HOSTED BY

ELSEVIER

Available online at www.sciencedirect.com

ScienceDirect

Journal of Otology 10 (2015) 7–12

www.journals.elsevier.com/journal-of-otology/

Advances in diagnosis and non-surgical treatment of Bell's palsy

Yang Zhao, Guodong Feng, Zhiqiang Gao*

Department of Otolaryngology, Peking Union Medical College Hospital, China Medical Science Academy, Beijing, 100730, China

Received 11 February 2015; revised 16 February 2015; accepted 23 February 2015

Abstract

Bell's palsy is a commonly seen cranial nerve disease and can result in compromised facial appearance and functions. Its etiology, prognosis and treatment are still being debated. This paper is a review of recent development in the understanding of etiology, diagnosis and non-surgical treatment of Bell's palsy.

Keywords: Facial paralysis; Non-surgical treatment; Steroids

1. Introduction

Facial paralysis is a common condition involving the facial nerve and can significantly impact a patient's quality of life. The facial nerve is a compound nerve comprised of motor, parasympathetic and sensory fibers. Damages to the facial nerve affect facial functions and appearance. Based on the location of the causal pathology, facial paralysis can be categorized as central or peripheral. Central facial paralysis results from disorders of the neural system above the facial nucleus, while peripheral facial paralysis is caused by damages to the facial nucleus or facial nerve. Bell's palsy is the most common peripheral facial paralysis. Diagnosis of facial paralysis is primarily based on clinical presentation, including weak eyebrow lifting, incomplete eye closure, drooping mouth corner, dry eye, loss of taste sensitivity, hyperacusis and ear pain (Stew and Williams, 2013). The etiology and degree of facial paralysis are quite variable and so are its treatment and treatment outcomes at this time (Kim and Lelli, 2013).

* Corresponding author.
E-mail address: tallee@sina.com (Z. Gao).

Peer review under responsibility of PLA General Hospital Department of Otolaryngology Head and Neck Surgery.

2. Etiology

There are roughly six types of peripheral facial paralysis: idiopathic (Bell's palsy), congenital, infection-related, traumatic, tumor-related and others (Bleicher et al., 1996). Bell's palsy has been used in lieu of "idiopathic" facial paralysis in the past, referring to idiopathic paralysis from lower facial neuron disorders and requiring exclusion of other etiologies (Dale, 1973). David proposed the hypothesis that Bell's palsy is a result of herpes virus infection, which has been supported by some studies at serology levels (Mccormick, 2000; Musani et al., 2009). Using polymerase chain reaction (PCR) technology, Murakami et al. (1996) was able to detect herpes virus genes in the geniculate ganglion area in facial paralysis patients but not in normal subjects. However, as indicated by Linder et al. (2005), detection of herpes virus in the geniculate ganglion in facial paralysis patients itself does not necessarily demonstrate the roles of the virus in the development of facial paralysis. In a prospective study involving 38 patients with Bell's palsy, specific serous IgM test showed possible infection in 11 patients, of which 6 were borrelia burgdorferi, 4 were chicken pox and only 1 was herpes virus (Imarhiagbe et al., 1993). Other reported possible etiologies include zoster sine herpete (Lee et al., 2012), Lyme disease (Oymar and Tveitnes,

http://dx.doi.org/10.1016/j.joto.2015.02.003

2009), parotitis, rubella (Morgan and Nathwani, 1992), vaccination (Mutsch et al., 2004), etc.

In adults, of all potential facial paralysis risk factors (including diabetes and pregnancy), only aging is supported by evidence (Monini et al., 2010). In children, Bell's palsy appears to be more common in cold seasons (Tsai et al., 2009). Some have found that the incidence of Bell's palsy in pregnant women is 45.1/100,000, almost three times as high as in non-pregnant women of similar age (Hilsinger et al., 1975), and possible causes may be hypercoagulability, elevated blood pressure, increased fluid load, virus infection and suppressed immunity (Cohen et al., 2000). But an analysis of these findings by Vrabec et al. (2007) showed that the rate of facial paralysis in pregnant women was not significantly higher than in non-pregnant women and that the seemingly high rate of facial paralysis in the third month of pregnancy might be related to increased susceptibility to herpes virus infection which was associated with unfavorable prognosis due to limitations on pharmacological interventions during pregnancy.

