Antiviral agents convey added benefit over steroids alone in Bell's palsy; decompression should be considered in patients who are not recovering

J A DE RU¹, P A BRENNAN², E MARTENS³

¹Department of Otolaryngology – Head and Neck Surgery, Central Military Hospital, Utrecht, the Netherlands, ²Department of Oral and Maxillofacial Surgery, University of Portsmouth, UK, and ³Statisticor, Rotterdam, the Netherlands

Abstract

Background: The management of Bell's palsy has been the subject of much debate, with corticosteroids being the preferred medication. However, evidence also supports the use of antiviral drugs for severe cases and even decompression surgery in patients who, despite medical treatment, are not recovering.

Method: A literature review was conducted on the management of Bell's palsy.

Results: This paper describes the background, statistical evidence, study results and pathophysiological theories that support more aggressive treatment for patients with severe palsy and those who have inadequate recovery.

Conclusion: Combination therapy including antiviral medication significantly improves outcomes in patients with severe Bell's palsy. Decompression should be considered in patients who have not recovered with drug treatment.

Key words: Antiviral Agents; Facial Nerve; Treatment Outcome; Drug Therapy; Human

Introduction

Disfiguring facial weakness, synkinesis, higher depression rates and lower self-esteem are some of the dramatic consequences of a non-completely recovered facial palsy.^{1,2} There is probably no benign ailment that causes more physical and emotional suffering.^{3,4} Therefore, everything should be done to promote recovery. Patients should be counselled and not forced into either therapy or 'watchful waiting'.⁵ Contraindications to treatment may in individual cases outweigh the potential benefits.

Decision makers need to assess and appraise all levels of evidence; the strengths and weaknesses of each need to be understood if reasonable and reliable conclusions are to be drawn.⁶ Much has been written about Bell's palsy in cohort and case studies. Every aspect of Bell's palsy has been the subject of a continuing dispute in the literature.^{7,8} Therefore, anatomy, relevant pathophysiology, natural course of the disease, relevant pharmacotherapy or surgical procedures, success and failure rates, and possible side effects of therapy, need to be reconsidered.

Pathophysiology

The term Bell's palsy is reserved for those cases in which there is no obvious cause (such as injury,

Accepted for publication 9 December 2014

infection or tumour), or in which there is nothing to suggest a more centrally placed lesion.⁹

Although it refers to a supposedly 'idiopathic' lesion, many theories have been developed. Bell's palsy has been attributed to cold exposure, chill or rheumatism.^{10–12} Nowadays, most literature suggests that Bell's palsy is caused by infection with the herpes simplex virus^{13–20} or varicella zoster virus.^{21–25} If this is true, the typical vesicles of the zoster are not present.

The inflammatory reaction against these viruses causes swelling of the facial nerve, which consequently becomes entrapped within its narrow bony canal.^{7,26} Many authors have described the swollen nerve.^{21,27–30} In the end, this theory might concur with a theory of ischaemic aetiology.^{31,32} In cases of longstanding paralysis, the facial nerve was reduced to a shrunken strand.^{33,34} Contrast enhancement of the facial nerve seen on magnetic resonance imaging, and the possible narrower canal on computed tomography scanning that patients with repeated palsies may have, provides circumstantial evidence that might support the theory.^{35,36}

Anatomy

The facial nerve runs through the temporal bone. The narrowest portion is found at the entrance. A tight

arachnoid band is found adherent to the nerve in this region, which contributes to the constriction.^{8,37}

Natural course

About 70 per cent of patients recover completely without any therapy,^{38,39} and 15 per cent more might still have a 'good' recovery.^{40,41}

Patients with an initial severe palsy, the elderly and patients with diabetes have a higher chance of non-recovery or complications.^{10,37,38,42–46} There is a less than 50 per cent chance of a spontaneous, complete recovery in those aged over 60 years.

Herpes zoster oticus is associated with a worse outcome than Bell's palsy; pain might be suggestive of a zoster sine herpete.^{2,37,47} The prognosis has been found to be worse when the onset of the palsy was accompanied by marked pain and loss of taste than when the onset was symptomless.^{9,27,41,47–49}

Because of the high spontaneous recovery rate, it is interesting to examine cases of non-recovery and failure rates. How well does a specific treatment prevent a disfiguring result?

Treatment

The main priority is to reduce nerve swelling. Corticosteroids are the first choice of treatment. Decompression gives more space to the swollen nerve. Given the probable viral pathogenesis, antiviral drugs could be useful.

Function assessment, grading and success rates

The use of different grading scales for the assessment of dynamic facial nerve function makes comparison regarding Bell's palsy therapy difficult.⁵⁰ Of note, the commonly used House–Brackmann grading scale was mainly based on patients diagnosed with cerebellopontine angle pathology. Is facial nerve function following such pathology comparable to Bell's palsy in terms of assessment?^{51–53} A scale with more possibilities for differentiation and one that integrates subjective scoring by the patient – the movement, rest, secondary defects, and subjective scoring grading scale ('MoReSS'),⁵⁴ for example – might be advisable for future studies.

