The Efficacy of Prednisone Versus Antivirals in the Complete Recovery of Patients With Bell’s Palsy: A Systematic Review

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The Efficacy of Prednisone Versus Antivirals in the Complete Recovery of Patients With Bell's Palsy: A Systematic Review

Abstract

Background: Bell's palsy is an idiopathic condition, caused by inflammatory injury to the facial nerve, resulting in a unilateral facial paralysis. This disfiguring disorder affects about 40,000 people in the U.S. each year and although many recover without treatment, there are serious physical and psychological complications for those that fail to recover completely. Due to its unknown etiology, the preferred treatment of Bell's palsy has been the subject of controversy for sometime. Current practice has demonstrated the use of steroids to counteract the inflammatory process and/or antivirals because of a hypothesized viral etiology. Does the use of antivirals alone or in conjunction with steroids substantially increase the overall recovery in patients with Bell's palsy?

Methods: An exhaustive search was conducted using Medline-OVID, CINAHL-EBSCOhost, EBMR Multifile, and Web of Science using the keywords: Bell's palsy, antiviral agents and prednisone or prednisolone. The NIH clinical trials site revealed no on-going or registered trials comparing the treatment of steroids and antivirals in patients with Bell's palsy. Relevant articles were assessed for quality using GRADE.

Results: Two randomized, double blind, placebo-controlled trials were included in this systematic review. One trial, with 829 participants, demonstrated a statistically significant increase in the recovery of patients treated with prednisolone as compared to valaciclovir. A second trial, with 496 participants, demonstrated a statistically significant increase in the recovery of patients treated with prednisolone as compared to aciclovir.

Conclusion: When initiated within 72 hours of symptom onset, prednisone has been shown to increase the overall number and rate of recoveries in patients being treated for Bell's palsy. The use of antivirals alone, as compared to placebo, did not increase the number of recoveries and in some cases slowed the rate at which patients recovered. Furthermore, when compared to prednisone alone, these two trials failed to produce results of statistically significant improvement in recovery when administering combination therapy of prednisone plus antivirals. This raises question as to whether combination therapy should be considered at all until further research proves a statistically significant improvement or a true etiology for Bell's palsy is identified.

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Degree Name
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Keywords
Bell's palsy, Antiviral agents, Prednisone, Prednisolone

Subject Categories
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Biography

Robin Tyner is a native of Texas. She received a Bachelors of Science degree with an emphasis in Health Sciences from Pacific University, Oregon, in 2012. Prior to PA school, she worked as a medical assistant at a hospital in San Antonio and served as a medic in the United States Army for 5 years. During her deployment to Iraq she worked with superbly skilled clinicians that enjoyed teaching, and had her dream of pursuing a career as a PA solidified. She is interested in serving the under-served and pursuing a career in Emergency Medicine.
Abstract

**Background:** Bell’s palsy is an idiopathic condition, caused by inflammatory injury to the facial nerve, resulting in a unilateral facial paralysis. This disfiguring disorder affects about 40,000 people in the U.S. each year and although many recover without treatment, there are serious physical and psychological complications for those that fail to recover completely. Due to its unknown etiology, the preferred treatment of Bell’s palsy has been the subject of controversy for sometime. Current practice has demonstrated the use of steroids to counteract the inflammatory process and/or antivirals because of a hypothesized viral etiology. Does the use of antivirals alone or in conjunction with steroids substantially increase the overall recovery in patients with Bell’s palsy?

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**Conclusion:** When initiated within 72 hours of symptom onset, prednisone has been shown to increase the overall number and rate of recoveries in patients being treated for Bell’s palsy. The use of antivirals alone, as compared to placebo, did not increase the number of recoveries and in some cases slowed the rate at which patients recovered. Furthermore, when compared to prednisone alone, these two trials failed to produce results of statistically significant improvement in recovery when administering combination therapy of prednisone plus antivirals. This raises question as to whether combination therapy should be considered at all until further research proves a statistically significant improvement or a true etiology for Bell’s palsy is identified.