3. Diagnosis

For comprehensive facial paralysis evaluation, a thorough history must include inquiry on exposure to various viruses (herpes, chicken pox-varicella zoster, HIV, etc) and history of stress and cold symptoms. All categories under the House-Brackmann grading system (H-BGS) must be covered in physical examination. Assessment of Bell's phenomenon and corneal reflex can help predict the risk of corneal injury. The ear should be examined for mass or herpes rash. Head and neck examination should include the parotid and the entire body should be examined for erythema migrans (Melvin and Limb, 2008). In patients with trauma to the temporal bone, audiometric tests should be performed to assess any hearing loss and its type and severity. Selection of imaging studies depends on the injury in a particular patient.

Localizing tests can help determine the location of facial nerve disorder. They are based on the fact that facial nerve functions proximal to the site of the disorder are preserved. In complete facial nerve damage, although localizing tests are reliable they may not be necessary; while in partial of mixed facial nerve injury, these tests may not be reliable and therefore their use is declining in recent years (Flint et al., 2010).

Electrophysiological tests include nerve excitability test, maximum stimulation test, electroneuronography, electromyography, etc, whose roles are limited in early stages of the condition and they should be applied at different time points (Table 1). Nerve degeneration continues in the first two weeks in most cases of Bell's palsy (Danielides et al., 1994), and it has therefore been recommended that nerve excitability test be repeated during this period. Nerve excitability test and maximum stimulation test rely on subjective observations and can be observer-biased. In contrast, electroneuronography (ENoG) and electromyography (EMG) are relative objective tests. ENoG records supra-maximum stimulation evoked compound action potentials (CAPs) from muscles and a loss of more than 90% of amplitude compared to normal side indicates poor prognosis. To avoid false positive results, ENoG should be performed a few days after facial nerve injury. EMG reflects post-synaptic potentials and can detect activities of a single motor unit. On AY et al. evaluated the consistency between EMG and clinical assessment and found they showed different validity levels for different areas on the face: *Kappa* = 0.87 for orbicularis oculi but only 0.59 for orbicularis oris. In about 65% of the cases where EMG detected no voluntary motions, their presence was reported in clinical evaluation, although EMG detected low grade synkinesis not noticeable to clinical assessment (On et al., 2007).

Table 1
Timing and interpretation in electrophysiological studies of facial nerve (Bonner et al., 1991).

Test	Time	Results	Interpretation
EMG	>2 weeks	Motor unit activities	Axon intact
		Multiphasic potentials	Nerve regeneration
		MU + fibrillation	Partial degeneration
ENoG	<3 weeks	Loss < 90%	Favorable prognosis
		Loss > 90%	Poor prognosis
Excitability Test	<3 weeks	Threshold < 3 mA	Favorable prognosis
Maximum stimulation	<3 weeks	Severely decreased or no response	Progressive degeneration

4. Management

4.1. Eye protection

Facial paralysis can lead to eye closure failure, which, without timely intervention, can result in corneal ulceration, scarring and vision loss (Lane, 2012). Intervention is based upon judgment on the prognosis of facial nerve function as well as the lagophthalmos (Lee et al., 2004). For mild lagophthalmos with optimistic prognosis, artificial tears, ointment, humidifying cover, eyelid implant, botulinum toxin or eyelid stitches can be effectively used. Artificial tears are usually the first choice measure and can be combined with ointment at night (Mavrikakis, 2008). If needed, eye patch or humidifying cover can be added, although adding humidifying cover has not been shown to significantly reduce the risk of eye complications (Sorce et al., 2009). In recent years, scleral contact lenses have been used to protect exposed cornea, including the prosthetic replacement of the ocular surface ecosystem (PROSE), which is a breathable scleral lens filled with saline. Gire et al. (2013) reported using the PROSE in patients with severe corneal complications from facial paralysis which provided vision improvement with no adverse effects. Eyelid implant can reduced eye exposure while improving appearance. Commonly used materials include gold and platinum, with the latter often being thinner with lower risk of protrusion or immune reactions (Bladen et al., 2012).

