ORIGINAL ARTICLE

The Effect of Prednisolone on Sequelae in Bell's Palsy

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Objective: To study whether prednisolone reduces sequelae in Bell's palsy.

Design: Prospective, randomized, double-blind, placebo-controlled, multicenter trial with 12 months of follow-up.

Setting: Seventeen referral centers.

Patients: In all, 829 patients aged 18 to 75 years.

Interventions: Randomization within 72 hours in a factorial fashion to placebo plus placebo (n=206); prednisolone, 60 mg/d for 5 days, with the dosage then tapered for 5 days, plus placebo (n=210); valacyclovir hydrochloride, 1000 mg 3 times daily for 7 days, plus placebo (n=207); or prednisolone plus valacyclovir (n=206).

Main Outcome Measures: Facial function at 12 months assessed with the Sunnybrook and House-Brackmann grading systems.

Results: In 184 of the 829 patients, the Sunnybrook score was less than 90 at 12 months; 71 had been treated with prednisolone and 113 had not ($P<.001$). In 98 patients, the Sunnybrook score was less than 70; 33 had received prednisolone and 65 had not ($P<.001$). The difference between patients who received prednisolone and who did not in House-Brackmann gradings higher than I and higher than II was also significant ($P<.001$ and $P=.01$, respectively). No significant difference was found between patients who received prednisolone and those who did not in Sunnybrook scores less than 50 ($P=.10$) or House-Brackmann grades higher than III ($P=.80$). Synkinesis was assessed with the Sunnybrook score in 743 patients. Ninety-six patients had a synkinesis score more than 2, of whom 33 had received prednisolone and 63 had not ($P=.001$). Sixty patients had a synkinesis score more than 4, of whom 22 had received prednisolone and 38 had not ($P=.005$).

Conclusion: Prednisolone significantly reduces mild and moderate sequelae in Bell's palsy.

Trial Registration: clinicaltrials.gov Identifier: NCT00510263

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THE ETIOLOGY OF BELL'S PALSY is by definition unknown. An inflammatory process with edema of the facial nerve is supported by the findings of facial nerve enhancement on magnetic resonance imaging and swelling of the nerve during decompression surgery.[1-3] One theory is that a reactivation of latent herpes simplex virus may cause the nerve injury.[4,5]

The prognosis in Bell's palsy is on the whole favorable, and about 70% recover completely within 6 months without treatment.[6] The remaining 30% have varying degrees of sequelae with functional, psychosocial, and esthetic disturbances. Treatment of Bell's palsy is aimed at preventing sequelae and is based on the presumed pathophysiological process of inflammation of the facial nerve.[7,8]

A recent Cochrane report[9] that included 1507 participants from 7 trials concluded that patients allocated to corticosteroid treatment had incomplete recovery of facial function 6 months or more after randomization, significantly less than in the control group. The reduction in the proportion of patients with disabling sequelae at 6 months was, however, not significant.

Contrary to the reported effect of corticosteroids, the updated Cochrane meta-analysis review of Lockhart and coworkers,[7] which included 1987 participants in 7 trials, found no significant benefit from herpes simplex virus antivirals compared with placebo in producing complete recovery from Bell's palsy. However, when antiviral agents are administered with corticosteroids, they may be associated with additional benefit.[10-13]

Despite the knowledge that prednisolone improves complete recovery rates in Bell's palsy,[9,14,15] large controlled studies on the effect of corticosteroids at reducing the severity of sequelae are lacking. As stated

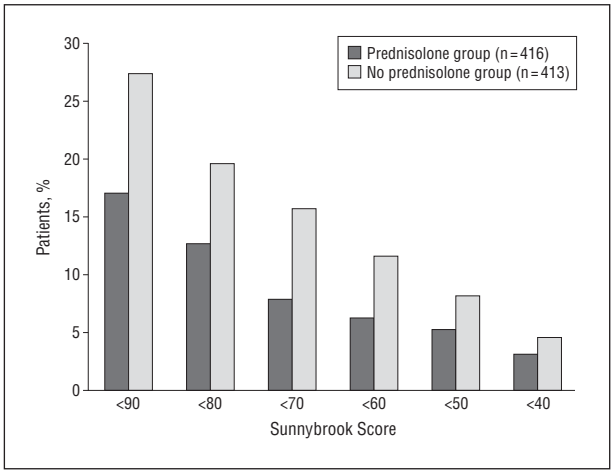

Figure. Patients with Bell's palsy grouped according to severity of sequelae by their Sunnybrook scores at 12 months.