**Keywords:** Bell’s palsy, Antiviral agents and Prednisone or Prednisolone
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Table I: GRADE Quality of Assessment
Table II: Summary of Findings

List of Abbreviations

AO   Aciclovir plus Placebo
AP   Aciclovir plus Prednisolone
BP   Bell’s palsy
GRADE Grading of Recommendations, Assessment, Development and Evaluations
GSK  GlaxoSmithKline
HBS  House-Brackmann Scale
HSV1 Herpes Simplex Virus-1
HTA  Health Technology Assessment
NIH  National Institute of Health
NNT Number Needed to Treat
OO   Double Placebo
OP   Prednisolone plus Placebo
RCT Randomized Controlled Trials
SS   Sunnybrook Scale
VO   Valaciclovir plus Placebo
VP   Valaciclovir plus Prednisolone
YS   Yanigahara Scale
The Efficacy of Prednisone Versus Antivirals in the Complete Recovery of Patients With Bell’s Palsy: A Systematic Review

BACKGROUND

Bell’s palsy, or idiopathic unilateral facial nerve paralysis, is a disfiguring disorder that acutely affects approximately 40 000 Americans each year. This condition is characterized by an inflammatory injury to the facial nerve, which renders the muscles of facial expression that it innervates, either partially or completely paralyzed. Although many patients can recover without intervention, up to 30% of the 15 to 30 new cases per 100 000 population reported worldwide annually suffer incomplete recovery or sequelae. In turn, those who do not fully recover may experience psychological effects due to a perceived loss of beauty and function as a result of prolonged or permanent facial asymmetry.

The exact etiology of Bell’s palsy (BP) remains unknown, but the accepted pathophysiology supports an inflammatory mechanism that compresses the seventh cranial nerve around the area where it exits the skull via the stylomastoid foramen. Upon exiting the skull, the facial nerve travels through the fallopian canal and then enters the parotid gland where it divides into the five terminal branches that are responsible for innervating the muscles of facial expression. Inflammation of the nerve itself, or anything else running inside the narrow canal, has the ability to compress and damage the facial nerve, resulting in weakness or paralysis of everything that it innervates. In addition to the muscles of facial expression, the nerve also stimulates secretions of the lower jaw, tear glands, and salivary glands, and is also responsible for taste sensation to
the anterior 2/3rds of the tongue as well as perceived sound volume.\textsuperscript{4} All of the structures that the facial nerve innervates account for the classic presentation associated with this condition.

The classic presentation of BP most often includes rapid onset of upper and lower facial paralysis which is typically unilateral and may also include post-auricular pain, decreased tearing, hyperacusis, alteration of taste and/or otalgia.\textsuperscript{2} Patients often present with complaints of an inability to smile, raise their eyebrow or blink naturally on the affected side. It is not uncommon for patients to have the affected eye roll upward on its own, in attempts to close their eye, which is known as Bell’s phenomenon. To accurately be diagnosed as BP, the paralysis must include both the lower portion of the face and the forehead. The onset of symptoms can be frightening as they often peak in less than 48 hours and, to an untrained eye, can mimic those of a stroke or central motor neuron lesion. It is important to be able to differentiate between a central motor neuron lesion, which is more serious and BP, which is a peripheral lower motor neuron lesion. Patients presenting with a history of gradual onset, ability to raise their eyebrow on the affected side and contralateral weakness should be worked up thoroughly to rule out a central lesion or stroke.\textsuperscript{2}

The diagnosis is often one of exclusion, based on a careful history and physical exam, as there are no specific diagnostic tests for BP. Prognosis and treatment choices are often guided by the severity of the paralysis, which can be assessed using a number of different scales including the House-Brackmann scale (HBS), the Sunnybrook scale (SS) or the Yanigahara scale (YS). The HBS and SS have been more widely used in the U.S. and Europe whereas the YS has been used most frequently in Japan. The HBS is a scale,
with grades I to VI, used to assess facial nerve function from three different standpoints, which include gross appearance, at rest, and in motion. Grade I indicates normal function in all branches, grade II indicates slight weakness or asymmetry, grade III indicates obvious weakness that is not disfiguring, grade IV in indicative of disfigurement with obvious weakness, grade V is considered severe with movement being barely perceptible, and grade VI indicates a complete lack of facial function altogether with no movement being visible at all. The SS is a scale that grades facial nerve function on a score from 1 to 100, with three domains, that includes resting symmetry, symmetry of voluntary movement and synkinesis. For resting symmetry, the eye, nasolabial fold and mouth of the affected side are compared with the normal side. The voluntary movements and synkinesis domains evaluate brow lift, gentle eye closure, open mouth smile, snarl, and lip pucker. These methods for grading severity have also been proven to be useful tools in documenting the recovery progress of individuals with BP.

