Bell's palsy treatment strategies

Antivirals may help some patients

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Is there a rational basis for treating facial nerve palsy (FNP) patients—or a definable subgroup—with antiviral agents? There is substantial evidence that infections—including with herpesviruses¹—can play an important etiologic role in FNP, although there are no systematic data to indicate the proportion in which this is the case. Paradoxically, the role of anti-infectious therapy is much less clear. An upcoming American Academy of Neurology Guideline² concludes, much like the original 2001 one, “Because of the possibility of a modest increase in recovery, patients may be offered antivirals (in addition to steroids).” Despite similarly cautious wording, the original guideline was followed by widespread use of antivirals in FNP—use that has decreased substantially in light of more recent data.

While antibacterial treatment is clearly needed in FNP caused by bacterial basilar meningitis, there is remarkably little evidence in support of anti-infectious treatment with other infectious etiologies. Antimicrobial therapy is recommended in FNP associated with Lyme disease, and seems reasonable to prevent long-term sequelae of this systemic infection; yet there are no studies to suggest that this in any way improves outcome of the FNP.

Similarly, antiviral treatment is recommended in the Ramsay Hunt syndrome—FNP due to reactivation of herpes zoster (VZV) infection, an infection said to represent up

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to 18% of FNP cases.³ However, while antivirals speed resolution of the zoster rash and probably lessen postherpetic neuralgia, there are no high-quality studies indicating that such treatment has any effect on the FNP outcome in this setting either.⁴ However, this recommendation is particularly relevant to the present discussion as some studies suggest VZV infection—without vesicles (zoster sine herpette)—may be responsible for up to 20% of cases of idiopathic FNP.³ The possibility that some apparently idiopathic FNP cases might be due to zoster sine herpette, coupled with experimental evidence linking herpes simplex virus 1 (HSV1) infection to facial nerve palsy in animals and the detection of HSV1 in saliva of some patients with idiopathic FNP,¹ provide a logical basis for antiviral treatment.

This rationale notwithstanding, the effect of antiherpes treatment on FNP outcome has been ambiguous at best. A recent Cochrane review¹ appears to put the matter firmly to rest, showing a clear lack of benefit of antivirals. But does it? First, in many of that review's subanalyses, studies were included in which patients received either acyclovir (or related drugs) or corticosteroids, not both. If antivirals had a benefit, but this was less than corticosteroids', such comparisons would appear to demonstrate antivirals' ineffectiveness. The subanalyses in which all patients received corticosteroids were inherently limited by the generally excellent outcomes with steroid treatment in patients with FNP. A recent meta-analysis⁵ demonstrated recovery in 91.2% of patients receiving antivirals plus corticosteroids, 88.2% in those receiving corticosteroids alone—a difference so small that a sufficiently powered study would need to be huge—and even then, the clinical relevance of such a small difference would be highly questionable, unless it were due to differences in selected subgroups.

The possible existence of different subgroups is suggested by the heterogeneity of the results in studies comparing steroid treatment of FNP patients with or without the addition of antivirals.⁵ Only one high-quality study showed a significant difference (a study cited in the 2001 Guideline, and the basis for the “possible” recommendation), and this study favored the addition of antiviral treatment. In contrast, the 2 methodologically highest quality studies were both clearly negative and were powerful enough to drive overall meta-analyses negative. However, in the analyses of antiviral use, these 2 studies both used an endpoint of complete FNP resolution; in contrast, the other studies (in which the odds ratios, while significant in only the 1 study, all favored using antivirals) used complete or near complete resolution as the endpoint.

Subgroup analyses⁵ have not shown a difference with earlier antiviral treatment or longer follow-up. However, there is a suggestion that antivirals might benefit patients with more severe involvement at presentation.^{1,5} The conflicting results of the various studies could be reconciled if antivirals improved outcomes in these severely affected patients, but their recovery was incomplete because of the severity at presentation. Moreover, if patients with FNP due to VZV (without the rash) were disproportionately represented among more severely affected patients (as some suggest), this would provide justification for antiviral use in individuals with severe involvement at presentation.

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What conclusions can be drawn from this? There appears to be compelling evidence that many cases of FNP are associated with herpes virus infections, both HSV and VZV. Corticosteroid treatment in these patients is quite effective; if antivirals provide any incremental benefit, the effect size must be small, perhaps because by the time of clinical presentation, most of the nerve damage that will occur has already happened. That said, the evidence to date is consistent with there being a subgroup of patients—perhaps presenting with more severe involvement at onset—in whom antivirals may be beneficial. Additional studies to resolve this question will need to 1) stratify patients by weakness severity at onset; 2) measure outcomes quantitatively to assess the degree of additional recovery potentially attributable to antivirals; and 3) use specific assays to identify potential involvement of VZV or HSV1. With such an approach, the role of antiviral therapy in patients with FNP should finally be resolved.

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DISCLOSURES

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