by Lockhart et al,[7] more work is needed to assess the likelihood of long-term sequelae. Our aim was therefore to study whether the severity of sequelae is reduced with prednisolone treatment in Bell's palsy and whether combination with the antiviral valacyclovir hydrochloride adds any further effect. The present study constitutes one of the secondary end points of the large Scandinavian Bell's Palsy Study.[14]

METHODS

PATIENTS

Data were drawn from the large collaborative Swedish and Finnish Scandinavian Bell's Palsy Study.[14] In this prospective, randomized, double-blind, placebo-controlled, multicenter trial, patients with acute, unilateral, peripheral facial palsy underwent screening for inclusion at 17 public otorhinolaryngological centers from May 1, 2001, through September 30, 2006. The last follow-up for included patients was September 2007. Patients aged 18 through 75 years with onset of palsy within 72 hours were considered for inclusion. Exclusion criteria were systemic therapy with antiherpetic medication within the past 2 weeks; ongoing systemic corticosteroid therapy; allergy to acyclovir, valacyclovir, famciclovir, or ganciclovir; pregnancy; breastfeeding; unwillingness by fertile women to use contraceptives during the medication period; the presence of other neurological diseases, diabetes mellitus, hypertension that was not well controlled, or serious heart disease; a history of serious heart disease, renal or hepatic disease, gastric or duodenal ulcer, glaucoma, acute otitis, ipsilateral chronic otitis, tuberculosis, or immunodeficiency syndromes; recent head injury; and psychiatric disease that is at risk of being influenced by the study medication or that might affect the patient's ability to complete the study. As part of the Scandinavian Bell's Palsy Study, this investigation was approved by regional ethics review boards and performed in accordance with the Declaration of Helsinki and good clinical practice guidelines. Written informed consent was obtained from all patients.

Patients were randomized to one of the following 4 treatment groups: placebo plus placebo, prednisolone plus placebo, valacyclovir plus placebo, or prednisolone plus valacyclovir. Prednisolone (or its placebo) was given as a single dose of 60 mg/d for 5 days, with the dosage then tapered to 10 mg/d for 5 days to give a total treatment time of 10 days. Valacyclovir hydrochloride (or its placebo) was given as two 500-mg tablets 3 times daily for 7 days. Follow-up visits were between days 11 to 17 and at 1, 2, 3, 6, and 12 months after randomization. If the recovery was complete (defined as a Sunnybrook score of 100) at 2 or 3 months, the next follow-up was at 12 months.

In total, 829 patients (341 women and 488 men) were included in the analysis. Of these, 206 received placebo plus placebo; 210, prednisolone plus placebo; 207, valacyclovir plus placebo; and 206, prednisolone plus valacyclovir. The study design was factorial and thus included 4 analysis groups; 416 of the patients received prednisolone (prednisolone plus placebo or prednisolone plus valacyclovir), whereas 413 did not (placebo plus placebo or valacyclovir plus placebo); 413 received valacyclovir (valacyclovir plus placebo or prednisolone plus valacyclovir), whereas 416 did not (placebo plus placebo or prednisolone plus placebo).[14]

The regionally weighted Sunnybrook score and the gross House-Brackmann facial grading system were used to assess facial function.[16,17] The Sunnybrook system evaluates resting symmetry, degree of voluntary movement, and synkinesis to form a composite score, for which 0 indicates complete paralysis and 100, normal function. The House-Brackmann system consists of a 6-grade scale (I to VI), in which I indicates normal function and VI, complete paralysis. Patients were grouped according to severity of sequelae by their Sunnybrook scores ($<$90, $<$80, $<$70, $<$60, and $<$50) and their respective House-Brackmann grades ($>$I, $>$II, $>$III, and $>$IV) at 12 months. The severity of synkinesis at the 12-month follow-up was analyzed using the synkinesis scores from the Sunnybrook score. In this system, synkinesis is graded from 1 (mildest) to 15 (most severe).