Due to its unknown etiology, the preferred treatment of Bell’s palsy has been the subject of controversy for sometime. Current practice has demonstrated the use of steroids to counteract the inflammatory process and/or antivirals because of a hypothesized viral etiology, namely Herpes Simplex Virus-1 (HSV1). Prednisone and prednisolone are analogues of one another that have been used as the steroid of choice for BP. To date, many randomized controlled trials (RCTs) have studied the efficacy of both steroids and antivirals, individually, as well as in combination. The study of antivirals in the treatment of BP has included the use of acyclovir/acyclovir, valacyclovir/valaciclovir and more recently famciclovir. “Valacyclovir is a prodrug and is nearly completely converted to acyclovir and L-valine. The bioavailability of valacyclovir is 3-5 times that
of acyclovir, implying a much higher antiviral activity against HSV. The controversy around the etiology of this condition, its treatment and the many clinical trials out there with conflicting results gave rise to the review of this clinical question. Is mono-therapy with prednisone or antivirals more efficacious in the complete recovery of patients with Bell’s palsy than combination therapy?

METHODS

An exhaustive search was conducted using the search engines Medline-OVID, CINAHL-EBSCOhost, EBMR Multifile, and Web of Science. Keywords such as Bell’s palsy, antiviral agents, and prednisone or prednisolone were used. The search was then narrowed to include only those trials that were conducted on humans, and published in English, within the last five years. Articles with primary data evaluating the efficacy of prednisone or prednisolone versus antiviral agents in the treatment of patients with new onset Bell’s palsy were included for review. The relevant articles were then critically appraised to assess for validity, and risk of bias, and to determine if they met pre-specified inclusion criteria for eligibility. To meet inclusion criteria, the studies had to be based on RCTs that had blind assessment of outcome and initiated treatment within 72 hours of symptom onset. The relevant articles, which met eligibility criteria, were then assessed for quality using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE). Lastly, a search on the National Institute of Health (NIH) clinical trials site revealed no currently registered trials, at any phase, relating to the use of steroids or antivirals in the treatment of Bell’s palsy.
RESULTS

The initial result of the search yielded 56 articles for review. After narrowing the original search with the aforementioned criteria, there were 31 articles that underwent further screening. After removing duplicates and irrelevant articles, six articles based on randomized controlled trials were critically appraised for validity and two of those met eligibility inclusion criteria. The two articles, which met inclusion criteria, were Engström et al (2008)\textsuperscript{10}, which was conducted in Sweden, and Sullivan et al (2009)\textsuperscript{11}, which was conducted in Scotland (see Table I). The authors of the four excluded articles were Hato et al (2007)\textsuperscript{8}, Kawaguchi et al (2007)\textsuperscript{12}, Minnerop et al (2008)\textsuperscript{13}, and Yeo et al (2008).\textsuperscript{14} The exclusion of these four studies was due to failure to blind or enrollment of some participants who had treatment initiated after the 72 hour cut-off mark.

Engström et al

This randomized, double blind, placebo-controlled trial\textsuperscript{10} investigated the short and long-term effects of valaciclovir and prednisolone in the recovery of the facial nerve of patients with BP. This study was set in Sweden and included 839 patients, aged 18 to 75 that presented, or were referred from EDs, or general practitioners within 72 hours of symptom onset of BP. Patients were considered ineligible, and therefore excluded, if they had had BP previously, waited more than 72 hours to seek care, did not fit the age range, were already taking antivirals or had signs of other infections known to contribute to facial paralysis. Additionally, patients were excluded if they had contraindications to any of the medications due to pre-existing health conditions such as peptic ulcer disease, recent head injury, renal or hepatic dysfunction, or were pregnant and or breastfeeding.\textsuperscript{10}
Once deemed eligible, patients were randomly assigned to one of four treatment groups by way of factorial method, via computer generation, that randomly selected groups of eight. The four treatment groups included double placebo (OO), prednisolone plus placebo (OP), valaciclovir plus placebo (VO) and prednisolone plus valaciclovir (VP). Patients allocated to receive prednisolone were given 60mg per day for five days and then had their dose reduced by 10mg each day for a total treatment time of 10 days. Patients allocated to receive valaciclovir were given 1000mg of valaciclovir three times per day for a total treatment time of 7 days. A bottle of prednisolone or its placebo, and valaciclovir or its placebo, was given to each patient in accordance with his or her group designation. Placebos were made to have the same smell, color and size of the drug it was mimicking, ensuring that patients were blind to their treatment group allocation. Additionally, study drugs were sealed in sequentially numbered, identical containers in accordance with allocation sequence and distributed in sealed envelopes that contained the randomization codes to ensure blinding of all study personnel and data analysts until all patients had completed follow-up.¹⁰

