

Critical Review Form

Meta-analysis

The benefits of steroids versus steroids plus antivirals for treatment of Bell's palsy: a meta-analysis, *BMJ* 2009; 339:b3354:1-7

Objective: “To determine whether steroids plus antivirals provide a better degree of facial muscle recovery in patients with Bell's palsy than steroids alone”. (p. 2)

Methods: Two SR authors performed an electronic search using PUBMED, EMBASE, Web of Science, and the Cochrane Central register of controlled trails in addition to searching bibliographies. Their search terms did not include steroids. Included studies had to be RCT's assessing steroids vs. steroids/antiviral combinations in adult non-pregnant Bell's palsy patients.

Two SR authors evaluated study quality using the [Jadad scale](#) and the analysis followed the [QUOROM](#) guidelines. This primary outcome was the proportion of patients with at least partial facial muscle recovery using a validated metric (example [House-Brackmann](#) score 1 or 2). Summary effects were generated using a random-effects model. Heterogeneity was assessed with the I^2 statistic. Publication bias was assessed using a [funnel plot](#) and [trim & fill](#) analysis. The SR authors planned *a priori* to conduct a sensitivity analysis by sequentially re-analyzing the summary effect size after removing one-study at a time. Sources of potential heterogeneity were identified *a priori*, these included study quality, treatment delays, length of follow-up, and type of antiviral studied.

Guide	Question	Comments
I	<i>Are the results valid?</i>	
1.	Did the review explicitly address a sensible question?	Yes. Does the summary of high quality trial evidence suggest that antiviral agents should or should not be added to corticosteroid?
2.	Was the search for relevant studies details and exhaustive?	No. The investigators neglected to search the gray literature, or contact experts/industry for unpublished trial data. Furthermore, they did not search for trials underway at www.clinicaltrials.gov .
3.	Were the primary studies of high methodological quality?	Yes. Two trials had Jadad score five (best possible), one had four, two had three, and one had one (p.5)
4.	Were the assessments of the included studies reproducible?	Uncertain since authors do not report on Kappa score for quality assessment nor do they note any disagreements.
II.	<i>What are the results?</i>	
1.	What are the overall results of the study?	<ul style="list-style-type: none"> • Six studies totaling 1145 patients were included in this meta-analysis including three acyclovir, two valciclovir and one famciclovir studies. • The vast majority of patients recover at least some facial function (89.7% overall cohort) including 88.2% of steroids alone and 91.2% of steroids antiviral. • The two highest quality studies (Jadad five) had non-significant point estimates favoring steroids alone, but random-effects model of all six trials also showed no benefit (OR 1.50, 95% CI 0.83 – 2.69, $I^2 = 47\%$). • The random-effects model was not significantly altered in sensitivity analysis except when the two highest quality studies were excluded which moved the joint-estimate in favor of combination therapy (Fig 4, p.6). • A funnel plot suggested publication bias and when (non-existent?) studies calculated using a trim & fill algorithm, were added the effects of steroids plus antivirals compared with steroids alone was eve less. • Subgroup analyses found no effect of treatment < 3 days, length of follow-up, or type of antiviral agent used.
2.	How precise are the results?	See 95% CI above.

3.	Were the results similar from study to study?	No. The point estimate for two trials favored steroids alone, while four favored combination therapy (Fig 2, p. 4) so $I^2 = 47\%$.
III.	<i>Will the results help me in caring for my patients?</i>	
1.	How can I best interpret the results to apply them to the care of my patients?	For Bell's palsy patients, antivirals provide no benefit for partial facial motor recovery over steroids alone.
2.	Were all patient important outcomes considered?	No. Secondary outcome measures such as facial pain or disfigurement were not consistently reported by investigators and were thus not analyzed in this meta-analysis". (p. 2). Furthermore, SR authors did not assess adverse drug events or POEMS like time to recovery or medication expenses relative to perceived or real therapeutic benefit.
3.	Are the benefits worth the costs and potential risks?	No cost-benefit analysis is presented or hypothesized.

Limitations

- 1) Incomplete search strategy neglecting the gray literature, ongoing clinical trials, or industry-experts as potential sources of difficult to find trial data.**
- 2) No assessment of patient-oriented outcomes like Quality of Life, time to recovery, or medication expense to benefit trade-offs.**
- 3) Insufficient data to assess important secondary outcomes like synkinesis or crocodile tears.**
- 4) No subgroup analysis of initial facial muscle impairment severity or dose of antiviral used.**
- 5) Exclusion of children and pregnant women limits external validity.**

Bottom Line

In clinically diagnosed Bell's palsy adding antiviral agents to corticosteroids does not improve the proportion of patients with at least partial facial motor function. Future trials will need to use newer technology (PCR) to assess the value of antiviral agents when Herpes virus is confirmed at the point-of-care while assessing the impact of antiviral dose and initial facial asymmetry severity on therapeutic effectiveness.

