HERU Briefing Paper

HEALTH ECONOMICS RESEARCH UNIT

Briefing paper **April 09**

ECONOMIC EVALUATION OF EARLY ADMINISTRATION OF PREDNISOLONE AND/OR ACYCLOVIR FOR THE TREATMENT OF BELL'S PALSY

Key Messages

1. Bell's palsy, which causes facial paralysis, affects 11-40 people per 100,000 per annum in the UK.
2. Standard treatment involves administration of prednisolone (steroids) and/or acyclovir (antivirals).
3. Early treatment with prednisolone significantly improves chances of complete recovery at 3 and 9 months and is likely to be considered cost-effective.
4. There is no evidence of a benefit of acyclovir and is highly unlikely to be considered cost-effective.

Background

Bell's palsy is an acute unilateral paralysis of the facial nerve.[1] Its cause is unknown but it affects 11-40 people per 100,000 in the population per annum, most commonly in the age group 30–45.[2] Although most recover, as many as 30% of people have a poor recovery with continuing facial disfigurement, psychological difficulties and sometimes facial pain.[2, 4] In the absence of an established aetiology, treatment continues to be based upon the established pathophysiology: swelling and entrapment of the nerve. Two Cochrane reviews have examined the effectiveness of oral prednisolone and acyclovir for the treatment of Bell's palsy [5, 6] and both report insufficient evidence on the effectiveness. Given this lack of evidence the UK NHS R&D Health Technology Assessment Programme commissioned a randomised controlled trial to determine the effectiveness and efficiency of prednisolone or Acyclovir, used separately or in combination in the early treatment of Bell's palsy. The aim of this briefing paper is to report evidence on the relative efficiency of these therapies.

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Methods

The primary study [7]

The primary study was a multi-centre, double-blind, placebo controlled, randomised, factorial trial involving patients with Bell's palsy who were recruited within 72 hours after onset of symptoms. Five hundred and fifty one patients were recruited from primary care settings and referred to 17 hospitals in Scotland between June 2004 and June 2006, where eligible patients were randomly assigned to receive 10 days of treatment of: 25mg twice daily with prednisolone (n=138), or 400mg five times daily with acyclovir (n=138), both agents (n=134), or placebo (n=141). Follow-up was 9 months. The primary outcome was complete recovery of facial function as rated on the House-Brackmann scale. Secondary outcomes included quality of life, appearance, pain, costs and relative efficiency. The study included adults of 16 years or older with unilateral facial weakness of no identifiable cause who presented to primary care or emergency department and could be referred to a collaborating otorhinolaryngologist within 72 hours of the onset of symptoms. The study concluded that early treatment with prednisolone significantly improves chances of complete recovery at 3 and 9 months and that there is no evidence of a benefit of acyclovir given alone or in combination with prednisolone.

Economic Evaluation

The economic evaluation adopted a modelling approach. Decision analytic models were constructed to compare the relative efficiency of the different treatments. An example of the model structure is shown in Figure 1. Within these models it is assumed that the different trial interventions affect the probability of being cured or not cured and the consequences thereafter are assumed to be independent of the assigned therapy.

Parameter estimates for probabilities, costs and effectiveness required to populate the model were developed from trial data. These data related to risk of being cured or not cured at different time points, health services resource use and costs and health state utilities. The costs estimates used in the model were based on the cost of the initial treatments and follow-up costs. The latter included the use of resources in primary and secondary care, and the subsequent use of other medications. All these resources were costed using readily available unit costs.

Figure 1 Decision tree model for early treatment for Bells palsy: Prednisolone alone vs. Acyclovir alone vs. prednisolone + Acyclovir vs. no treatment (placebo)

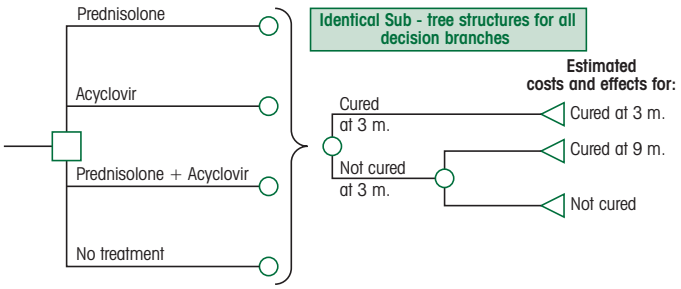


Figure 1a. The four decision branches reflect the four groups provided by the 2 x 2 factorial trial design.

The main comparison compared all four randomised arms (e.g. four arms model). Secondary analyses comparing prednisolone vs. no prednisolone and acyclovir vs. no acyclovir were also conducted. For all analyses cumulative mean costs were estimated for the nine months follow-up period of the trial. All costs were expressed in 2006/07 pounds Sterling. The perspective of the analyses was that of the National Health Service. Effectiveness was measured in terms of number of cases cured (e.g. House-Brackmann score = 1), and mean QALYs for the nine month time horizon. As the time horizon for the analyses was less than a year, neither cost nor effectiveness outcomes were discounted.