STATISTICAL ANALYSIS

A slightly modified intention-to-treat analysis was used according to a preestablished analysis plan.[14] We used the last-observation-carried-forward method for recovery rates and imputed missing data points in the postbaseline follow-up visits from the last observation available for each patient. For the analysis of synkinesis at 12 months, a complete case analysis method was used, that is, only the 743 patients who attended the 12-month follow-up visit were included. To reveal any synergistic effect of the combination of prednisolone and valacyclovir, we performed an interaction test. Results are given with dichotomous data as proportions with 95% CIs using the normal approximation approach. Categorical variables were compared by means of the Fisher exact test. We performed statistical analysis using commercially available software (SAS statistical program, version 9.2; SAS Institute, Inc).

RESULTS

Baseline characteristics were similar in the 4 treatment groups and have previously been reported.[14]

PREDNISOLONE VS NO PREDNISOLONE

Of the 829 patients, 184 had a Sunnybrook score less than 90 at 12 months. Of these 184 patients, 71 were treated with prednisolone (prednisolone plus placebo or prednisolone plus valacyclovir) and 113 were not (placebo plus placebo or valacyclovir plus placebo) ($P<.001$). A total of 134 patients had a Sunnybrook score less than 80. Fifty-three of these had received prednisolone and 81 had not ($P=.01$). In the 98 patients with a Sunnybrook score less than 70, 33 had received prednisolone and 65 had not ($P<.001$). In the 74 patients with a Sun-

Table 1. Sequelae at 12 Months in Patients Who Received Prednisolone vs Those Who Did Not

	Total No. of Patients	Patients With Sequelae, No. (%) [95% CI]		Difference (95% CI)	*P* Value
		Prednisolone (n=416)	No Prednisolone (n=413)		
Sunnybrook score[a]					
<90	184	71 (17.1) [13.4 to 20.7]	113 (27.4) [23.0 to 31.7]	−10.3 (−15.9 to −4.7)	<.001
<80	134	53 (12.7) [9.5 to 16.0]	81 (19.6) [15.8 to 23.5]	−6.9 (−11.9 to −1.9)	.01
<70	98	33 (7.9) [5.3 to 10.5]	65 (15.7) [12.2 to 19.3]	−7.8 (−12.1 to −3.4)	<.001
<60	74	26 (6.3) [3.9 to 8.6]	48 (11.6) [8.5 to 14.7]	−5.4 (−9.3 to −1.5)	.01
<50	56	22 (5.3) [3.1 to 7.5]	34 (8.2) [5.6 to 10.9]	−2.9 (−6.4 to 0.5)	.10
<40	32	13 (3.1) [1.5 to 4.8]	19 (4.6) [2.6 to 6.6]	−1.5 (−4.1 to 1.2)	.29
House-Brackmann grade[a]					
>I	239	92 (22.1) [18.1 to 26.1]	147 (35.6) [31.0 to 40.2]	−13.5 (−19.6 to −7.4)	<.001
>II	95	35 (8.4) [5.7 to 11.1]	60 (14.5) [11.1 to 17.9]	−6.1 (−10.4 to −1.8)	.01
>III	44	21 (5.1) [2.9 to 7.2]	23 (5.6) [3.4 to 7.8]	−0.5 (−3.6 to 2.5)	.80
>IV	18	12 (2.9) [1.3 to 4.5]	6 (1.5) [0.3 to 2.6]	1.4 (−0.6 to 3.4)	.23
Synkinesis score[b]					
>2	96	33 (8.9) [6.0 to 11.8]	63 (16.9) [13.1 to 20.7]	−8.0 (−12.8 to −3.2)	.001
>4	60	22 (6.0) [3.5 to 8.4]	38 (10.2) [7.1 to 13.3]	−4.2 (−8.2 to −0.3)	.005
>6	37	13 (3.5) [1.6 to 5.4]	24 (6.4) [3.9 to 8.9]	−2.9 (−6.1 to 0.2)	.09

[a] Modified intention-to-treat analysis based on all 829 patients.
[b] Complete-case analysis based on the 743 patients who attended the 12-month follow-up visit, including 370 patients who received prednisolone and 373 who did not.

nybrook score less than 60, 26 had received prednisolone and 48 had not ($P=.01$). There was no significant difference between the patients who received or did not receive prednisolone in the number of patients with Sunnybrook scores of less than 50 and less than 40 ($P=.10$ and $P=.29$, respectively) (**Figure** and **Table 1**).