Current treatment

Based on the 'probable pathophysiology', on the best available research and on our clinical expertise, the main points in Bell's palsy treatment are as follows. Firstly, treatment should start as early as possible. Secondly, treatment with steroids is indicated in most patients; the cost is low and the side effects are minor. Thirdly, one should identify the patients with a likelihood of non-recovery (House–Brackmann grades IV, V and VI), and treat them with a combination of steroids and antivirals. Fourthly, if complete recovery is not likely to be achieved, as can be assessed with electrophysiological tests (e.g. electroneurography (ENoG) and electromyography (EMG)), the patients should be referred (if that is their wish) to the 'best' surgeons for decompression surgery as soon as possible.^{8,10,25,45,50,55-63}

Over the last 15 years, patients in our clinics with moderate and severe palsy (House–Brackmann grades IV, V and VI) have been treated with corticosteroids and antivirals. Prednisone 1 mg/kg or 80 mg for one week is prescribed; we want a high dose for prompt relief of the nerve. In severe cases, valaciclovir 1000 mg three times a day for one week is prescribed.

This regime has been maintained because of the good results. With this medication scheme, indications for decompression surgery to treat Bell's palsy were rare. Surgical intervention can be helpful in those cases that do not respond to medical measures. The results of our clinical practice are in line with those of Yanagihara *et al.*,³¹ which showed that the number of patients undergoing a decompression operation was in decline.

Treatment revisited

What is the evidence for our protocol? This issue is important because on average 85 per cent of patients have a 'rather good' recovery without therapy. Furthermore, this percentage might be higher when corticosteroids are prescribed, and it will be difficult to prove any added value of antivirals or decompression surgery as there will be a ceiling effect.^{10,64,65}

Our questions are as follows. Firstly, does antiviral medication, combined with steroids, improve the recovery of patients with severe palsy? Secondly, does decompression surgery ameliorate the outcome in severe cases that do not show improvement with medical therapy?

This paper is not just another new systematic review. Reviews on Bell's palsy have been published on many occasions. In those, the same articles seem to be reviewed over and over again. In our opinion, another meta-analysis with no new results would not be useful if any outcome was measured in the traditional way.⁶⁶ Therefore, we have used the data and reference lists of previous systematic reviews, but we focus on a different interpretation of the current literature.

Antiviral medication

Over the last 75 years, a viral cause for Bell's palsy has been suggested. Therefore, antiviral treatment is likely to benefit patients, providing that treatment is started early and that the severe cases are given a high enough dose to cover an infection with varicella as well.^{15,22–24,66}

Hato *et al.*²⁵ has previously described the difference in recovery in severely affected patients treated with combination therapy versus monotherapy steroid treatment in a retrospective study conducted in 2003. If the data from the paper by Quant *et al.*⁶⁷ are updated, the results of combination therapy in prospective trials are likely to be significantly better than those for monotherapy, with

an odds ratio of 1.712 (95 per cent confidence interval (CI) = 1.172-2.501) (Table I).^{19,24,43,63,68-71}

Table II shows that the pooled odds ratio for patients with initial severe palsy recovering to at least House–Brackmann grade II is 1.985 (95 per cent CI = 1.334-2.952).^{9,24,43,63,68–73}

Only one outlier exists, namely the study by Sullivan *et al.*⁶⁸ Criticism of that particular study has already been described extensively.⁷⁴

In cases where the ENoG responsive level was less than 10 per cent compared to the contralateral side, indicating that patients had severe palsy, the recovery rate for combination therapy was 63.6 per cent (7 out of 11 patients recovered), and for steroids only it was 36.4 per cent (4 out of 11 patients recovered).⁷¹ Twenty-eight per cent of patients on combination therapy showed recovery of four House–Brackmann points or more, versus only 11.9 per cent of patients on corticosteroids.⁷⁰

As well as having a higher percentage of full recovery, combination therapy results in significantly fewer sequelae and fewer patients with an unsatisfactory recovery (worse than House–Brackmann grade III) compared with those treated with steroids only (Table III).^{25,63,70,71,75} In the studies by Minnerop *et al.*⁷⁰ and Lee *et al.*,⁷¹ the patients who did not recover to House–Brackmann grade IV were all in the monotherapy group. Synkinesis more frequently occurs following therapy with steroids only than following combination therapy.^{73,76}

In line with the consistency criterion for causation, we could ask 'has the outcome been repeatedly observed by different persons, in different places, circumstances and times?'⁷⁷ With combination therapy, broadly the same answer has been reached in quite a variety of situations. Hence, we can justifiably infer that the effect is not due to some constant error.

| TABLE I PROSPECTIVE TRIALS COMPARING COMBINATION THERAPY WITH STEROIDS ONLY* | | | | |
|--|----------|------------------------|--|--|
| Study | Succ | Successes/failures (n) | | |
| | Steroids | Combination therapy | | |
| Yeo et al. ¹⁹ | 40/7 | 41/3 | | |
| Adour <i>et al.</i> ⁶³ | 35/11 | 49/4 | | |
| Hato <i>et al.</i> ²⁴ | 96/11 | 110/4 | | |
| Sullivan et al.68 | 122/5 | 115/9 | | |
| Engström <i>et al.</i> ⁶⁹ | 160/26 | 164/16 | | |
| Minnerop et al. ⁷⁰ | 53/14 | 42/8 | | |
| Lee et $a\hat{l}$. ⁷¹ | 71/36 | 82/17 | | |
| Ryu <i>et al.</i> ⁴³ | 74/18 | 91/19 | | |

Pooled values: I² index = 27.4 per cent; *p*-value Q = 0.210; metaanalysis random-effects model odds ratio = 1.712 (95 per cent confidence interval (CI) = 1.172–2.501). 'Odd ones out' principle values (deleting the studies with the most negative and most positive results, i.e. deleting Sullivan *et al.*⁶⁸ and Adour *et al.*⁶³): I² index = 0.0 per cent; *p*-value Q = 0.606; meta-analysis random-effects model odds ratio = 1.787 (95 per cent CI = 1.277–2.500). *Based on the meta-analysis by Quant *et al.*⁶⁷ (and their correction); the data of Ryu *et al.*⁴³ and Lee *et al.*⁷¹ have been added.