Compliance was evaluated by counting the tablets in each container at each follow-up visit. Follow-up visits were conducted to assess progression or improvement of facial function using the HBS and SS scales at days 11 and 17, and monthly for months 1, 2, 3, 6 and 12. Although secondary outcomes such as facial function and synkinesis were evaluated, the primary endpoint was defined as time to complete recovery of facial recovery. Complete recovery was determined by a grade of I on the HBS or a score of 100 on the SS. In addition, data were collected on adverse events experienced during treatment, which included but was not limited to, palpitations,
headache, fatigue, dizziness, paraesthesia, gastrointestinal complaints, and polyuria.\textsuperscript{10}

Of the 829 patients who took any medication at all, 206 patients received OO, 210 received OP, 207 received VO and 206 received VP. Therefore, 416 patients received prednisolone and 413 received valaciclovir. Patients were analyzed by whether or not they received prednisolone or valaciclovir using an intention to treat method. In addition, they were also analyzed in their individual group allocations so that data could be compared to establish the difference in effect between the two drugs as well as the effect of combining the two treatments against placebo. The time to complete recovery was much shorter (75 days) for the 416 patients that received prednisolone compared with the 413 patients that did not (135 days). Additionally, it was noted that those patients who received double placebo experienced a complete recovery in about 104 days on average, which was nearly 1 month sooner than those treated with the antivirals. Furthermore, of the patients treated with OP, 160/210 (76\%) had a complete recovery at 12 months, which was significantly more when compared with the 133/207 (64\%) receiving VO and the 133/206 (65\%) receiving OO (see Table II). These statistics correlate with a number needed to treat (NNT) with prednisolone, when compared with antivirals or placebo, of eight to see one additional complete recovery, which is statistically significant.\textsuperscript{10}

\textbf{Sullivan et al}

This randomized, double blind, placebo-controlled trial\textsuperscript{11} sought to determine whether the early use of oral prednisone or aciclovir, used separately or in combination, improved the recovery of patients with BP at three and nine months. This study was set in Scotland and included 551 patients, aged 16 years and older, that were referred to 17 different hospital trial sites from general practices with new onset of BP. Patients were
considered ineligible, and therefore excluded, if they had had BP previously, waited more than 72 hours to seek care, did not fit the age range, were already taking antivirals or had signs of other infections known to contribute to facial paralysis. Additionally, patients were excluded if they had contraindications to any of the medications due to pre-existing health conditions such as peptic ulcer disease, multiple sclerosis, uncontrolled diabetes, sarcoidosis, and herpes zoster, or were pregnant and or breastfeeding.¹¹

Once deemed eligible, patients were randomly assigned to one of four treatment groups by an independent, secure, automated telephone service using a permuted block randomization technique without stratification and block sizes of 4 or 8. The four treatment groups included double placebo (OO), prednisolone plus placebo (OP), aciclovir plus placebo (AO) and prednisolone plus aciclovir (AP). All patients were treated for 10 days and those allocated to receive prednisolone were given enough 25mg tablets to take 50mg per day. Patients allocated to receive aciclovir were given enough 400mg tablets to take 2000mg each day. A bottle of prednisolone or its placebo, and aciclovir or its placebo, was given to each patient in accordance with his or her group designation. Placebos were indistinguishable in appearance from their respective drugs and with regard to their bottle packaging. Each of the different treatment combinations was provided in packs labeled 1 through 4 to ensure that the referrers, recruiters, patients, researchers, and later, assessors were all blinded to treatment allocation and outcome.¹¹

The primary outcome, complete recovery of the facial nerve, was measured in this trial using the HBS. After diagnosis, all patients were re-assessed in an at home visit, 3 to 5 days post randomization into the trial. Further follow-up and assessment was conducted at three months and again at nine months if a patient had not completely
recovered at the three-month visit. Although a complete recovery of facial function was initially defined, by this trial, as an HBS score of II or better, the cutoff was changed to a score of I shortly after the study commenced. Therefore, anyone with a score of II or higher at their three month follow-up visit was scheduled for a nine month visit.

