyses were repeated with the results weighted according to the propensity of patients to withdraw from the study, there was no appreciable change.

A total of 34 patients (6.9% of those who completed follow-up) were assessed as fully recovered at the time of the first assessment visit (i.e., within at most 8 days after the onset of symptoms). For patients receiving double placebo, 64.7% were fully recovered after 3 months, and 85.2% after 9 months. Table 3 gives comparisons of all four treatment groups relative to each other. Prednisolone was highly effective, both separately and in combination with acyclovir. Acyclovir was ineffective, both separately and as an addition to prednisolone. Figure 2 shows the proportion of patients assessed as having normal facial function at baseline, at 3 months, and at 9 months in the four study groups.

Generally, there were no significant differences among the groups in secondary measures (Table 2). However, only patients who received prednisolone had an improvement in the appearance score over time. Also, pain scores tended to be lower in the prednisolone group than in the group that did not receive prednisolone. On the other hand, the quality of life at 9 months was significantly higher for patients who did not receive prednisolone than for those who did (P=0.04). Given that the secondary measures were obtained only in patients who had not recovered at 3 months and given the problem of multiple testing, this result should be interpreted with caution.

At 3 months, the absolute risk reduction associated with prednisolone treatment was 19%. Therefore, the number needed to treat in order to achieve one additional complete recovery was 6 (95% CI, 4 to 9). At 9 months, the equivalent numbers were an absolute risk reduction of 12% and a number needed to treat of 8 (95% CI, 6 to 14).

Adverse events included the expected range of minor symptoms associated with the drugs used (Table 4). During follow-up, three patients died. All three deaths were deemed to be unrelated to treatment: two patients had received double placebo and one had received acyclovir alone. No other major adverse events were reported. There was no need for patients or study personnel to be informed about study-group assignments.

Table 3. Complete Recovery at 3 Months and 9 Months, According to Treatment Combination, Adjusted for Baseline Characteristics.*

Variable	Prednisolone		No Prednisolone	
	Odds Ratio (95% CI)	P Value†	Odds Ratio (95% CI)	P Value†
At 3 mo				
Patients who received acyclovir	1.73 (0.96–3.12)	0.07	0.85 (0.49–1.47)	0.57
Patients who did not receive acyclovir	2.58 (1.37–4.88)	0.003	1.00	
At 9 mo				
Patients who received acyclovir	1.76 (0.74–4.16)	0.20	0.58 (0.29–1.16)	0.12
Patients who did not receive acyclovir	3.23 (1.13–9.22)	0.03	1.00	

* Odds ratios are for complete recovery, defined as grade 1 on the House–Brackmann scale, which ranges from 1 to 6, with higher scores indicating worse facial paralysis. Odds ratios and P values were adjusted for age, sex, baseline House–Brackmann grade, and the time from the onset of symptoms to the initiation of treatment. Odds ratios were calculated by comparing all three active treatments with double placebo. Significance testing for comparisons at 3 and 9 months had the following results: combination therapy versus prednisolone only, P=0.18 (3 months) and P=0.28 (9 months); combination therapy versus acyclovir only, P=0.004 (3 months) and P=0.001 (9 months); acyclovir only versus double placebo, P=0.79 (3 months) and P=0.19 (9 months); and prednisolone only versus double placebo, P<0.001 (3 months) and P=0.004 (9 months).

† P values are for the comparison with double placebo.

DISCUSSION

In this large, randomized, controlled trial of the efficacy of treatment for Bell's palsy, we confirmed the generally favorable outcome for patients receiving double placebo, with 64.7% of patients fully recovered at 3 months and 85.2% at 9 months.[9,10] Early treatment (within 72 hours after the onset of symptoms) with prednisolone increased these rates to 83.0% and 94.4%, respectively. Acyclovir produced no benefit over placebo, and there was no benefit in its addition to prednisolone.

The results of previous trials have been inconsistent.[21] Our trial included twice as many patients as were included in the Cochrane systematic reviews.[11,12] We recruited most patients from primary care practices, thus reducing the selection bias inherent in hospital-based studies. The high rate of acceptance of randomization and the low dropout rate during the study suggest that our results can probably be applied to other settings with similar populations. It is possible that genetic polymorphisms that are prevalent in some populations or environmental factors such as diet could alter the response. We used drugs that are relatively inexpensive and are readily available worldwide. The assessment of outcomes with the use of validated study tools was undertaken by observers who were unaware of the assignments to study groups.

We used the House–Brackmann scale to grade facial-nerve function because it reliably assigns patients to a recovery status. 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.[22,23] This observation, as well as rapid recovery between randomization and the home visit in some cases, may explain why 34 patients received grade 1 on the House–Brackmann scale at their baseline assessment. Alternative scales, such as the Sydney and Sunnybrook facial grading systems, are available but are more difficult to use in clinical practice.[24]

We did not observe any benefits with respect to our secondary outcome measures (quality of life, appearance, and pain) in any study group, including patients who received prednisolone. There was some suggestion of a benefit from prednisolone in terms of reduced pain and improved appearance, but these differences were not significant. In the subgroup of patients who did not have a complete recovery at 3 months and who underwent the 9-month assessment, there were reduced quality-of-life scores among patients who were treated with prednisolone and also among those treated with acyclovir. Given the evidently reduced health status of those who required a health assessment at 9 months, this result is perhaps not surprising.