| TABLE II | | | | |
|---|--|--|--|--|
| PROSPECTIVE TRIALS COMPARING COMBINATION | | | | |
| THERAPY WITH STEROIDS ONLY IN PATIENTS WITH | | | | |
| SEVERE PALSY* | | | | |

| Study | Succ | Successes/failures (n) | | |
|--|----------|------------------------|--|--|
| | Steroids | Combination therapy | | |
| Yeo et al. ¹⁹ | 23/7 | 23/2 | | |
| Adour et al. ⁶³ | 5/5 | 7/3 | | |
| Hato et al. ²⁴ | 71/11 | 88/4 | | |
| Sullivan et al. ⁶⁸ | 19/2 | 23/5 | | |
| Engström et al. ⁶⁹ | 19/19 | 20/19 | | |
| Minnerop ₇ et al. ⁷⁰ | 8/9 | 13/5 | | |
| Lee <i>et al.</i> ⁷¹ | 71/36 | 82/17 | | |
| Ryu <i>et al.</i> ⁴³ | 15/9 | 15/5 | | |

Pooled values related to the likelihood of 'good' recovery: $I^2 = 0.0$ per cent; *p*-value Q = 0.493; meta-analysis randomeffects model odds ratio = 1.985 (95 per cent confidence interval (CI) = 1.334–2.952). 'Odd ones out' principle values (deleting the studies with the most negative and most positive results, i.e. deleting Sullivan *et al.*⁶⁸ and Yeo *et al.*¹⁹): $I^2 = 0.0$ per cent; *p*-value Q = 0.636; meta-analysis random-effects model odds ratio = 2.078 (95 per cent CI = 1.365–3.164). Based on a previous article;⁷² the data of Ryu *et al.*⁴³ and Lee *et al.*⁷¹ have been added. The Engström *et al.*⁶⁹ findings have been updated with data from Axelsson *et al.*⁷³

Considering the above, we think that antiviral medication can improve recovery in patients with severe Bell's palsy.

Davenport *et al.*⁷⁸ stated that the Scottish Bell's palsy study was performed because of a concern regarding the longstanding acceptance of steroid use, and the increasing acceptance of acyclovir use, despite insufficient evidence. The authors concluded that 'steroids are now evidence based, but we have shown acyclovir to be ineffective'. They urged colleagues to consider further trials rather than propagate the use of an unproven treatment.⁷⁸

In our opinion, it should have been clear in 2000 that corticosteroids ameliorate the outcome. However, because of doubts regarding the longstanding acceptance of steroid use, two double-blind, randomised trials were performed at this point.^{68,69} In these trials (n = 416 and n = 245), patients were randomised to receive no steroids. Of these, about 66 more (10 per cent – a conservative low estimate) would have recovered with steroids. In our opinion, this indicates a lot of

| TABLE III NUMBERS OF PATIENTS WITH POOR RECOVERY, IN PROSPECTIVE AND RETROSPECTIVE STUDIES | | | | | |
|--|---------------|--------------------|------------------------|--|--|
| Study | Design | Failures/total (n) | | | |
| | | Steroids | Combination therapy | | |
| Adour <i>et al</i> . ⁶³ | Prospective | 11/46 | 4/53 | | |
| Minnerop et al. ⁷⁰ | Prospective | 3/17 | 0/18 | | |
| Lee et al. ⁷¹ | Prospective | 10/107 | 5/99 | | |
| Hato et al. ²⁵ | Retrospective | 44/386 | 4/94 | | |

Retrospective 22/248

11/248

Ahangar et al.75

missed chances for recovery. We urge colleagues not to ignore history once again when it comes to the use of antivirals.

Combination therapy meta-analyses

Meta-analyses have generally concluded that antiviral therapy has no significant effect. However, if antiviral drugs have little added value when all patients are considered without differentiation, this does not necessarily mean that specific groups might not benefit from their prescription.

There were a number of points raised in the recent meta-analyses (Table IV); these are described briefly below.^{62,67,79–82}

Firstly, in the conclusion of the abstract, the Cochrane review does not refer to combination therapy, but only to antivirals versus placebo or corticosteroids.⁷⁹ This really is not the issue anymore.

Secondly, the Cochrane review ignores the fact that its own results indicate there was 'a significant but slight reduction in the rate of incomplete recovery, favouring the combination of antivirals and corticosteroids over corticosteroids alone; RR [relative risk] 0.64 (0.50 to 0.82)'.⁷⁹ Thus, only one study reports negative findings; yet still the Cochrane review concludes that antivirals, though in contradiction with their own calculations, are not effective. Does this reflect a bias given the overlap between the authors of the only study with negative findings and the Cochrane review authors?

Thirdly, the Cochrane review concludes that 'there was no significant difference in long-term sequelae comparing antivirals + corticosteroids with corticosteroids alone, RR [relative risk] = 0.39, (CI 95% = 0.14, 1.07)'.⁷⁹ This result might be clinically very relevant.