Judgments of recovery were determined by expert medical review of four posed portrait photographs taken at each follow-up visit. The four photographed positions, utilized to evaluate the progression of recovery for each patient, were at rest, smiling, eyebrows raised and eyes tightly shut. Three different clinicians (a plastic surgeon, neurologist and otolaryngologist) independently graded the photos of each patient. Where difference of more than one point occurred between evaluators, the grading was redone. Secondary outcomes that were evaluated included pain associated with the palsy, cost of the different treatment modalities and psychological distress associated with concern about personal appearance. Furthermore, the trial collected and analyzed data on all adverse events that were experienced with each individual or combined pharmaceutical treatment. These included, but were not limited to, nausea, vomiting, night sweats, and pruritus.¹¹

Of the 551 patients that were originally randomized, final outcomes were available for 496 patients, resulting in a 90% completion rate and 10% loss to follow-up overall. Intention to treat analyses were conducted for all four treatment groups individually, as well as for combined grouping, to assess the difference in treatment effect for those receiving prednisolone as compared to those receiving antiviral treatment. For the three month follow-up appointment, approximately 86% of patients (107/124) that received OP had made a full recovery, which was significantly more than the 63% (75/120) that received AO and the 65% (77/119) that received OO (see Table II). These
numbers correlated to a NNT with prednisolone in order to see one additional improvement of six patients at three months and an NNT of eight patients at nine months. The collected data from this trial did not correlate with a statistical significance between the placebo group as compared with the antiviral group. In addition to the percentage of full recoveries, the authors of this study also analyzed the average time that it took each individual treatment group to achieve complete recovery. That analysis found that treatment with prednisolone substantially shortened the duration of time needed to make a full recovery. The mean time to full recovery for the OP group was 67 days as compared to 85 days for the AP group, 126 days for the OO group and 150 days for the AO group.11

DISCUSSION

Corticosteroids, namely prednisone or prednisolone, have proven to be both cost effective and very successful in the treatment of patients with Bell’s palsy. Due to its idiopathic nature and proposed viral etiology, recent research has revolved around studying the use of antivirals alone or in conjunction with steroids for the treatment of BP. To date, cost effectiveness aside, RCTs have produced conflicting results regarding the benefit of treating BP patients with antivirals alone or in conjunction with corticosteroids. Both and Engström et al10 and Sullivan et al11 determined that the use of prednisolone was superior to either antiviral drug evaluated. There was a significant difference in complete recovery as early on as 3 months in the groups that received prednisolone with both trials. This trend continued to show statistically significant differences at all points of follow-up as evidenced in the Summary of Findings, which can be found in Table II.10,11
Both Engström\textsuperscript{10} and Sullivan et al\textsuperscript{11} reported an absence of statistical significance in the difference found between patients that received an antiviral plus placebo and those that received double placebo. Furthermore, there was a decrease in the recovery rate for patients that received an antiviral in both trials. This decrease balanced out to an equal recovery by the completion of the Engström et al study\textsuperscript{10} but continued to increase as time went on in the Sullivan et al study. This data indicates a need for further research to be conducted before giving serious consideration to the prescription of antivirals at all. Although neither of these studies determined that adding an antiviral to placebo was beneficial, there is room for more research to be done with regard to serological studies determining an underlying cause of Bell’s palsy. Sullivan et al sited an area of further research opportunity to be in determining if higher tissue concentrations (higher doses) of antiviral agents could result in a more detectable benefit than that which they were able to find.\textsuperscript{10,11}

Additionally, systematic reviews and meta-analyses on variations of this subject have been published recently utilizing different eligibility criteria and quality stipulations.\textsuperscript{15-18} The eligibility criteria for inclusion in this review was slightly different than that of those reviews or analyses and, therefore, revealed some different articles for consideration. Of the studies reviewed in consideration for this review, there were four RCTs that were assessed for quality of evidence in addition to the two, which were included in this review. Although those four failed to meet all of the inclusion criteria, they served to gauge the strength or quality of evidence produced by the two articles that did meet all eligibility criteria.
The Hato et al study (2007)\textsuperscript{8} failed to meet inclusion criteria because it initiated treatment up to seven days after the onset of symptoms. Nonetheless, the authors reported a slight increase in the recovery of 221 patients with BP that received combination therapy of valacyclovir and prednisolone when compared to prednisolone alone. However, 52/296 (>17\%) of the patients, who were originally randomized to receive treatment were lost to follow-up without explanation. Furthermore, the physicians were not completely blinded during the trial limiting the strength or value of the study because of failure to uphold allocation concealment.\textsuperscript{8}

