

## Letter from the editor

### Bell's palsy: are commonly used treatments effective?

#### Context:

Bell's palsy results from inflammation of the facial nerve, leading to impairment of facial movement, often accompanied by pain, numbness, and alteration in taste.<sup>[1]</sup> There is some evidence that Bell's palsy is caused by herpes viruses, although this is based on weak observational evidence, and other causes need to be excluded. Bell's palsy resolves spontaneously in around 71% of patients, but 13% are left with slight weakness, and 16% with moderate weakness in their facial muscles.

Corticosteroids are widely used to treat early stages of Bell's palsy because of their known effectiveness in reducing inflammation. Antiviral agents are also used because of their effectiveness in treating herpes viruses.<sup>[1]</sup> However, two Cochrane systematic reviews have concluded that there is insufficient randomised controlled trial (RCT) evidence to assess either treatment.<sup>[2][3]</sup> The [Bell's palsy systematic review](#) in *BMJ Clinical Evidence* also suggests that the combination of corticosteroids and antiviral agents is 'Likely to be beneficial', but this conclusion is based on a single RCT of 119 people suggesting that aciclovir plus prednisolone may be more effective than prednisolone alone. The evidence for the effectiveness of combined treatment with antivirals plus prednisolone compared with placebo is even less robust — the *BMJ Clinical Evidence* review found only one small observational study in 56 people. This observational study suggested that combined treatment, in this case valaciclovir plus prednisolone, may be more effective than no treatment at all. A recent large multicentre study conducted in Scotland has investigated the benefits of the combination of prednisolone and aciclovir, either drug alone, or placebo, in people with Bell's palsy.<sup>[4]</sup>

#### Results:

Sullivan et al investigated 551 people "with unilateral facial weakness of no identifiable cause who presented to primary care or the emergency department and could be referred to a participating otorhinolaryngologist within 72 hours of onset of symptoms", using an RCT design.<sup>[4]</sup> They randomised participants into four groups: aciclovir plus prednisolone, aciclovir plus placebo, prednisolone plus placebo, and placebo plus placebo. The primary outcome assessed by the investigators was facial nerve function as assessed by the House–Brackmann Scale, where grade 1 indicates normal facial function and grade 6 indicates complete paralysis. Secondary outcomes assessed were health-related quality of life, pain, facial appearance, and adverse effects. Data were available for 496/551 (90%) of participants at follow-up of 3 and 9 months. Of these participants, 357/496 (72%) had recovered by 3 months.

The investigators assessed all participants receiving prednisolone (either alone or in combination with aciclovir) and found that prednisolone significantly increased the proportion of people with normal facial function after 3 months compared with placebo. A similar assessment of all participants receiving aciclovir (either alone or in combination with prednisolone) found no significant difference between groups in facial function at 3 months. Comparison of prednisolone plus aciclovir with placebo also found no significant difference between groups in facial function after 3 months, but it is unclear whether there were sufficient people in this group to detect a significant difference in outcomes. Differences between

groups persisted after 9 months although absolute differences between prednisolone and placebo were smaller than they were at 3 months. See table below for full details.

<b>Grade 1 on House– Brackmann scale at 3 months</b>	<b>Prednisolone</b>	<b>Placebo</b>	<b>Odds ratio*</b>
	205/247 (83%)	152/239 (64%)	2.44, 95% CI 1.55 to 3.84
	<b>Aciclovir</b>	<b>Placebo</b>	
	173/243 (71%)	184/243 (76%)	0.86, 95% CI 0.55 to 1.34
	<b>Combined prednisolone plus aciclovir</b>	<b>Placebo</b>	<b>Odds ratio</b>
Absolute numbers not reported	65%; absolute numbers not reported	1.73, 95% CI 0.96 to 3.12	
<b>Grade 1 on House– Brackmann scale at 9 months</b>	<b>Prednisolone</b>	<b>Placebo</b>	<b>Odds ratio*</b>
	237/251 (94%)	200/245 (82%)	3.32, 95% CI 1.55 to 3.84
	<b>Aciclovir</b>	<b>Placebo</b>	
	211/247 (85%)	226/249 (91%)	0.61, 95% CI 0.33 to 1.11
	<b>Combined prednisolone plus aciclovir</b>	<b>Placebo</b>	<b>Odds ratio</b>
Absolute numbers not reported	85.2%; absolute numbers not reported	0.58, 95% CI 0.29 to 1.16	
*Adjusted for age, sex, time from onset of symptoms to initiation of treatment, and baseline scores for facial function, quality of life, appearance, and pain			

There was no significant difference between prednisolone and no prednisolone or aciclovir and no aciclovir in secondary outcomes of quality of life, pain, and appearance. No data were reported on secondary outcomes in people receiving combined treatment.