Fourthly, the study by Goudakos and Markou includes two trials that are not accessible to us, one of which, according to the title, appears not to concern Bell's palsy.⁸¹

Fifthly, an important fact in the meta-analysis by Quant *et al.*⁶⁷ is that the figures from Engström's trial have been reversed. If the analysis was performed with the correct figures, the odds ratio becomes 1.72

(95 per cent CI = 1.02-2.88).⁶⁴ The correct difference in the proportion of recovered patients amongst those who received steroids alone and those who received combination therapy now becomes 92.2 per cent minus 87.2 per cent. This 5 per cent is a clinically very relevant effect. Another effect of using the correct figures is that the heterogeneity index drops from 47.1 to 32.4 per cent, making a fixed-effects model instead of a random-effects model a serious option, resulting in a smaller confidence interval odds ratio of 1.69 (95 per cent CI = 1.12-2.53).

Sixthly, there are two meta-analyses that include trials in their funnel plot by means of a 'trim and fill' algorithm employed to correct for possible publication bias. Although this method can be valuable, it relies heavily on the assumption that unpublished, extremely negative studies exist. In fact, this is a very unlikely assumption when it concerns studies in which antivirals are used to treat a viral cause.^{67,82}

Nevertheless, 'extreme' effects might be influencing outcomes. Therefore, we suggest using the 'odd ones out' principle as a sensitivity analysis, leaving out the studies with the most negative result (Sullivan et al.⁶⁸) and the most positive result (Adour et al.⁶³ in Table I and Yeo et al.¹⁹ in Table II). This method leads to a dramatic drop of the heterogeneity index in both tables ($I^2 = 0.0$ per cent). This is mainly because of the removal of the Sullivan et al.⁶⁸ trial, which reported results that do not concur at all with our clinical expectations (i.e. that patients with severe palsy using a combination of antivirals and corticosteroids recover worse than those using corticosteroids only). In Table I, the odds ratio becomes 1.787 (95 per cent CI = 1.277 - 2.500) and in Table II it becomes 2.078 (95 per cent CI = 1.365 - 3.164). Both results indicate a larger effect of using combination therapy.

The real outlier would seem to be the Sullivan *et al.*⁶⁸ study. The authors suggested that the detrimental effect on recovery of antiviral medication could be due to a Jarisch–Herxheimer reaction.⁷⁹ In our clinical experience, we have never seen this reaction. Moreover, no other study has reported such an adverse effect.

| TABLE IV OVERVIEW OF CONCLUSIONS MADE IN META-ANALYSIS STUDIES | | | | |
|---|------|---|--|--|
| Study | Year | Conclusion | | |
| Cochrane review ⁷⁹ | 2009 | High quality evidence showed no significant benefit from anti-herpes simplex antivirals compared with placebo in producing complete recovery; moderate quality evidence showed that antivirals were significantly less likely than corticosteroids to produce complete recovery | | |
| De Almeida <i>et al</i> . ⁸⁰ | 2009 | Corticosteroids associated with reduced risk of unsatisfactory recovery; antiviral agents, administered with corticosteroids, may be associated with additional benefit | | |
| Goudakos & Markou ⁸¹ | 2009 | Addition of an antiviral agent to corticosteroids not associated with an increase in complete recovery of facial motor function | | |
| Numthavaj <i>et al</i> . ⁸² | 2011 | Treatment with antivirals plus corticosteroids may lead to slightly higher recovery rates compared with prednisone alone, but findings did not quite reach statistical significance | | |
| Quant et al. ⁶⁷ | 2009 | Antivirals did not provide an added benefit in achieving at least partial facial muscle recovery compared with steroids alone; hence, study does not support routine use of antivirals. Benefit of antiviral therapy with steroids for patients with severe facial muscle paralysis remains unclear | | |
| Thaera et al. ⁶² | 2010 | Corticosteroids effectively reduce risk of an unfavourable outcome; antiviral agents, administered with corticosteroids, may result in additional benefit | | |

What is the harm of adding antiviral therapy? Theoretically, antivirals can cause gastroesophageal complaints, renal failure and headache; however, in the studies analysed, the side effects did not differ significantly amongst study groups. Famciclovir is sometimes recommended over acyclovir because of an easier dosage schedule and fewer gastrointestinal side effects.⁸³

The effect of non-complete recovery is lifelong morbidity. The price of valaciclovir or Famvir[™] to prevent sequelae is about €150.

Thus, the answer to the first question, does antiviral medication combined with steroids improve the recovery of patients with severe palsy, is affirmative. Antivirals should be given to patients with (moderate) severe palsy.

Decompression surgery

Does decompression surgery ameliorate the outcome in severe cases of Bell's palsy that do not show improvement with medical therapy? The swollen nerve can be given more space with decompression and therefore this treatment fits well with the pathophysiology.⁸ The earlier it is done, the less danger there will be of permanent impairment.^{21,29,46,84} Theoretically, the only hope of restoring bilaterally co-ordinated emotional expression after paralysis of the facial nerve lies in restoration of the functional integrity of that nerve.¹¹

All agree that decompression is not the mainstay of treatment for Bell's palsy. It should be preserved for special cases; it is more relevant in patients who are less likely to recover spontaneously.^{8,9,85} Decompression is indicated for a medically treated patient with no signs of recovery of a total paralysis, and ENoG findings showing more than 95 per cent loss of activity, and without voluntary movement potentials on EMG.^{8,27,86–88} From reports by McNeill,⁷ Gantz *et al.*,⁸ Yanagihara *et al.*⁸⁹ and Alford *et al.*,⁹⁰ it is clear that the timing and extent of decompression are of utmost importance for the recovery and development of sequelae.

