Bell's palsy treatment strategies

No obligation to use antivirals

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A 48-year-old woman presents to your office with upper and lower left-sided facial weakness she noticed while applying mascara that morning. Other than the peripheral pattern of left facial weakness and absent taste of the left tongue, her neurologic examination is normal. You see no signs to suggest Ramsay Hunt syndrome¹ and your practice is not in a Lyme disease endemic area. You make a diagnosis of idiopathic Bell's palsy.

Because of strong evidence of the efficacy of steroids in patients with Bell's palsy,² you plan to give your patient a short course of oral steroids to improve her chances of facial functional recovery. Although some of your colleagues have also used antivirals such as acyclovir in this situation, you do not feel obligated to offer antivirals to your patient. Why not?

There is evidence suggesting that herpes simplex virus type 1 (HSV-1) may be the cause of some cases of idiopathic Bell's palsy.³ PCR studies for HSV-1 of aspirates of facial nerve endoneurial fluid in patients with Bell's palsy are commonly positive. Patients without Bell's palsy who also have the endoneurial fluid studied by PCR are usually negative for HSV-1. Other studies have isolated herpes simplex virus from the nasopharynx of patients with Bell's palsy. These studies suggest that HSV may play an etiologic role in patients with Bell's palsy. Thus, it is biologically plausible that antivirals might improve outcomes in patients with Bell's palsy.

Although suggestive, this evidence is not convincing. HSV-1 is a common virus that often lies dormant in the nervous system.³ Any inflammatory condition of the facial nerve could potentially result in a reactivation of the virus. The identification of the HSV-1 virus in an inflamed facial nerve may simply represent a consequence of and not the cause of the inflammation. Additionally, even if HSV-1 causes Bell's palsy, there is no guarantee that

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antiviral medications will affect its natural history.⁴ Antibiotics do not always effectively treat an infection—especially one that is self-limited. Biological plausibility is not enough.

What happens to patients with Bell's palsy who receive antivirals? A search of the American Academy of Neurology Web site identifies a recently updated practice guideline⁵ regarding the treatment of Bell's palsy. The guideline reviews all comparative studies of patients with Bell's palsy who were treated with antivirals including acyclovir, valacyclovir, and famciclovir. In these studies, outcomes of patients treated with the combination of steroids and antivirals were compared to outcomes of patients receiving steroids alone. Of the 9 antiviral studies reviewed in the guideline, 5 demonstrated a significant and important effect of antivirals and 4 failed to show any benefit from antivirals.

Which studies are more likely to be correct? The 4 studies showing a potentially important treatment effect of antivirals all had a high risk of bias (Class IV) because of unmasked outcome assessment. In these studies, investigators were aware of which patients received antivirals. Observer expectation bias might have influenced investigators to believe that antiviral treated patients did better than they actually did. Although determining whether somebody has complete facial paralysis is straightforward, identifying mild to moderate residual facial dysfunction in a patient recovering from Bell's palsy requires a more subtle judgment. This judgment can be affected by observer expectation.

The studies that failed to show a benefit of antivirals were randomized trials with masked outcome assessment. These studies were unlikely to be affected by observer expectation bias and were judged to have a low or moderately low risk of bias (Class I or II). None of these studies demonstrated a significant effect of antivirals when added to steroids in patients with Bell's palsy.

The absence of a significant effect in the Class I and II studies does not necessarily mean that antivirals provide no important benefit. When assessing apparently negative studies, it is important to determine if they enrolled sufficient patients (i.e., had the power) to confidently reject a benefit. Inspecting the 95% confidence intervals (CIs) is an easy way to make this determination. Combining the studies with the lowest risk of bias (Class I) in a meta-analysis reveals a risk difference of zero (no benefit), with the 95% CI going from -8% favoring steroids alone to 7% favoring steroids plus antivirals.

The 95% CIs tell us 2 things: 1) we can be confident that the studies had adequate power to exclude a benefit of antivirals greater than 7% ; and 2) we cannot confidently reject the possibility that up to 7 additional Bell's palsy patients out of 100 do better when given antivirals with steroids (or that 8 would do worse, although worsening caused by antivirals seems less biologically plausible). Despite 2 Class I trials demonstrating no benefit, antivirals might still provide a modest benefit.

Given that antivirals might work, why not offer them to patients in addition to steroids? In fact, this would be a reasonable course of action. However, any such offer should be accompanied by an explanation that at best the antivirals will have a modest effect and indeed they may provide no benefit (or might even be harmful). Faced with that information, the patient might reasonably decline the offer.

Given the limitations in the evidence, the offer of antivirals is reasonable. However, there is no obligation to make such an offer. There are many Bell's palsy therapies without strong

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evidence of ineffectiveness. These include hyperbaric oxygen, acupuncture, and facial nerve decompression. Even though better studies may someday demonstrate that these modalities are effective, there is no obligation to offer these therapies to patients. The only medication a physician should feel obligated to offer a patient with Bell's palsy is oral steroids—there is strong evidence of steroid efficacy.

REFERENCES

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DISCLOSURES

G. Gronseth serves as an editorial advisory board member of *Neurology Now*, served on a speakers' bureau for Boehringer Ingelheim, and received honoraria from Boehringer Ingelheim. He is the compensated Evidence-based medicine methodologist for the American Academy of Neurology. Go to Neurology.org/cp for full disclosures.