Among the patients with a House-Brackmann grade higher than I, 92 received prednisolone and 147 did not ($P<.001$). The corresponding number of patients with a House-Brackmann grade higher than II was 35 in the prednisolone group and 60 in the no prednisolone group ($P=.01$). The number of patients in the House-Brackmann grading intervals higher than III to higher than IV did not differ significantly in those who received prednisolone and those who did not (Table 1).

Synkinesis was present in 158 of the 743 patients with a 12-month follow-up (complete-case analysis). Of these 158 patients, 96 had a synkinesis score more than 2; 33 had received prednisolone, whereas 63 had not ($P=.001$). In the 60 patients with a synkinesis score more than 4, 22 had received prednisolone, whereas 38 had not ($P=.005$). In the 37 patients with a synkinesis score more than 6, there was no significant difference between the groups who did and did not receive prednisolone ($P=.09$) (Table 1).

VALACYCLOVIR VS NO VALACYCLOVIR

We found no significant difference at 12 months in the number of patients in any of the Sunnybrook score intervals less than 90 to less than 40 when we compared the 413 patients who received valacyclovir and the 416 who did not. Similarly, no significant difference between the valacyclovir and no valacyclovir groups was found for House-Brackmann grading intervals of higher than I to higher than IV. When analyzing synkinesis at 12 months, no difference was found between the 2 treatment groups (**Table 2**).

PREDNISOLONE VS PREDNISOLONE PLUS VALACYCLOVIR

When comparing the 210 patients given prednisolone alone (prednisolone plus placebo) and the 206 given prednisolone plus valacyclovir, there was no significant difference in the number with sequelae in the Sunnybrook score intervals less than 90 to less than 40 (**Table 3**).

In addition, no significant difference in synkinesis at 12 months was found between patients receiving prednisolone alone and those receiving prednisolone plus valacyclovir (Table 3).

COMMENT

Treatment with prednisolone for Bell's palsy within 72 hours significantly reduced the number of patients with mild to moderate severity of palsy at 12 months when we assessed the condition of patients with the Sunnybrook scale and the House-Brackmann grading system. In addition, we found a significant reduction of patients with mild to moderate synkinesis in the patients receiving prednisolone. We found no additive effect of valacyclovir to prednisolone on sequelae.

In the Cochrane meta-analysis by Salinas et al,[9] the number of patients with severe paralysis or what may be judged as disabling persistent sequelae 6 months or more after randomization was used as an outcome measure. When 5 corticosteroid trials with a total of 668 participants were included in the analysis of disabling sequelae, a nonsignificant reduction in the number of participants with this outcome was reported.[9] We found that prednisolone significantly reduced the proportion of patients who would be classified as having mild or moderate sequelae (Sunnybrook score <90 to <50) at 12 months. The number of patients with more severe sequelae, however, was not reduced by treatment with this drug. These results are in agreement with

Table 2. Sequelae at 12 Months in Patients Who Received Valacyclovir vs Those Who Did Not

	Total No. of Patients	Patients With Sequelae, No. (%) [95% CI]		Difference (95% CI)	*P* Value
		Valacyclovir (n=413)	No Valacyclovir (n=416)		
Sunnybrook score[a]					
<90	184	93 (22.5) [18.5 to 26.6]	91 (21.9) [17.9 to 25.9]	0.6 (–5.0 to 6.3)	.87
<80	134	68 (16.5) [12.9 to 20.1]	66 (15.9) [12.3 to 19.4]	0.6 (–4.4 to 5.6)	.85
<70	98	49 (11.9) [8.7 to 15.0]	49 (11.8) [8.7 to 14.9]	0.1 (–4.3 to 4.5)	>.99
<60	74	35 (8.5) [5.8 to 11.2]	39 (9.4) [6.6 to 12.2]	–0.9 (–4.8 to 3.0)	.72
<50	56	27 (6.5) [4.1 to 8.9]	29 (7.0) [4.5 to 9.4]	–0.4 (–3.8 to 3.0)	.89
<40	32	14 (3.4) [1.6 to 5.1]	18 (4.3) [2.4 to 6.3]	–0.9 (–3.6 to 1.7)	.59
House-Brackmann grade[a]					
>I	239	116 (28.1) [25.2 to 34.0]	123 (29.6) [25.2 to 34.0]	–1.5 (–7.7 to 4.7)	.64
>II	95	49 (11.9) [8.7 to 15.0]	46 (11.1) [8.0 to 14.1]	0.8 (–3.5 to 5.2)	.74
>III	44	23 (5.6) [3.4 to 7.8]	21 (5.1) [2.9 to 7.2]	0.5 (–2.5 to 3.6)	.76
>IV	18	9 (2.2) [0.8 to 3.6]	9 (2.2) [0.8 to 3.6]	0 (–2.0 to 2.0)	>.99
Synkinesis score[b]					
>2	96	42 (11.4) [8.1 to 14.6]	54 (14.4) [10.9 to 18.0]	–3.1 (–7.9 to 1.8)	.23
>4	60	25 (6.8) [4.2 to 9.4]	35 (9.4) [6.4 to 12.3]	–2.6 (–6.5 to 1.3)	.23
>6	37	16 (4.3) [2.3 to 6.4]	21 (5.6) [3.3 to 8.0]	–1.3 (–4.4 to 1.9)	.50