| TABLE V OUTCOME OF SURGERY VERSUS NO SURGERY IN | | | | | |
|--|-------------------|---------------|-------------------|---------------|--|
| PATIENTS WITH SEVERE PALSY OR TOTAL PARALYSIS | | | | | |
| Study | Good recovery (n) | | Poor recovery (n) | | |
| | Surgery | No surgery | Surgery | No surgery | |
| Fish & Esslen ⁹⁷ | 79%* | 64%* | _ | _ | |
| McNeill ⁷ | 10/19 | 8/11 | 9/19 | 3/11 | |
| Giancarlo & | 12/19 | 0/8 | 0/19 | 6/8 | |
| Mattucci ²⁷ | | | | | |
| May et al. ⁹⁸ | 5/25 | 3/13 | 20/25 | 10/13 | |
| Brown ⁵⁵ | 25/41 | 24/51 | 6/41 | 11/51 | |
| Gantz <i>et al.</i> ⁸ | | | | | |
| – Iowa | 18/19 | 4/11 | _ | _ | |
| Michigan | 7/9 | 11/27 | 1/9 | 4/27 | |
| Yanagihara <i>et al</i> . ⁸⁶ | 41/58 | 26/43 | 0/58 | 6/43 | |
| | | | | | |

*Numbers not available

Thus, the very nature and duration of the lesion for which decompression is justified make complete recovery unlikely. Yanagihara *et al.*⁸⁹ and others have reported an interesting and significant feature: in some patients who have undergone decompression, there is some return of movement within a week of the operation.⁹ This is a striking effect, and, as described by Glaziou *et al.*,⁹¹ is strongly suggestive of a genuine treatment consequence.

Tumarkin⁴¹ reported that in the 20 per cent of patients who are not likely to recover spontaneously, the evidence indicates a more central involvement (herpes oticus) extending to the genu. Gantz *et al.*⁸ stated correctly that the findings of previous studies evaluating the efficacy of surgical decompression in Bell's palsy that did not include decompression of the nerve medial to the generalised to support the notion that surgical decompression is not effective.⁵⁰

If a surgical intervention is established as a useful treatment option based on the good results shown by some surgeons, it does not necessarily mean that any surgeon should perform this treatment. Rather, it means that special cases are better off in special hands.⁵⁰ Whereas the effects of treatment with medication are probably generalisable to a certain extent, surgical results are – because of individual skills and the rarity of cases needing surgery – definitely not. Hence, to quote Sir Terence Cawthorne, who, when asked – discussing the vestibulocochlear nerve – to state which datum would most strongly influence his decision whether to proceed to an operation or not, answered: 'the name of the surgeon'.⁸⁴

Decompression surgery is associated with a broad range of possible collateral damage, varying from hearing loss to intracranial complications. Nevertheless, as concluded by Morris²¹ (who admittedly performed only transmastoid surgery), 'there is no reason why, if decompression is carried out carefully, there should be any injury to the nerve at all, and the hearing will not be interfered with'. Gantz *et al.*⁸ and Yanagihara *et al.*⁸⁶ have reported a low incidence of collateral damage, even when more extensive types of surgery were undertaken.

Sinha *et al.*⁹² concluded that, of the patients who showed greater than 90 per cent of compound action potential reduction in the affected side, almost half (47 per cent) had normal to near normal recovery, indicating no need for therapy. However, if we reverse our thinking, more than half will end up with sequelae. In addition, other studies have shown no benefit and other authors were sceptical.^{93,94}

Reports published in the last five years show good outcomes after decompression surgery in the patient group with a poor prognosis.^{95,96}

With regard to question two, does decompression surgery ameliorate the outcome in severe cases that do not show improvement with medical therapy, we conclude that decompression surgery, performed for the right indication, by the most skilful surgeons, might be effective in preventing sequelae (Table V).^{7,8,27,55,86,97,98}

Conclusion

In view of these results, the probable pathogenesis and, in particular, the severe morbidity of permanent sequelae, antivirals can be crucial. They should be prescribed in combination with steroids in the event of severe deficit and for elderly patients. In cases of complete paralysis with no sign of recovery, and electrophysiological confirmation of a high chance of non-recovery, decompression might be indicated. Patients should be informed about the possibility of this treatment option.