4.2. Steroids

A British study at the end of last century showed that among patients with Bell's palsy in England, about 36% used

glucosteroids, 0.6% used anti-viral agents, and only 0.4% used both (Rowlands et al., 2002), indicating a wide divergence in pharmacological interventions for facial paralysis by clinicians.

In the 2013 AAO-HNS guidelines for diagnosis and treatment of Bell's palsy, oral steroids within 72 h of occurrence of Bell's palsy are strongly recommended, while sole use of anti-viral drugs or in patients with newly developed Bell's palsy is advised against (Baugh et al., 2013). The 2014 guidelines by the Canadian Bell's Palsy Task Force also recommend oral steroids and no sole use of anti-viral medicines, although the treatment initiation time window is reduced to within 48 h (De Almeida et al., 2014).

A meta-analysis by De Almeida et al. (2009) that included 8 studies and a total of 1285 subjects indicated that steroids might reduce the rate of incomplete recovery and synkinesis. A Cochrane study involving 7 studies and 1507 subjects showed that, after 6 months, the rate of incomplete recovery and synkinesis in the randomly allocated treatment group was significantly lower than the control group, although there was no significant differences in cosmetic outcomes between the two groups. It should be noted that a fixed effect model was used in the variance test in this meta-analysis report with $P = 0.04$, suggesting a risk of forced combination effect.

From these meta-analysis studies, it appears that existing evidence essentially supports the use of steroids in the treatment of facial paralysis, which may shorten disease course and reduce complications. It also appears that, with increasing sample sizes, multi-center random comparative studies tend to show positive results, but it is difficult to show statistical significance in small sample reports.

The timing of intervention in facial paralysis has been controversial. In a large sample random comparative study by Mats et al. (Axelsson et al., 2011), the rate of complete recovery in Bell's palsy was 66% (103/156) when steroids were started within 24 h of occurrence and increased to 76% (128/168) if initiated between 25 and 48 h (significantly different from the control), but similar to the control when steroids were given between 49 and 72 h (65/92 vs. 58/83, $P = 0.5$), indicating that steroids should be administered within 48 h of occurrence of facial paralysis.

Steroids can not only improve prognosis in facial paralysis, but also improve quality of life and sleep (Whitley et al., 1996), although they do not provide pain relief (Axelsson et al., 2011; Berg et al., 2009). Facial paralysis associated pain usually lasts for 2 weeks followed by gradual decrease. A report from Taiwan by Lee et al. (2013a) found that facial paralysis was a high risk for stroke (incidence of stroke in facial paralysis patients was 2.02 times of that in "normal" population), and steroid therapy might lower the risk.

4.3. Anti-viral therapy

Based upon the hypothesis that facial paralysis may result from viral infection, anti-viral measures have been used in treating Bell's palsy. In a recent Cochrane systemic assessment that included 1987 subjects, the combined results showed no significant differences between the anti-viral drug treated group and placebo control group regarding facial paralysis recovery. Compared to steroids, prognosis was worse in patients receiving anti-viral agents. The same assessment also revealed that rate of long term complications was not significantly different regardless if steroids or anti-viral agents were used. The number of literature included in a web-based meta-analysis by Numthavaj et al. (2011) is only one short of that in the Cochrane assessment (Kawaguchi et al., 2007). Using a mixed effects model, this report assessed efficacies of steroids and antivirals at 3 and 6 months following facial paralysis and showed that recovery outcomes at 3 months were significantly worse when using acyclovir or valaciclovir alone then when using only steroids. The authors believed that while antivirals might have some effects in treating peripheral facial paralysis, the effects were small. In contrast, the meta-analysis by Quant et al. (2009), including the study by Minnerop et al. (2008) but excluding those by Kawaguchi et al. (2007) and De Diego et al. (1998), concluded that antivirals did not add additional benefits in treating facial paralysis patients. In examining the bar graphs in the report, it is clear that the inclusion of two high quality studies (Sullivan et al., 2007; Engstrom et al., 2008) led to their conclusion.