[a] Modified intention-to-treat analysis based on all 829 patients.
[b] Complete-case analysis based on the 743 patients who attended the 12-month follow-up visit, including 369 patients who received valacyclovir and 374 who did not.

Table 3. Sequelae at 12 Months in Patients Who Received Prednisolone Plus Placebo vs Those Who Received Prednisolone Plus Valacyclovir

	Total No. of Patients	Patients With Sequelae, No. (%) [95% CI]		Difference (95% CI)	*P* Value
		Prednisolone Plus Placebo (n=210)	Prednisolone Plus Valacyclovir (n=206)		
Sunnybrook score[a]					
<90	71	38 (18.1) [12.9 to 23.3]	33 (16.0) [11.0 to 21.1]	2.1 (–5.2 to 9.3)	.60
<80	53	27 (12.9) [8.3 to 17.4]	26 (12.6) [8.1 to 17.2]	0.3 (–6.2 to 6.7)	>.99
<70	33	18 (8.6) [4.8 to 12.4]	15 (7.3) [3.7 to 10.9]	1.3 (–3.9 to 6.5)	.72
<60	26	14 (6.7) [3.3 to 10.1]	12 (5.8) [2.6 to 9.1]	0.9 (–3.8 to 5.5)	.84
<50	22	13 (6.2) [2.9 to 9.5]	9 (4.4) [1.6 to 7.2]	1.8 (–2.5 to 6.1)	.51
<40	13	8 (3.8) [1.2 to 6.4]	5 (2.4) [0.3 to 4.6]	1.4 (–2.0 to 4.7)	.58
House-Brackmann grade[a]					
>I	92	50 (23.8) [18.0 to 29.6]	42 (20.4) [14.8 to 25.9]	3.4 (–4.6 to 11.4)	.41
>II	35	19 (9.1) [5.1 to 13.0]	16 (7.8) [4.1 to 11.5]	1.3 (–4.1 to 6.6)	.72
>III	21	10 (4.8) [1.9 to 7.7]	11 (5.3) [2.2 to 8.4]	–0.6 (–4.8 to 3.7)	.83
>IV	12	7 (3.3) [0.9 to 5.8]	5 (2.4) [0.3 to 4.6]	0.9 (–2.3 to 4.1)	.77
Synkinesis score[b]					
>2	33	21 (11.3) [6.7 to 15.9]	12 (6.5) [2.9 to 10.1]	4.8 (–1.1 to 10.6)	.14
>4	22	14 (7.5) [3.7 to 11.4]	8 (4.4) [1.4 to 7.3]	3.2 (–1.7 to 8.0)	.27
>6	13	9 (4.8) [1.7 to 8.0]	4 (2.2) [0.1 to 4.3]	2.6 (–1.1 to 6.4)	.26

[a] Modified intention-to-treat analysis based on all 829 patients.
[b] Complete-case analysis based on the 743 patients who attended the 12-month follow-up visit, including 186 who received prednisolone plus placebo and 184 who received prednisolone plus valacyclovir.

those reported by Salinas et al[9] concerning the absent effect of prednisolone on the reduction of severe sequelae.