References

- 1 Walker DT, Hallam MJ, Ni Mhurchadha S, McCabe P, Nduka C. The psychosocial impact of facial palsy: our experience in one hundred and twenty six patients. Clin Otolaryngol 2012; 37:474-7
- Gilden DH. Bell's palsy. N Engl J Med 2004;351:1323-31
- 3 Pulec JL. Acute facial paralysis. In: Pensak ML. Controversies in Otolaryngology. New York: Thieme Medical Publishers, 2001;223-6
- 4 Pulec JL. Early decompression of the facial nerve in Bell's palsy. Ann Otol Rhinol Laryngol 1981;90(6 Pt 1):570-7
- 5 Mulley AG, Trimble C, Elwyn G. Stop the silent misdiagnosis: patients' preferences matter. BMJ 2012;345:ee6572
- 6 Rawlins M. De testimonio: on the evidence for decisions about the use of therapeutic interventions. Lancet 2008;372:2152-61
- 7 McNeill R. Facial nerve decompression. J Laryngol Otol 1974; 88:445-55
- 8 Gantz B, Rubinstein JT, Gidley P, Woodworth GG. Surgical management of Bell's palsy. Laryngoscope 1999;109:1177-88
- 9 Cawthorne T. The pathology and surgical treatment of Bell's palsy. Proc R Soc Med 1951;44:565-72
- 10 Aminoff MJ. Bell's palsy and its treatment. Postgrad Med J 1973:49:46-51
- 11 Ney KW. Facial paralysis and the surgical repair of the facial nerve. Laryngoscope 1922;5:327-47
- 12 Van der Graaf RC, Ijpma FFA, Nicolai JP, Werker PMN. Bell's palsy before Bell: Evert Jan Thomassen à Thuessink and idiopathic peripheral facial paralysis. J Laryngol Otol 2009;123: 1193-8
- 13 Sade J. Pathology of Bell's palsy. Arch Otolaryngol 1972;95: 406 - 13
- 14 McCormick DP. Herpes-simplex virus as cause of Bell's palsy. Lancet 1972;1:937-9
- 15 Murakami S, Mizobuchi M, Nakashiro Y, Doi T, Hato N, Yanagihara N. Bell palsy and herpes simplex virus: identification of viral DNA in endoneurial fluid and muscle. Ann Intern Med 1996;124:27-30
- 16 Holland NJ, Weiner GM. Recent developments in Bell's palsy. BMJ 2004;329:553-7
- 17 Alberton DL, Zed PJ. Bell's palsy: a review of treatment using antiviral agents. Ann Pharmacother 2006;40:1838-42
- 18 Finsterer J. Management of peripheral facial nerve palsy. Eur Arch Otorhinolaryngol 2008;265:743-52
- 19 Yeo SG, Lee YC, Park DC, Cha CI. Acyclovir plus steroid vs steroid alone in the treatment of Bell's palsy. Am J Otolaryngol 2008;29:163-6
- 20 Kennedy PG. Herpes simplex virus type 1 and Bell's palsy a current assessment in the controversy. J Neurovirol 2010;161: 1 - 5
- 21 Morris WM. Surgical treatment of Bell's palsy. Lancet 1938;19: 429 - 31
- 22 Morgan M, Moffat M, Ritchie L, Collacott I, Brown T. Is Bell's palsy a reactivation of varicella zoster virus? J Infect 1995;30: 29-36
- 23 Hato N, Murakami S, Gyo K. Steroid and antiviral treatment for Bell's palsy. Lancet 2008;37:1818-20
- 24 Hato N, Yamada H, Kohno H, Matsumoto S, Honda N, Gyo K et al. Valacyclovir and prednisolone treatment for Bell's palsy: a

- 25 Hato N, Matsumoto S, Kisaki H, Takahashi H, Wakisaka H, Honda N et al. Efficacy of early treatment of Bell's palsy with oral acyclovir and prednisolone. Otol Neurotol 2003;24: 948-51
- 26 Duel AB. The operative treatment of facial palsy. Br Med J 1934;2:1027-32
- 27 Giancarlo HR, Mattucci KF. Facial palsy; facial nerve decompression. Arch Otolaryngol 1970;91:30-6
- 28 Kettel K. Pathology and surgery of Bell's palsy. Laryngoscope 1963;73:837-49
- 29 Jongkees LBW. On peripheral facial nerve paralysis. Arch Otolaryngol 1972;95:317–23
- 30 Hagino K, Tsunoda A, Tsunoda R, Kishimoto S. Measurement of the facial nerve calibre in facial palsy: implications for facial nerve decompression. Otol Neurotol 2011;32:686-9
- 31 Yanagihara N, Honda N, Hato N, Murakami S. Edematous swelling of the facial nerve in Bell's palsy. Acta Otolaryngol 2000; 120:667-71
- 32 Taverner D. Bell's palsy: a clinical and electromyographic study. Brain 1955;78:209-10
- 33 McGovern FH, Hansel JS. Decompression of the facial nerve in experimental Bell's palsy. Laryngoscope 1961;71:1090-104
- 34 McGovern FH. A review of the experimental aspects of Bell's palsy. Laryngoscope 1968;78:324-34
- 35 Millen SJ, Daniels D, Meyer G. Gadolinium-enhanced magnetic resonance imaging in facial nerve lesions. Otolaryngol Head Neck Surg 1990;102:26–33
- 36 Murai A, Kariya S, Tamura K, Doi A, Kozakura K, Okano M et al. The facial nerve canal in patients with Bell's palsy: an investigation by high-resolution computed tomography with multiplanar reconstruction. Eur Arch Otorhinolaryngol 2013; 270:2035-8
- 37 Ge XX, Spector GJ. Labyrinthine segment and geniculate ganglion of facial nerve in fetal and adult human temporal bones. Ann Otol Rhinol Laryngol Suppl 1981;90:1–12
- 38 Peitersen E. Bell's palsy: the spontaneous course of 2,500 peripheral facial nerve palsies of different etiologies. Acta Otolaryngol Suppl 2002;(549):4-30
- 39 Mathews WB. Prognosis in Bell's palsy. Br Med J 1961;2: 215 - 17
- 40 Pickerill HP, Pickerill CM. Early treatment of Bell's palsy. Br Med J 1945;2:457-9
- 41 Tumarkin IA. Some aspects of the problem of facial paralysis. Proc R Soc Med 1936;29:1685-91
- 42 Lejeune D, Bernat I, Vitte E, Lamas G, Willer JC, Soudant J et al. Treatment of Bell's palsy with acyclovir and methylprednisolone [in French]. Ann Otolaryngol Chir Cervicofac 2002; 119:209-15
- 43 Ryu EW, Lee HY, Lee SY, Park MS, Yeo SG. Clinical manifestations and prognosis of patients with Ramsay Hunt syndrome. Am J Otol 2012;33:313-18
- 44 Langworth EP, Taverner D. The prognosis in facial palsy. Brain 1963;86:465-80
- 45 Williamson IG, Whelan TR. The clinical problem of Bell's palsy: is treatment with steroids effective? Br J Gen Pract 1996;**46**:743–7
- 46 Kanazawa A, Haginomori S, Takamaki A, Nonaka R, Araki M, Takenaka H. Prognosis for Bell's palsy: a comparison of diabetic and nondiabetic patients. Acta Otolaryngol 2007;127:888-91
- 47 Pulec JL. Bell's palsy: diagnosis, management and results of treatment. Laryngoscope 1974;84:2119-40
- 48 Dalton GA. Bell's palsy: some problems of prognosis and treatment. Br Med J 1960;1:1765-70
- 49 Peiris OA, Miles DW. Galvanic stimulation of the tongue as a prognostic index in Bell's palsy. Br Med J 1965;2:1162-3
- 50 De Ru JA, Van Benthem PPG, Janssen LM. All evidence is equal, but some is more equal than others. Otol Neurotol 2010;31:551-3
- 51 House JW, Brackmann DE. Facial nerve grading system. Otolaryngol Head Neck Surg 1985;93:146-7
- 52 Browning GG. A facial palsy grading system that appears to be invalid. Clin Otolaryngol 2007;32:396
- 53 Wormald RN, Ahmed I, Fenton JE. The facial nerve: one editorial, two authors, top-cited. *Clin Otolaryngol* 2007;**32**:397–8 De Ru JA, Braunius WW, Van Benthem PP, Busschers WB,
- 54 Hordijk GJ. Grading facial nerve function. Why a new grading