The Kawaguchi et al study (2007)\textsuperscript{12} was another RCT that failed to meet the inclusion criteria because it also initiated treatment up to seven days after the onset of initial symptoms. This study evaluated the etiology of BP and sought to determine the effectiveness of valacyclovir and prednisone in treating it. This RCT found no statistical difference in cumulative recovery rates between those treated with combination therapy and prednisolone alone. However, this trial failed to blind the patients or physicians evaluating the progress of those enrolled in the study. This limited the results of the study because it introduced bias.\textsuperscript{12}

The Minnerop et al study (2008)\textsuperscript{13} failed to meet inclusion criteria as they initiated treatment up to five days after initial symptom onset. This study evaluated the combination therapy of famciclovir and prednisone in the treatment of patients with BP. Similar to valacyclovir, famcyclovir is another anologue of acyclovir, which is regarded to have greater bioavailability and therefore to be more effective overall. Minnerop et al\textsuperscript{13} reported a significantly better outcome for BP patients treated with combination therapy as compared with prednisone alone. However, the design of this study utilized
pseudo-randomization and failed to blind patients to their treatment group allocation. Additionally, 48/167 (30%) patients that were randomized were lost during follow-up, which severely limited the usefulness of this study.\textsuperscript{13}

The Yeo et al study (2008)\textsuperscript{14} also failed to meet inclusion criteria due to initiation of treatment greater than 72 hours after onset of symptoms and because other treatment mechanisms were also employed during this study. The design of this study differed from all others in that all patients were admitted to the hospital for at least seven days to receive treatment. Participants were given either prednisone and acyclovir or prednisone alone. Additionally, the patients were also administered peripheral blood circulation supplements, plasma volume extenders and also received physical therapy services. Yeo et al reported a greater recovery for those that received combination therapy as compared to prednisone alone. However, they had a very small sample size of patients (n=91) and admittedly reported that the differences they found were not statistically significant. Furthermore, no discussion was made as to how allocation was concealed or whether or not a placebo was used to increase blinding. All of these factors grossly limited the results of this study.\textsuperscript{14}

Due to the conflicting outcomes of the many RCTs conducted to date, including those above, it is imperative that one considers the quality of evidence for each study before basing clinical decisions on the information it provides. Engström et al\textsuperscript{10} and Sullivan et al\textsuperscript{11} had superior methodology when compared to any of the other trials considered for this review. The Engström et al\textsuperscript{10} study was a well-conducted study with a large sample size and complete follow-up. Approximately ninety percent (743/829) of patients attended 12-month follow-up accounting for 90% completion and only a 10%
loss to follow-up overall. Additionally, 728 of 829 patients returned no excess medication resulting in an 88% complete compliance rate. Furthermore, 96% of patients were more than 80% compliant with taking their medication and there were only 16 patients for which compliance data was missing. Sullivan et al\textsuperscript{11} was also a well-conducted study with a large sample size and complete follow-up. Ninety percent of the patients (496/551) randomized to receive treatment completed follow-up, accounting for only 10% lost to follow-up. A strength for both of these trials was that the authors of each study acknowledged and addressed their losses to follow-up. Another strength of both trials was that they both employed otolaryngologists to assess all participants being admitted into the trials to ensure that they didn’t meet any of the exclusion criteria. Additionally, the participants were each assessed for progression of recovery, using the HBS, by an experienced clinician that was blinded to the treatment group allocation to reduce the risk for bias.\textsuperscript{10,11}

To fully assess for bias, financial or otherwise, a GRADE\textsuperscript{9} review was conducted on each of these trials. The Health Technology Assessment (HTA)\textsuperscript{19}, who acts to bridge the gap between policy making and evidence by examining the safety, efficacy and cost effectiveness primarily through research and RCTs, was solely responsible for the funding of the Sullivan et al study.\textsuperscript{11,19} Engström et al\textsuperscript{10} was funded by numerous entities including GlaxoSmithKline (GSK) and Pfizer AB of Sweden. These pharmaceutical companies helped with the study design and also supplied the drugs for their study. Despite the obvious conflict of interest with their participation, the authors of this study openly admitted the involvement. Additionally, the authors reported that none of the funding sources, including GSK and Pfizer had a role in the data collection or its analysis.
and interpretation. In conclusion, due to the superb methodology of these trials, their completion of follow-up, and the consistency between their results, these trials should be considered of the highest quality.