Rates of adverse effects were similar in all four study groups and included dizziness, dyspepsia, and nausea. No statistical assessment of differences between groups was reported.

### Limitations of the study:

In their power calculation, the investigators suggested that it would need 236 patients receiving each treatment (a total of 944 patients in the trial), in order to achieve 80% power to detect a clinically meaningful difference between treatments — that is a difference in complete recovery of at least 10–12 percentage points. In recruiting only 551 patients, the authors assumed that there was no interaction between treatments, and that results in different groups could, therefore, be combined after randomisation. However, this combination of data means that people receiving combined treatment were in fact analysed twice, firstly in the analysis of prednisolone alone versus no prednisolone, and again in the analysis of aciclovir alone versus no aciclovir. This weakens the data that the authors present on prednisolone alone, as some of the patients' response rates may have been influenced by the addition of aciclovir. Conversely, some of the patients' response rates in the analysis of aciclovir alone may well have been affected by the addition of prednisolone. In addition, the lack of sufficient

patients in the trial means that the group of people receiving combined treatment was too small to detect possibly significant differences between combined treatment and placebo or either drug alone.

The authors state that: "prednisolone was highly effective, both separately and in combination with aciclovir. Aciclovir was ineffective, both separately and as an addition to prednisolone." This conclusion seems to be based on the inference that, as prednisolone alone improved facial function and aciclovir alone did not, both drugs must therefore perform in the same way when used in combination. There are no data reported by the authors to support this inference; the data reported simply suggest that there was no significant difference between combined treatment and placebo. Presentation of results made it difficult to ascertain exactly what the combination treatment was being compared with when non-significant odds ratios were reported (I assumed placebo rather than prednisolone alone or aciclovir alone).

Furthermore, most participants in the trial (54%) initiated treatment within 24 hours of symptom onset, and all initiated treatment within 72 hours. This means that we still don't know whether corticosteroids are effective if commenced more than 72 hours after the onset of Bell's palsy.

## Conclusions:

This is the first large RCT<sup>[4]</sup> assessing commonly used treatments for Bell's palsy, being four times larger than any previously conducted trial. The results support the use of prednisolone as first-line treatment in early presentations of Bell's palsy, and suggest that aciclovir may be ineffective. These conclusions may well alter established clinical practice. However, trial design flaws mean that it remains unclear whether combining treatments may be valuable, or whether the addition of aciclovir reduces the effectiveness of prednisolone. Given that there is some evidence that combined treatment with valaciclovir plus prednisolone may be valuable,<sup>[5]</sup> further research is warranted before combined treatment for this common neurological problem is abandoned. Sullivan et al recruited widely and, as such, provide strong data for people presenting to both primary and secondary care with symptoms and signs of Bell's palsy. However, as all participants included had experienced symptoms for 72 hours or less, it is still not certain whether clinicians treating patients with a longer duration of symptoms can apply these results to their decision making. Finally, when advising patients, clinicians may well wish to place the long-term results in people receiving prednisolone (94% response) in context of long-term results in people receiving placebo (82–91% response), so that a fully informed decision about whether it is worthwhile to undertake treatment can be made.

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## References

1. Managing Bell's palsy. *Drug Ther Bull* 2006;44:49–53. Review.
2. Salinas RA, Alvarez G, Ferreira J. Corticosteroids for Bell's palsy (idiopathic facial paralysis). In: The Cochrane Library, Issue 1, 2008. Chichester, UK. John Wiley & Sons, Ltd
3. Allen D, Dunn L. Aciclovir or valaciclovir for Bell's palsy (idiopathic facial paralysis). In: The Cochrane Library, Issue 1, 2008. Chichester, UK: John Wiley & Sons, Ltd.
4. [Sullivan FM](#), Swan IR, [Donnan PT](#), et al. Early treatment with prednisolone or acyclovir in Bell's palsy. *Clin Otolaryngol* 2007;32:460.
5. Hato N, Yamada H. Valaciclovir and prednisolone treatment for Bell's palsy: a multicenter, randomized, placebo-controlled study. *Otol Neurotol* 2007;28:408–413.