Sensitivity analysis

Deterministic and probabilistic sensitivity analyses were conducted. The latter involved attaching probability distributions to the model parameters and conducting Monte Carlo simulations (MCS). One thousand iterations were obtained for each MCS conducted. These results were used to produce cost-effectiveness scatterplots and cost-effectiveness acceptability curves (CEACs) from which the likelihood of an intervention being considered cost-effective for society's willingness to pay at threshold values of £10,000, £20,000, £30,000 and £50,000 were calculated.

Table 1 Cost-effectiveness results

Treatment	Cost (£)	Cured cases* at 9 months (%)	ICER**	QALYs	ICER***	Probability that intervention is cost-effective for different threshold values for society's willingness to pay for a QALY (%)			
						£10,000	£20,000	£30,000	£50,000
Four arms model									
Prednisolone only	182	86%		0.719		79%	77%	77%	76%
Acyclovir + Prednisolone	198	78%	Dominated	0.718	Dominated	0%	0%	0%	0%
No treatment	205	78%	Dominated	0.717	Dominated	13%	10%	7%	5%
Acyclovir only	220	78%	Dominated	0.716	Dominated	8%	13%	16%	19%
Prednisolone vs. No prednisolone model									
Prednisolone	232	94%		0.718		79%	78%	77%	76%
No Prednisolone	248	82%	Dominated	0.717	Dominated	21%	22%	23%	24%
Acyclovir vs. No Acyclovir model									
No Acyclovir	235	91%		0.718		91%	85%	82%	79%
Acyclovir	247	85%	Dominated	0.717	Dominated	9%	15%	18%	21%

* Cured cases defined as HB score = 1; ** Incremental cost effectiveness ratio using % cured cases; ***Incremental cost effectiveness ratio using QALYs

Results

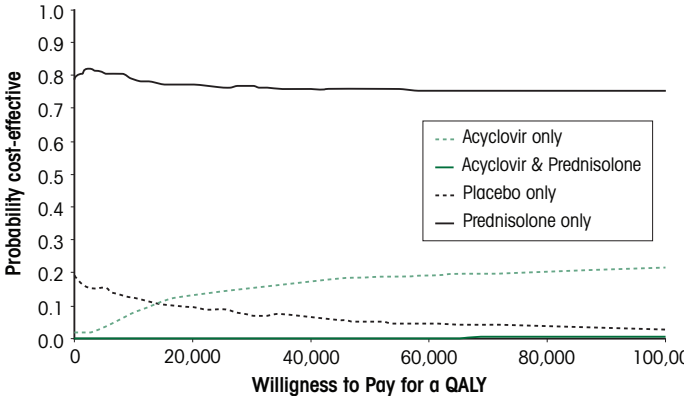
Comparison of all four randomised groups

On average, prednisolone only is the least costly and most effective of the four alternative interventions (Table 1). Furthermore, it has approximately an 80% chance of being considered cost-effective compared with the other treatments (Figure 2 & Table 1).

Prednisolone vs. no prednisolone model

When the proportion of cases cured (Cost-effectiveness analysis) or QALYs (Cost-utility analysis) are used as the measure of effectiveness prednisolone has a lower mean cost and is more effective than the no prednisolone alternative (Table 1). There is almost a 60% chance of prednisolone being less costly and more effective than no prednisolone.

Figure 2 Cost-effectiveness acceptability curves. Four arms model.



These CEACs indicate that collectively the other interventions have only a 20% chance of being considered cost-effective.

Acyclovir vs. no acyclovir model

Table 1 shows the incremental cost per case cured and per QALY for the comparison of acyclovir with no acyclovir. The no acyclovir alternative has on average lower costs and a higher proportion of individuals recovered. Therefore, on average no acyclovir dominates acyclovir treatment. The probabilistic analysis reinforces this finding (Table 1).

Sensitivity Analysis

A wide range of sensitivity analyses were conducted. Results were only sensitive to the probability of being cured at three months within the acyclovir vs. no acyclovir model. When the difference in the probability of being cured at three months between the acyclovir arm and no acyclovir arm was 3.3% (the upper limit of the 95%CI), the ICER was approximately £9,600. Therefore, the confidence interval surrounding the difference in cure rates between the acyclovir arm and the no acyclovir arm is sufficiently wide to contain clinically and economically important differences.

Conclusions

Based on the data available it appears that treatment of Bell's palsy with prednisolone is likely to be cost-effective. Treatment with acyclovir is highly unlikely to be cost-effective. Given the limited data available on costs and utilities further data would be useful to confirm findings. Similarly even though it is unlikely to change conclusion further data on costs and outcomes in the longer term (i.e. for a follow-up greater than nine months) would also serve to confirm the findings of the study.

For further details about this study see:

RA Hernández, F Sullivan, P Donnan, I Swan, L Vale, for the BELLS Trial Group. "Economic evaluation of early administration of prednisolone and/or aciclovir for the treatment of Bell's palsy". Family Practice 2009 26(2):137-144; doi:10.1093/fampra/cmn107

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For further details about HERU:

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