CONCLUSION

Corticosteroids (CS) have proven to increase the rate and overall amount of recoveries in patients with Bell’s palsy when initiated within the first 72 hours of symptom onset. Despite the controversy surrounding a viral etiology, and the proposed benefit of using antivirals alone or in conjunction with CS, no quality RCTs have been published within the last five years to support that theory. Additionally, both Engström\textsuperscript{10} and Sullivan et al\textsuperscript{11} determined that the administration of antivirals actually slowed the rate of recovery when compared to treatment with CS or to no treatment at all. The benefits of treatment with CS result in a NNT of eight in order to produce one more complete recovery. The risks associated with a short course of CS treatment were reported to be very mild, and unless contraindicated for other medical conditions, the statistical significance of the evidence reported in these two trials should warrant the use of CS as the primary method of treatment. The overall combined quality of the studies reviewed is high based on the GRADE criteria with no downgrading required. A strong recommendation for the use of prednisone as the single pharmaceutical treatment can be made until further evidence reports a reliable difference in treatment outcome with antivirals or until a true etiology is established.
References


Table I: GRADE Quality of Assessment

<table>
<thead>
<tr>
<th>Study Detail</th>
<th>Downgrade Criteria</th>
<th>Quality</th>
<th>Comments</th>
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<tr>
<td>839</td>
<td>RCT</td>
<td>High</td>
<td>Allocation concealment and blinding maintained until trial completion with minimal loss to follow up.</td>
</tr>
<tr>
<td>551</td>
<td>RCT</td>
<td>High</td>
<td>Allocation concealment and blinding maintained until trial completion with minimal loss to follow up.</td>
</tr>
<tr>
<td>RCT</td>
<td>3 months</td>
<td>6 months</td>
<td>9 months</td>
</tr>
<tr>
<td>---------------------</td>
<td>----------</td>
<td>----------</td>
<td>----------</td>
</tr>
<tr>
<td><strong>Engström et al</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Double placebo (OO)</td>
<td>111/206</td>
<td>127/206</td>
<td>133/206</td>
</tr>
<tr>
<td></td>
<td>(54%)</td>
<td>(62%)</td>
<td>(65%)</td>
</tr>
<tr>
<td>Valaciclovir (VO)</td>
<td>113/207</td>
<td>120/207</td>
<td>133/207</td>
</tr>
<tr>
<td></td>
<td>(55%)</td>
<td>(58%)</td>
<td>(66%)</td>
</tr>
<tr>
<td>Valaciclovir +</td>
<td>134/206</td>
<td>149/206</td>
<td>164/206</td>
</tr>
<tr>
<td>Prednisolone (VP)</td>
<td>(65%)</td>
<td>(72%)</td>
<td>(80%)</td>
</tr>
<tr>
<td>Prednisolone (OP)</td>
<td>137/210</td>
<td>150/210</td>
<td>160/210</td>
</tr>
<tr>
<td></td>
<td>(65%)</td>
<td>(71%)</td>
<td>(76%)</td>
</tr>
<tr>
<td><strong>Sullivan et al</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Double placebo (OO)</td>
<td>77/119</td>
<td>104/122</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(65%)</td>
<td>(85%)</td>
<td></td>
</tr>
<tr>
<td>Aciclovir (AO)</td>
<td>75/120</td>
<td>96/123</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(63%)</td>
<td>(78%)</td>
<td></td>
</tr>
<tr>
<td>Aciclovir +</td>
<td>98/123</td>
<td>115/124</td>
<td></td>
</tr>
<tr>
<td>Prednisolone (AP)</td>
<td>(80%)</td>
<td>(93%)</td>
<td></td>
</tr>
<tr>
<td>Prednisolone (OP)</td>
<td>107/124</td>
<td>122/127</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(86%)</td>
<td>(96%)</td>
<td></td>
</tr>
</tbody>
</table>