When analyzing the additive effect of antivirals on corticosteroid therapy, previous studies have mainly reported recovery rates and not the severity of sequelae. In the double-blind study by Adour et al[10] with a follow-up time of 4 months, combined acyclovir-prednisone treatment in 53 patients with Bell's palsy was statistically more effective in restoring volitional muscle motion than that in 46 patients treated with placebo and prednisone. Hato et al[12] studied 221 patients with Bell's palsy (not a double-blinded study) and reported that the recovery rate for treatment with valacyclovir plus prednisolone was significantly better than that with prednisolone alone. In contrast, Kawaguchi et al[18] enrolled 150 patients and found no significant difference in recovery rates between patients given combination therapy with prednisolone plus valacyclovir and those treated with prednisolone only. Furthermore, Engström et al[19] reported no additive effect of valacyclovir to prednisolone in severe palsies. In the present study, we found no additive effect of valacyclovir to prednisolone on sequelae from Bell's palsy.

The amount of synkinesis correlates with the severity of nerve injury.[20] We found that prednisolone re-

duced the number of patients with Bell's palsy who had mild and moderate sequelae and also the number with mild and moderate synkinesis. Because synkinesis measurement is incorporated with the assessment of resting symmetry and voluntary facial movement in the Sunnybrook system, the composite Sunnybrook score is influenced by all 3 measures. Our results, however, indicate that there is a relationship between severity of palsy and grade of synkinesis, as stated by Linder et al.[20]

Because facial functional outcome assessments are semisubjective, a level of bias in the final outcome assessment scores should be considered in all trials. Revealing the statistical significance of treatment benefit in studies of Bell's palsy requires a large number of patients owing to the variable and spontaneous recovery profile of patients.[6,21] As stated by de Ru and coworkers,[22] mistaken patient populations, clinically irrelevant intervention, faulty comparison, and erroneous assessment of the measure of outcome due to a mediocre measuring instrument are medically substantive points of criticism regarding a great deal of research. For assessing the degree of a facial paralysis, the House-Brackmann grading scale is often used. This scale, however, has been judged to be rather insensitive, and its role as a criterion standard has therefore been questioned.[22,23] In the present study, measurement of outcome was assessed with 2 systems: the gross House-Brackmann grading scale[16] and the more sensitive Sunnybrook scoring system.[17] Furthermore, data were obtained from the Scandinavian Bell's Palsy Study,[14] which, in analogy with the trial of Sullivan et al,[15] was summarized with the lowest risk of bias of the 7 trials included in the Cochrane report by Lockhart et al.[7]

There are drawbacks to the present study. Subgroup analyses led to a reduction of patients in the analysis groups, which makes statistical comparisons more hazardous. Furthermore, we did not make the distinction between incomplete and complete palsy at baseline as advocated by Linder et al.[20] We analyzed the median baseline scoring levels, which were found to be similar in the different treatment groups.[14] One cannot, however, exclude the occurrence of more complete palsies in 1 or more of the groups. The number of patients with severe palsy (Sunnybrook score ≤20) at baseline was nevertheless evenly distributed between the treatment groups.[19]

To conclude, treatment with prednisolone significantly reduced mild and moderate sequelae in Bell's palsy at 12 months. Prednisolone did not reduce the number of patients with severe sequelae. Valacyclovir alone did not affect the severity of sequelae. The combination of prednisolone plus valacyclovir did not reduce the number of patients with sequelae compared with prednisolone alone.

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Author Contributions: Drs Berg, Jonsson, and Engström, had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design:* Berg, Jonsson, Kanerva, Hultcrantz, and Engström. *Acquisition of data:* Berg, Jonsson, Kanerva, and Engström. *Analysis and interpretation of data:* Berg, Bylund, Marsk, Jonsson, and Engström. *Drafting of the manuscript:* Berg and Jonsson. *Critical revision of the manuscript for important intellectual content:* Berg, Bylund, Marsk, Jonsson, Kanerva, Hultcrantz, and Engström. *Obtained funding:* Jonsson and Engström. *Administrative, technical, and material support:* Berg, Jonsson, and Kanerva. *Study supervision:* Jonsson.