Acyclovir, famciclovir and valaciclovir are commonly used antivirals. Taken orally, acyclovir is low in bioavailability (Bentz et al., 2006), and its compliance is difficult to monitor. Famciclovir is a prodrug of penciclovir and has high bioavailability and long half-life inside cells when taken orally (Lee et al., 2013b). Valaciclovir is the prodrug of acyclovir with even higher bioavailalbility and can be dosed only twice a day (Kawaguchi et al., 2007).

4.4. Hyperbaric oxygen

Facial nerve swelling inside the fallopian canal in the temporal bone can lead to anoxia status in nerve cells (Fisch and Felix, 1983), which is believed to be one of the mechanisms in Bell's palsy. Inflammation and anoxia of the facial nerve causes reversible neurapraxia initially, which can be followed by Wallerian degeneration. Hyperbaric oxygen increases the oxygen diffusion gradient around anoxic tissues, which may facilitate resolution of edema and promote regeneration (Holland et al., 2012). In studying a mouse model of facial nerve injury, Toros et al. (2013) found that the combination of hyperbaric oxygen and steroids resulted in reduced axonal degeneration and blood vessel blockage and increased axonal diameter. Racic et al. (1997) compared results of hyperbaric oxygen and prednisone treatments at 9 months follow up in 79 cases of facial paralysis and reported rates of complete recovery of 95.2% and 75.7%, and average recovery time of 22 and 34.4 days, respectively. They concluded that hyperbaric oxygen yielded better outcomes than steroids. However, the study was not blinded and therefore prone to study bias. Furthermore, hyperbaric therapy is not risk free. The pressure inside a hyperbaric chamber is 1.5–3 times of atmosphere pressure and can potentially cause round window rupture, vision change, tingling in fingers and

claustrophobia, which practitioners must be aware of Plafki et al. (2000).

4.5. Electric stimulation

Electrical stimulation can cause contraction of muscles that have lost innervation (Sheffler and Chae, 2007) and promote nerve regeneration and expression of growth-related genes (Geremia et al., 2007). In recent years, electric stimulation has been used in repair of injured nerves. Lal et al. (2008) established a facial nerve electric stimulation model using rats and found that electric stimulation significantly reduced time needed for recovery of blink reflex. Hyvärinen from Finland (Hyvarinen et al., 2008) tried 6 months of skin electric stimulation with gradually increased intensity in 10 patients considered unlikely to recover (disease course longer than 1 year) and reported improvement in H-BGS scores, ENoG findings and self-evaluation with no treatment-related adverse incidents. But the number of cases in the study was small, there was no controls and daily 6 h of treatment required incredibly high compliance on the patient's part. Hyvärinen's findings are contradicted by conclusions in a South Africa study (Alakram and Puckree, 2010), which reported no significant difference in H-BGS scores between the control and patients who received electric stimulation at an early time following facial paralysis (<30 days). The discrepancy between the two studies may have something to do with the timing of electric stimulation intervention. In China, Cui (2011) established an EMG signals based functional electric stimulation system, in which a trigger threshold was set in reference to EMG amplitudes from auricular muscles on the healthy side and stimulation voltage set in reference to response of auricular muscles on the paralyzed side to electric stimulation. As EMG potentials from contralateral auricular muscles reached the set threshold, the system was triggered to deliver stimulation to ipsilateral auricular muscles, causing contraction and auricle movements synchronized to the healthy side. Similarly, Yi et al. (2013) were able to stimulate blink reflex using EMG signals from the contralateral side.

Regeneration following nerve injury requires multiple processes including the survival and regrowth of neurons, budding of nerves, as well as axonal elongation, connection and synapses formation. It is currently believed that electric stimulation may be able to affect the early stage of nerve regeneration, such as the survival of neurons and budding of nerves. Future studies need to cover the entire course of nerve regeneration (Lal et al., 2008).