system, the MoReSS, should be proposed. *Otol Neurotol* 2006; **27**:1030-6

- 55 Brown JS. Bell's palsy: a 5 year review of 174 consecutive cases: an attempted double blind study. *Laryngoscope* 1982; 92:1369–73
- 56 Tang IP, Lee SC, Shashinder S, Raman R. Outcome of patients presenting with idiopathic facial nerve paralysis (Bell's palsy) in a tertiary centre--a five year experience. *Med J Malaysia* 2009; 64:155–8
- 57 Shafshak TS, Essa AY, Bakey FA. The possible contributing factors for the success of steroid therapy in Bell's palsy: a clinical and electrophysiological study. *J Laryngol Otol* 1994;**108**: 940–3
- 58 Taverner D, Cohen SB, Hutchinson BC. Comparison of corticotrophin and prednisolone in treatment of idiopathic facial paralysis (Bell's palsy). *Br Med J* 1971;4:20–2
- 59 Stillman JS, Niparko JK, Lee SS, Lileny PR. Prognostic value of evoked and standard electromyography in acute facial paralysis. *Otolaryngol Head Neck Surg* 1992;107:377–81
- 60 Thomander L, Stalberg E. Electroneurography in the prognostication of Bell's palsy. Acta Otolaryngol 1981;92:221–37
- 61 Steiner JF. Treatment of Bell palsy; translating uncertainty into practice. *JAMA* 2009;**302**:1003–4
- 62 Thaera GM, Wellik KE, Barrs DM, Dunckley ED, Wingerchuk DM, Demaerschalk BM. Are corticosteroid and antiviral treatments effective for Bell palsy? A critically appraised topic. *Neurologist* 2010;16:138–40
- 63 Adour KK, Ruboyianes JM, Von Doersten PG, Byl FM, Trent CS, Quesenberry CP Jr *et al.* Bell's palsy treatment with acyclovir and prednisone compared with prednisone alone: a doubleblind, randomized, controlled trial. *Ann Otol Rhinol Laryngol* 1996;**105**:371–8
- 64 De Ru JA, Martens EP, Van der Veen EL. Antivirals for a possible viral cause (Rapid response to Quant *et al.*, 1 November 2011). *BMJ* 2009;**339**:b3354
- 65 Burgess LPA, Yim DWS, Lepore ML. Bell's palsy: the steroid controversy revisited. *Laryngoscope* 1984;94:1472–6
- 66 Moher D. The problem of duplicate systematic reviews. BMJ 2013;347:f5040
- 67 Quant EC, Jeste SS, Muni RH, Cape AV, Bhussar MK, Peleg AY. The benefits of steroids versus steroids plus antivirals for treatment of Bell's palsy: a meta-analysis. *BMJ* 2009;**339**: b3354. Erratum in: *BMJ* 2013;**346**:f151
- Sullivan FM, Swan IRC, Donnan PT, Morrison JM, Smith BH, McKinstry B *et al.* Early treatment with prednisolone or acyclovir in Bell's palsy. *N Engl J Med* 2007;**357**:1598–607
 Engström M, Berg T, Stjernquist-Desatnik A, Axelsson S,
- 69 Engström M, Berg T, Stjernquist-Desatnik A, Axelsson S, Pitkaranta A, Hultcrantz M *et al.* Prednisolone and valaciclovir in Bell's palsy: a randomised, double-blind, placebo-controlled, multicentre trial. *Lancet Neurol* 2008;7:993–1000
- 70 Minnerop M, Herbst M, Fimmers R, Kaabar P, Matz B, Klockgelter T *et al.* Bell's palsy; combined treatment of famciclovir and prednisone is superior to prednisone alone. *J Neurol* 2008;255:1726–30
- 71 Lee HY, Byun JY, Park MS, Yeo SG. Steroid-antiviral treatment improves the recovery rate in patients with severe Bell's palsy. *Am J Med* 2013;**126**:336–4172
- 72 Van der Veen EL, Rovers MM, De Ru JA, Van der Heijden GJ. A small effect of adding antiviral agents in treating patients with severe Bell palsy. *Otolaryngol Head Neck Surg* 2012;146: 353–7
- 73 Axelsson S, Berg T, Jonsson L, Engström M, Kanerva M, Stjernquist-Desatnik A. Bell's palsy – the effect of prednisolone and/or valaciclovir versus placebo in relation to baseline severity in a randomised controlled trial. *Clin Otolaryngol* 2012;37: 283–90
- 74 De Ru JA. Re: The benefits of steroids versus steroids plus antivirals for treatment of Bell's palsy: a meta-analysis (Rapid response to Quant *et al.*, 1 June 2013). *BMJ* 2009;**339**: b3354
- 75 Ahangar AA, Hosseini S, Saghebi R. Comparison of the efficacy of prednisolone versus prednisolone and acyclovir in the treatment of Bell's palsy. *Neurosciences (Riyadh)* 2006;11:256–9
- 76 De Ru JA, Blackburn TK, McAlister K, Brennan PA, Featherstone C, Van der Veen EL. Valaciclovir in combination with prednisolone for Bell's palsy. *Clin Otolaryngol* 2014;**39**: 321–22