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REFERENCES

1. Fisch U, Esslen E. Total intratemporal exposure of the facial nerve: pathologic findings in Bell's palsy. *Arch Otolaryngol*. 1972;95(4):335-341.
2. Schwaber MK, Larson TC III, Zealear DL, Creasy J. Gadolinium-enhanced magnetic resonance imaging in Bell's palsy. *Laryngoscope*. 1990;100(12):1264-1269.
3. Burmeister HP, Baltzer PA, Volk GF, et al. Evaluation of the early phase of Bell's palsy using 3 T MRI. *Eur Arch Otorhinolaryngol*. 2011;268(10):1493-1500.
4. McCormick DP. Herpes-simplex virus as a cause of Bell's palsy. *Lancet*. 1972;1 (7757):937-939.
5. Murakami S, Mizobuchi M, Nakashiro Y, Doi T, Hato N, Yanagihara N. Bell palsy and herpes simplex virus. *Ann Intern Med*. 1996;124(1, pt 1):27-30.
6. Peitersen E. Bell's palsy: the spontaneous course of 2,500 peripheral facial nerve palsies of different etiologies. *Acta Otolaryngol Suppl*. 2002;(549):4-30.
7. Lockhart P, Daly F, Pitkethly M, Comerford N, Sullivan F. Antiviral treatment for Bell's palsy (idiopathic facial paralysis). *Cochrane Database Syst Rev*. 2009;(4):CD001869.
8. Quant EC, Jeste SS, Muni RH, Cape AV, Bhussar MK, Peleg AY. The benefits of steroids versus steroids plus antivirals for treatment of Bell's palsy: a meta-analysis. *BMJ*. 2009;339:b3354. doi:10.1136/bmj.b3354.
9. Salinas RA, Alvarez G, Daly F, Ferreira J. Corticosteroids for Bell's palsy (idiopathic facial paralysis). *Cochrane Database Syst Rev*. 2010;(3):CD001942.
10. Adour KK, Ruboyianes JM, Von Doersten PG, et al. Bell's palsy treatment with acyclovir and prednisone compared with prednisone alone: a double-blind, randomized, controlled trial. *Ann Otol Rhinol Laryngol*. 1996;105(5):371-378.
11. de Almeida JR, Al Khabori M, Guyatt GH, et al. Combined corticosteroid and antiviral treatment for Bell palsy. *JAMA*. 2009;302(9):985-993.
12. Hato N, Yamada H, Kohno H, et al. Valacyclovir and prednisolone treatment for Bell's palsy. *Otol Neurotol*. 2007;28(3):408-413.
13. Numthavaj P, Thakkinstian A, Dejthevaporn C, Attia J. Corticosteroid and antiviral therapy for Bell's palsy: a network meta-analysis. *BMC Neurol*. January 5 2011; 11:1. doi:10.1186/1471-2377-11-1.
14. Engström M, Berg T, Stjernquist-Desatnik A, et al. Prednisolone and valaciclovir in Bell's palsy. *Lancet Neurol*. 2008;7(11):993-1000.
15. Sullivan FM, Swan IR, Donnan PT, et al. Early treatment with prednisolone or acyclovir in Bell's palsy. *N Engl J Med*. 2007;357(16):1598-1607.
16. House JW, Brackmann DE. Facial nerve grading system. *Otolaryngol Head Neck Surg*. 1985;93(2):146-147.
17. Ross BG, Fradet G, Nedzelski JM. Development of a sensitive clinical facial grading system. *Otolaryngol Head Neck Surg*. 1996;114(3):380-386.
18. Kawaguchi K, Inamura H, Abe Y, et al. Reactivation of herpes simplex virus type 1 and varicella-zoster virus and therapeutic effects of combination therapy with prednisolone and valacyclovir in patients with Bell's palsy. *Laryngoscope*. 2007;117 (1):147-156.
19. Engström M, Berg T, Stjernquist-Desatnik A, et al. Is antiviral medication for severe Bell's palsy still useful [authors' reply]? *Lancet Neurol*. 2009;8(6):509-510. doi:10.1016/S1474-4422(09)70115-2.
20. Linder TE, Abdelkafy W, Cavero-Vanek S. The management of peripheral facial nerve palsy. *Otol Neurotol*. 2010;31(2):319-327.
21. Goudakos JK, Markou KD. Corticosteroids vs corticosteroids plus antiviral agents in the treatment of Bell palsy. *Arch Otolaryngol Head Neck Surg*. 2009;135 (6):558-564.
22. de Ru JA, van Benthem PP, Janssen LM. All evidence is equal, but some is more equal than others. *Otol Neurotol*. 2010;31(4):551-553.
23. Browning GG. Bell's palsy. *Clin Otolaryngol*. 2010;35(1):56-58.