4.6. Mime play

Dutch clinicians and mime artists first developed mime therapies for patients with facial paralysis, which were further developed at several German centers. To start, the patient is instructed to massage the face and neck for 10–15 min/day, including gentle touch and kneading that involved gentle pulling of the paralyzed side to reduce synkinesis. The patient is then taught to recognize facial tension and relaxation and specific exercises to synchronize the face on both sides. The last training session involved eye and lip closure exercises (see description by Beurskens and Heymans (2004) for details). Beurskens evaluated the efficacy of this therapy using the Sunnybrook facial function grading system in 50 patients with facial paralysis who were randomly divided into a treatment and a control group. After 3 months, the treatment groups showed a 20.4 points improvement compared to the control group (Beurskens and Heymans, 2006).

4.7. Biofeedback

Following facial paralysis, the lack of feedback from facial movements disrupts reception of information regarding facial motion by the brain (Baricich et al., 2012). Biofeedback helps the brain in instant analysis and correction of facial motions. Frequently used modalities in facial paralysis patients include EMG and mirror feedbacks. Most studies at this time conclude that efficacies of EMG and mirror feedbacks are similar. In a retrospective clinical study by Dalla Toffola et al. (2012), all subjects were assigned to groups based on disease severity and received EMG/ENoG tests at 3–4 weeks following the onset of their facial paralysis. EMG results indicated that recovery was complete in those with neurapraxia, while those with sectioned axons achieved similar recovery outcomes with either EMG or mirror biofeedback treatments. Nakamura from Japan (Nakamura et al., 2003) studied prevention of synkinesis by biofeedback. Twenty seven patients with facial paralysis were randomly divided in two groups and those in the test group were required to move the mouth while keeping eyes equally open in front of a mirror for 30 min every day. Assessment 10 months later showed that the rate of synkinesis was significantly lower in the biofeedback treatment group than in the control group. Pourmomeny et al. (2014) also confirmed that EMG biofeedback might lower the rate and degree of synkinesis.

4.8. Acupuncture

Acupuncture has been used to treat diseases for a long time in China, but its efficacy is yet to be proven in evidence-based medicine. Available literature at this time mostly show that acupuncture is effective, although all studies are blemished by flaws like lack of randomization or blinding. Existing studies on acupuncture are also highly heterogeneous, making combined analysis difficult. To overcome this obstacle and assess efficacy of acupuncture in Bell's palsy patients, Cumberworth et al. (2012) performed literature search using evidence-based medicine standards and identified 3 reports, including 2 systematic evaluations and 1 RCT. From their comparison, the authors concluded that acupuncture might be an effective or highly effective treatment. But for the evidence that can be searched at this time, one should be cautious in assessing its efficacy. Even if it is effective, differences in individual techniques used by a particular practitioner may still result in different efficacies. Traditionally, acupuncture therapy emphasizes on acquiring “Qi” to obtain the best results (Xu et al., 2013).

The aim of treatment in Bell's palsy is to restore symmetry in facial appearance and synchronized movements of facial muscles for desired facial expressions, while protecting the eye (Terzis and Anesti, 2011). The complexity in facial paralysis determines the complexity in its treatments, although it also drives the development of various therapies. In the future, management of facial paralysis should be a combined approach encompassing patient education, drug therapies, physiotherapies and surgical treatments.

Funding

This work was supported by China National Science and Technology Support Program (Grant No. 2012BAI12B01) and China National Natural Science Foundation Grant No. 81341031.

References

Alakram, P., Puckree, T., 2010. Effects of electrical stimulation on House-Brackmann scores in early Bell's palsy. Physiother. Theory Pract. 26 (3), 160–166.

Axelsson, S., Berg, T., Jonsson, L., et al., 2011. Prednisolone in Bell's palsy related to treatment start and age. Otol. Neurotol. : Off. Publ. Am. Otol. Soc. Am. Neurotol. Soc. Eur. Acad. Otol. Neurotol. 32 (1), 141–146.

Baricich, A., Cabrio, C., Paggio, R., et al., 2012. Peripheral facial nerve palsy: how effective is rehabilitation? Otol. Neurotol. : Off. Publ. Am. Otol. Soc. Am. Neurotol. Soc. Eur. Acad. Otol. Neurotol. 33 (7), 1118–1126.