- 77 Hill AB. The environment and disease: association or causation? Proc R Soc Med 1965;58:295–300
- 78 Davenport RJ, Sullivan F, Smith B, Morrison J, McKinstry B. Treatment for Bell's palsy. *Lancet* 2008;**372**:1219–20
- 79 Lockhart P, Daly F, Pitkethly M, Comerford N, Sullivan F. Antiviral treatment for Bell's palsy (idiopathic facial paralysis). *Cochrane Database Syst Rev* 2009;(4):CD001869
- 80 De Almeida JR, Al Khabori M, Guyatt GH, Witterick IJ, Lin VYW, Nedzelski JM *et al.* Combined corticosteroid and antiviral treatment for Bell palsy: a systematic review and metaanalysis. *JAMA* 2009;**302**:985–93
- 81 Goudakos JK, Markou KD. Corticosteroids versus corticosteroids plus antiviral agents in the treatment of Bell palsy: a systematic review and meta-analysis. *Arch Otolaryngol Head Neck* Surg 2009;135:558–64
- 82 Numthavaj P, Thakkinstian A, Dejthevaporn C, Attia J. Corticosteroid and antiviral therapy for Bell's palsy: a network meta-analysis. *BMC Neurol* 2011;11:1
 83 Ramsey MJ, DerSimonian R, Holtel MR, Burgess LPA.
- 83 Ramsey MJ, DerSimonian R, Holtel MR, Burgess LPA. Corticosteroid treatment for idiopathic facial nerve paralysis: a meta-analysis. *Laryngoscope* 2000;**110**:335–41
- 84 Jongkees LBW. Surgery of the facial nerve. J Laryngol Otol 1968;82:575-84
- 85 Huizing EH, Mechelse K, Staal A. Treatment of Bell's palsy: an analysis of the available studies. *Acta Otolaryngol* 1981;92: 115–21
- 86 Yanagihara N, Hato N, Murakami S, Honda N. Transmastoid decompression as a treatment of Bell palsy. *Otolaryngol Head Neck Surg* 2001;**124**:282–6
- Jongkees LB. The timing of surgery in intratemporal facial paralysis. *Laryngoscope* 1969;79:1557–61
- 88 Hopp ES, Hambley WM. Bell's palsy. A ten-year review of cases at the University of California Medical Center. *Laryngoscope* 1961;71:823–9
- 89 Yanagihara N, Gyo K, Yumoto E, Tamaki M. Transmastoid decompression of the facial nerve in Bell's palsy. Arch Otolaryngol 1979;105:530–4
- 90 Alford BR, Sessions RB, Weber SC. Indications for surgical decompression of the facial nerve. *Laryngoscope* 1971;81: 620–35
- 91 Glaziou P, Chalmers I, Rawlins M, McCulloch P. When are randomised trials unnecessary? Picking signal from noise. *BMJ* 2007;**334**:349–51
- 92 Sinha PK, Keith RW, Pensak ML. Predictability of recovery from Bell's palsy using evoked electromyography. *Am J Otol* 1994;15:769–71
- 93 Mechelse K, Goor G, Huizing EH, Hammelburg E, van Bolhuis AH, Staal A *et al.* Bell's palsy: prognostic criteria and evaluation of surgical decompression. *Lancet* 1971;**2**:57–9
- 94 Adour KK. Decompression for Bell's palsy: why I don't do it. Eur Arch Otorhinolaryngol 2002;259:40-7
- 95 Hato N, Nota J, Komobuchi H, Teraoka M, Yamada H, Gyo K et al. Facial nerve decompression surgery using bFGF-impregnated biodegradable gelatin hydrogel in patients with Bell's palsy. Otolaryngol Head Neck Surg 2012;146:641–6
- 96 Cannon RB, Gurgel RK, Warren FM, Shelton C. Facial nerve outcomes after middle fossa decompression for Bell's palsy. *Otol Neurol* 2014. Epub 2014 Jul 23
- 97 Fish U, Esslen E. Total intratemporal exposure of the facial nerve. Arch Otolaryngol 1972;95:335-41
- 98 May M, Klein SR, Taylor FH. Idiopathic (Bell's) facial palsy: natural history defies steroid or surgical treatment. *Laryngoscope* 1985;95:406–9

Address for correspondence:

Dr J A de Ru,

Department of Otolaryngology – Head and Neck Surgery, Central Military Hospital 'Dr A Mathijsen',

Lundlaan 1,

3584EZ Utrecht, the Netherlands

E-mail: j.a.deru@umcutrecht.nl

Dr J A de Ru takes responsibility for the integrity of the content of the paper Competing interests: None declared