Bell’s Palsy — Is Glucocorticoid Treatment Enough?
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Approximately a third of cases of acute peripheral facial weakness are caused by trauma, diabetes mellitus, hypertension, eclampsia, the Ramsay Hunt syndrome (facial palsy with zoster oticus caused by varicella–zoster virus), Lyme disease, sarcoidosis, Sjögren's syndrome, parotid gland tumors, and amyloidosis and may even be a complication of intranasal influenza vaccine. The remaining two thirds of cases are idiopathic (Bell’s palsy).

Bell’s palsy occurs in 20 to 32 persons per 100,000 per year and affects both sexes and all ages. Fortunately, most patients with Bell’s palsy recover completely, but 20 to 30% may have permanent, disfiguring facial weakness or paralysis. Besides the asymmetry evident from limited retraction of the muscles around the angle of the mouth on one side and an inability to close the eye (Fig. 1), there may be other permanent sequelae, such as synkinesis, hyperacusis, a loss of taste, and an inability to produce tears. It is this substantial minority of patients with Bell’s palsy on whom early treatment is focused.

The rationale for early and aggressive treatment is based on long-standing observations by surgeons who have reported the presence of facial-nerve swelling during decompression operations in patients with Bell’s palsy. Edema may be secondary to ischemia or inflammation, as evidenced by contrast enhancement of the facial nerve seen on magnetic resonance imaging 9 to 23 days after the onset of Bell’s palsy. For years, physicians have treated patients with Bell’s palsy as early as possible with glucocorticoids. In addition, the detection of herpes simplex virus in the endoneurial fluid of patients with Bell’s palsy has led to the widespread use of antiviral agents along with glucocorticoids in the past decade, although the exact role of the virus in disease pathogenesis is unknown. Most, but not all, of the numerous studies that have compared glucocorticoid treatment with placebo in patients with Bell’s palsy have shown significant improvement with glucocorticoids. Glucocorticoids also appear to confer a greater benefit than acyclovir in these patients. Although the collective data suggest that glucocorticoids decrease the incidence of permanent facial paralysis, whether antiviral therapy confers additional benefits has not been known.

In this issue of the Journal, Sullivan et al. report on a large study involving the treatment of
patients with Bell’s palsy. The study was randomized, controlled, and double-blind, with predefined and specified outcome measures and follow-up for 9 months. Patients were recruited within 72 hours after the onset of symptoms from 17 hospitals in Scotland and were randomly assigned to treatment for 10 days with prednisolone, acyclovir, or both or with placebo. The House–Brackmann scale was used to assess recovery of facial function. Assessment of final outcomes at 9 months, which was possible in 496 patients, revealed complete facial-nerve recovery in 85.2% of patients who received placebo, supporting earlier reports in untreated patients.12,13 Furthermore, 96.1% of patients who received prednisolone alone recovered completely, an absolute risk reduction of 11%, as compared with those receiving placebo alone. This absolute risk reduction means that 9 patients (95% confidence interval, 6 to 14) would need to be treated to achieve one additional full recovery.

Surprisingly, only 78.0% of patients who received acyclovir alone had recovered fully at 9 months, a proportion somewhat less than that after placebo treatment, and the percentage of patients who were completely recovered after treatment with a combination of acyclovir and prednisolone was slightly less (92.7%) than after treatment with prednisolone alone (96.1%). Overall, there was no evidence of benefit from acyclovir over placebo or from the combination of acyclovir and prednisolone over prednisolone alone.

The lack of benefit from antiviral therapy that is reported by Sullivan et al. conflicts with the results of a recent prospective, randomized, placebo-controlled study by Hato et al.14 that compared a combination of valacyclovir (at a dose of 500 mg twice daily for 5 days) and prednisolone with placebo and prednisolone.14 A complete recovery was seen in 96.5% of 107 patients who received valacyclovir and prednisolone, as compared with 89.7% of 107 patients who received placebo and prednisolone (an absolute risk reduction of 6.8%). More striking was the report of the full recovery of 90.1% of patients with complete facial palsy who were treated with valacyclovir and prednisolone, as compared with 75.0% of those treated with placebo and prednisolone. This finding extrapolates to a need to treat approximately 15 patients among the total group with Bell’s palsy or approximately 7 patients in the subgroup with complete facial palsy to achieve one additional full recovery. The patients in the study by Hato et al. appear to have had more severe facial palsy than those in the study by Sullivan et al. (The average Yanagihara score in the study by Hato et al. was approximately 15, which falls between House–Brackmann grades 4 and 5, as compared with a mean score of 3.6 in the study by Sullivan et al.). In the study by Hato et al., the benefit of valacyclovir and prednisolone over placebo and prednisolone appeared to correlate with the severity of the facial palsy (an absolute risk reduction of 15.1% in patients with complete palsy and 5.7% in those with severe palsy, as compared with no reduction in those with moderate palsy). However, there were several methodologic limitations in the study by Hato et al. First, the investigators who were administering the treatment and assessing the outcome were aware of study-group assignments. Second, only 75% of patients who were enrolled in the study and underwent randomization were ultimately analyzed, as compared with 91 to 95% in their similar groups in the study by Sullivan et al.

How are the results from these two studies to be integrated into clinical practice? Although most patients with Bell’s palsy improve spontaneously, the use of prednisolone within 72 hours after the onset of symptoms decreases permanent facial disfigurement. In the United States, oral prednisone (at a dose of 1 mg per kilogram of body weight for 7 to 10 days) is used more often than prednisolone, and the cost of prednisone is less than $11 for a course of 7 to 10 days. Furthermore, the number needed to treat (approximately nine) to see one additional complete recovery from facial palsy is small.

The study by Sullivan et al. clearly indicates that the addition of acyclovir provides no additional benefit to treatment with glucocorticoids alone. But what about valacyclovir? Valacyclovir is a pro-drug that is nearly completely converted to acyclovir and L-valine and has substantially increased bioavailability, as compared with acyclovir. Both Hato et al. and Sullivan et al. show no benefit of antiviral therapy in patients with moderate palsy and thus provide no rationale for treating these patients with valacyclovir. The cost of a 5-day course of 500 mg of valacyclovir twice daily is approximately $70, and the number needed to treat for one additional full recovery in patients with complete facial palsy is approximately seven. Although the study by Hato et al. was methodologi-
cally flawed, the use of valacyclovir in combination with glucocorticoids could still be considered in patients with severe or complete facial palsy.

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