Baugh, R.F., Basura, G.J., Ishii, L.E., et al., 2013. Clinical practice guideline: Bell's palsy. Otolaryngol. Head Neck Surg. : Off. J. Am. Acad. Otolaryngol. Head Neck Surg. 149 (3 Suppl), S1–S27.

Bentz, B.G., Maxwell, L.K., Erkert, R.S., et al., 2006. Pharmacokinetics of acyclovir after single intravenous and oral administration to adult horses. J. Vet. Intern. Med./Am. Coll. Vet. Intern. Med. 20 (3), 589–594.

Berg, T., Axelsson, S., Engstrom, M., et al., 2009. The course of pain in Bell's palsy: treatment with prednisolone and valacyclovir. Otol. Neurotol. : Off. Publ. Am. Otol. Soc. Am. Neurotol. Soc. Eur. Acad. Otol. Neurotol. 30 (6), 842–846.

Beurskens, C.H., Heymans, P.G., 2004. Physiotherapy in patients with facial nerve paresis: description of outcomes. Am. J. Otolaryngol. 25 (6), 394–400.

Beurskens, C.H., Heymans, P.G., 2006. Mime therapy improves facial symmetry in people with long-term facial nerve paresis: a randomised controlled trial. Aust. J. Physiother. 52 (3), 177–183.

Bladen, J.C., Norris, J.H., Malhotra, R., 2012. Cosmetic comparison of gold weight and platinum chain insertion in primary upper eyelid loading for lagophthalmos. Ophthal. Plastic Reconstr. Surg. 28 (3), 171–175.

Bleicher, J.N., Hamiel, S., Gengler, J.S., et al., 1996. A survey of facial paralysis: etiology and incidence. Ear Nose Throat J. 75 (6), 355–358.

Bonner, F.T., Hughes, M.N., Poole, R.K., et al., 1991. Kinetics of the reactions of trioxodinitrate and nitrite ions with cytochrome d in Escherichia coli. Biochim. Biophys. Acta 1056 (2), 133–138.

Cohen, Y., Lavie, O., Granovsky-Grisaru, S., et al., 2000. Bell palsy complicating pregnancy: a review. Obstet. Gynecol. Surv. 55 (3), 184–188.

Cui, T., 2011. Functional Electric Stimulation for Recovery of Paralyzed Auricular Muscles in Rats (Doctoral degree thesis). Peking Union Medical College.

Cumberworth, A., Mabvuure, N.T., Norris, J.M., et al., 2012. Is acupuncture beneficial in the treatment of Bell's palsy?: best evidence topic (BET). Int. J. Surg. 10 (6), 310–312.

Dale, C.C., 1973. Recognizing Bell's palsy: what the family physician should know. Can. Fam. Physician Med. famille Can. 19 (5), 59–61.

Dalla Toffola, E., Tinelli, C., Lozza, A., et al., 2012. Choosing the best rehabilitation treatment for Bell's palsy. Eur. J. Phys. Rehab. Med. 48 (4), 635–642.

Danielides, V., Skevas, A., Kastanioudakis, I., et al., 1994. Comparative study of evoked electromyography and facial nerve latency test in the prognosis of idiopathic facial nerve palsy in childhood. Child's Nerv. Syst. : ChNS : Off. J. Int. Soc. Pediatr. Neurosurg. 10 (2), 122–125.

De Almeida, J.R., Al Khabori, M., Guyatt, G.H., et al., 2009. Combined corticosteroid and antiviral treatment for Bell palsy: a systematic review and meta-analysis. JAMA : J. Am. Med. Assoc. 302 (9), 985–993.

De Almeida, J.R., Guyatt, G.H., Sud, S., et al., 2014. Management of Bell palsy: clinical practice guideline. CMAJ : Can. Med. Assoc. J.=J. l'Assoc. med. Can. 186 (12). http://www.cmaj.ca/content/186/12/917.full.

De Diego, J.I., Prim, M.P., De Sarria, M.J., et al., 1998. Idiopathic facial paralysis: a randomized, prospective, and controlled study using single-dose prednisone versus acyclovir three times daily. Laryngoscope 108 (4 Pt 1), 573–575.