In conclusion, we have provided evidence that the early use of oral prednisolone in patients with Bell's palsy is an effective treatment. The mechanism of action may involve modulation of the immune response to the causative agent or direct reduction of edema around the facial nerve within the facial canal. Treatment with unesterified acyclovir at doses used in other trials either alone or with corticosteroids had no effect on the outcome. Therefore, we cannot recommend acyclovir for use in the treatment of Bell's palsy.[25,26] A recent study in Japan suggested that valacyclovir (a prodrug that achieves a level of bioavailability that is three to five times that of acyclovir) may be a useful addition to prednisolone.[27] However, the Japanese study was smaller than ours, patients were treated in tertiary centers, and the outcome assessors were aware of the study-group assignments; therefore, the results of that study should be interpreted with caution.

No data are available regarding how best to treat patients who present more than 72 hours after the onset of symptoms, so all patients with suspected Bell's palsy should be assessed as early as possible. Since most patients with this condi-

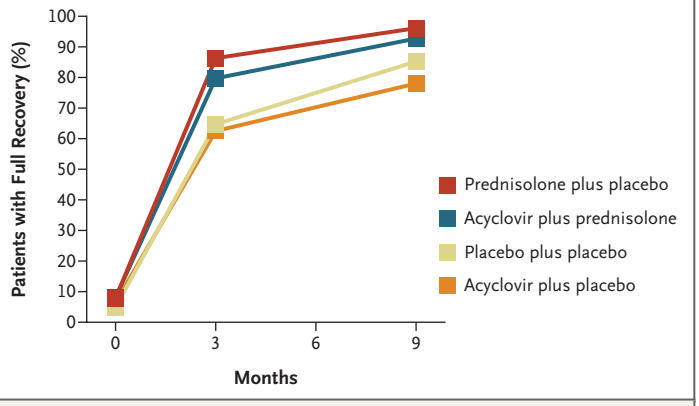

Figure 2. Patients Who Had a Full Recovery at 3 Months and 9 Months, According to Study Group.

Full recovery was defined as grade 1 on the House–Brackmann facial-nerve grading scale, which ranges from 1 to 6, with higher grades indicating worse facial paralysis.

Table 4. Adverse Events.

Event	Prednisolone–Placebo	Acyclovir–Prednisolone	Placebo–Placebo	Acyclovir–Placebo	Total
			number of events		
Dizziness	5	4	4	5	18
Dyspepsia	2	4	3	1	10
Nausea	1	2	3	3	9
Constipation	3	2	1	0	6
Hunger	1	1	0	2	4
Vomiting	0	2	1	0	3
Insomnia	1	1	1	0	3
Night sweats	2	1	0	0	3
Rash	0	1	0	2	3
Hot flushes	1	1	0	0	2
Depression	0	0	0	1	1
Thirst	0	0	1	0	1
Anorexia	0	1	0	0	1
Diarrhea	0	0	0	1	1
Drowsiness	0	0	1	0	1
Pruritus	0	1	0	0	1
Combinations of minor symptoms*	8	4	3	3	18
Death	0	0	2	1	3
Total	24	25	20	19	88

* Patients with two or more symptoms (e.g., dizziness and vomiting) are listed in this category only and are not duplicated in categories corresponding to a separate symptom (i.e., dizziness or vomiting).

tion recover fully without any treatment, withholding treatment will remain an appropriate strategy for some patients. Our study showed that the administration of prednisolone can increase the probability of complete recovery at 9 months, a finding that should help inform discussions about the use of corticosteroids for patients with Bell's palsy.

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The views and opinions expressed in this article are those of the authors and do not necessarily reflect those of the Department of Health (England).

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APPENDIX

In addition to the authors, the following investigators participated in the study. **Trial Steering Committee:** C. van Weel, *University of Nijmegen*; I. Williamson, *University of Southampton*; S. Wyke, *University of Stirling*; C. Hamilton (patient representative); **Temporary Researcher:** D. Gray, *University of Aberdeen.* **Local Principal Investigators:** K. Ah-See, *Aberdeen Royal Infirmary*; N. Balaji, *Monklands Hospital, Airdrie*; H. Beg, *Victoria Hospital, Kirkcaldy*; Q. Gardiner, *Perth Royal Infirmary*; M. Hussain, *Ninewells Hospital, Dundee*; A. Kerr, *Western General Hospital and Royal Infirmary, Edinburgh*; J. Marshall, *Southern General Hospital, Glasgow*; W. McKerrow, *Raigmore Hospital, Inverness*; M. Shanks, *Crosshouse Hospital, Kilmarnock*; D. Simpson, *Stobhill Hospital, Glasgow*; G. Vernham, *St. John's Hospital, Livingston*; A. White, *Royal Alexandra Hospital, Paisley.* **Scottish School of Primary Care:** L. McCloughan, *Scottish Primary Care Research Network*; M. Pitkethly, *East of Scotland Node*; S. Campbell, *North of Scotland Node*; A. Cardy, *North of Scotland Node*; C. Fulton, *East of Scotland Node*; J. McGill, *West of Scotland Node*; K. Bell, *National Health Service Ayrshire and Arran*; B. Rae, *North Glasgow Hospitals Trust.* **Data Monitoring and Ethics Committee:** M. Campbell, C. Counsell, *University of Aberdeen*; R. Mountain, S. Ogston (statistician), *University of Dundee.*

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