Engstrom, M., Berg, T., Stjernquist-Desatnik, A., et al., 2008. Prednisolone and valaciclovir in Bell's palsy: a randomised, double-blind, placebo-controlled, multicentre trial. Lancet Neurol. 7 (11), 993–1000.

Fisch, U., Felix, H., 1983. On the pathogenesis of Bell's palsy. Acta oto-laryngol. 95 (5–6), 532–538.

Flint, P.W., Haughey, B.H., Lund, V.J., et al., 2010. Cummings Otolaryngology - Head and Neck Surgery [M]. Mosby.

Geremia, N.M., Gordon, T., Brushart, T.M., et al., 2007. Electrical stimulation promotes sensory neuron regeneration and growth-associated gene expression. Exp. Neurol. 205 (2), 347–359.

Gire, A., Kwok, A., Marx, D.P., 2013. PROSE treatment for lagophthalmos and exposure keratopathy. Ophthal. Plastic Reconstr. Surg. 29 (2), e38–40.

Hilsinger Jr., R.L., Adour, K.K., Doty, H.E., 1975. Idiopathic facial paralysis, pregnancy, and the menstrual cycle. Ann. Otol. Rhinol. Laryngol. 84 (4 Pt 1), 433–442.

Holland, N.J., Bernstein, J.M., Hamilton, J.W., 2012. Hyperbaric oxygen therapy for Bell's palsy. Cochrane Database Syst. Rev. 2, CD007288.

Hyvarinen, A., Tarkka, I.M., Mervaala, E., et al., 2008. Cutaneous electrical stimulation treatment in unresolved facial nerve paralysis: an exploratory study. Am. J. Phys. Med. Rehab./Assoc. Acad. Physiatr. 87 (12), 992–997.

Imarhiagbe, D., Prodinger, W.M., Schmutzhard, E., 1993. Infective pathogens as a possible etiology of idiopathic peripheral facial paralysis. Wien. Klin. Wochenschr. 105 (21), 611–613.

Kawaguchi, K., Inamura, H., Abe, Y., et al., 2007. Reactivation of herpes simplex virus type 1 and varicella-zoster virus and therapeutic effects of combination therapy with prednisolone and valacyclovir in patients with Bell's palsy. Laryngoscope 117 (1), 147–156.

Kim, C., Lelli Jr., G.J., 2013. Current considerations in the management of facial nerve palsy. Curr. Opin. Ophthalmol. 24 (5), 478–483.

Lal, D., Hetzler, L.T., Sharma, N., et al., 2008. Electrical stimulation facilitates rat facial nerve recovery from a crush injury. Otolaryngol. Head Neck Surg. : Off J. Am. Acad. Otolaryngol. Head Neck Surg. 139 (1), 68–73.

Lane, C., 2012. Management of ocular surface exposure. Br. J. Ophthalmol. 96 (4), 471–472.

Lee, V., Currie, Z., Collin, J.R., 2004. Ophthalmic management of facial nerve palsy. Eye 18 (12), 1225–1234.

Lee, H.Y., Kim, M.G., Park, D.C., et al., 2012. Zoster sine herpete causing facial palsy. Am. J. Otolaryngol. 33 (5), 565–571.

Lee, C.C., Su, Y.C., Chien, S.H., et al., 2013. Increased stroke risk in Bell's palsy patients without steroid treatment. Eur. J. Neurol. : Off. J. Eur. Fed. Neurol. Soc. 20 (4), 616–622.

Lee, H.Y., Byun, J.Y., Park, M.S., et al., 2013. Steroid-antiviral treatment improves the recovery rate in patients with severe Bell's palsy. Am. J. Med. 126 (4), 336–341.

Linder, T., Bossart, W., Bodmer, D., 2005. Bell's palsy and Herpes simplex virus: fact or mystery? J. Otology Neurotol. : Off. Publ. Am. Otol. Soc. Am. Neurotol. Soc. Eur. Acad. Otol. Neurotol. 26 (1), 109–113.

Mavrikakis, I., 2008. Facial nerve palsy: anatomy, etiology, evaluation, and management. Orbit 27 (6), 466–474.

Mccormick, D.P., 2000. Herpes simplex virus as a cause of Bell's palsy. 1972. Rev. Med. Virol. 10 (5), 285–289.

Melvin, T.A., Limb, C.J., 2008. Overview of facial paralysis: current concepts. Facial Plast. Surg. : FPS 24 (2), 155–163.

Minnerop, M., Herbst, M., Fimmers, R., et al., 2008. Bell's palsy: combined treatment of famciclovir and prednisone is superior to prednisone alone. J. Neurol. 255 (11), 1726−1730.

Monini, S., Lazzarino, A.I., Iacolucci, C., et al., 2010. Epidemiology of Bell's palsy in an Italian Health District: incidence and case-control study. Acta Otorhinolaryngol. Ital. organo Uff. della Soc. Ital. Otorinolaringol. Chir. Cerv.-facc. 30 (4), 198.

Morgan, M., Nathwani, D., 1992. Facial palsy and infection: the unfolding story. J. Clin. Infect. Dis. : Off. Publ. Infect. Dis. Soc. Am. 14 (1), 263−271.

Murakami, S., Mizobuchi, M., Nakashiro, Y., et al., 1996. Bell palsy and herpes simplex virus: identification of viral DNA in endoneurial fluid and muscle. Ann. Intern. Med. 124 (1 Pt 1), 27−30.

Musani, M.A., Farooqui, A.N., Usman, A., et al., 2009. Association of herpes simplex virus infection and Bell's palsy. JPMA J. Pak. Med. Assoc. 59 (12), 823−825.

Mutsch, M., Zhou, W., Rhodes, P., et al., 2004. Use of the inactivated intranasal influenza vaccine and the risk of Bell's palsy in Switzerland. N. Engl. J. Med. 350 (9), 896−903.

Nakamura, K., Toda, N., Sakamaki, K., et al., 2003. Biofeedback rehabilitation for prevention of synkinesis after facial palsy. Otolaryngol. Head Neck Surg. : Off. J. Am. Acad. Otolaryngol. Head Neck Surg. 128 (4), 539−543.

Numthavaj, P., Thakkinstian, A., Dejthevaporn, C., et al., 2011. Corticosteroid and antiviral therapy for Bell's palsy: a network meta-analysis. BMC Neurol. 11 (1).

On, A.Y., Yaltirik, H.P., Kirazli, Y., 2007. Agreement between clinical and electromyographic assessments during the course of peripheric facial paralysis. Clin. Rehabil. 21 (4), 344−350.

Oymar, K., Tveitnes, D., 2009. Clinical characteristics of childhood lyme neuroborreliosis in an endemic area of northern Europe. Scand. J. Infect. Dis. 41 (2), 88−94.

Plafki, C., Peters, P., Almeling, M., et al., 2000. Complications and side effects of hyperbaric oxygen therapy. Aviat. Space, Environ. Med. 71 (2), 119−124.

Pourmomeny, A.A., Zadmehre, H., Mirshamsi, M., et al., 2014. Prevention of synkinesis by biofeedback therapy: a randomized clinical trial. Otol. Neurotol. : Off. Publ. Am. Otol. Soc. Am. Neurotol. Soc. Eur. Acad. Otol. Neurotol. 35 (4), 739−742.

Quant, E.C., Jeste, S.S., Muni, R.H., et al., 2009. The benefits of steroids versus steroids plus antivirals for treatment of Bell's palsy: a meta-analysis. BMJ 339 (b3354).

Racic, G., Denoble, P.J., Sprem, N., et al., 1997. Hyperbaric oxygen as a therapy of Bell's palsy. Undersea Hyperb. Med. : J. Undersea Hyperb. Med. Soc. Inc. 24 (1), 35−38.

Rowlands, S., Hooper, R., Hughes, R., et al., 2002. The epidemiology and treatment of Bell's palsy in the UK. Eur. J. Neurol. : Off. J. Eur. Fed. Neurol. Soc. 9 (1), 63−67.

Sheffler, L.R., Chae, J., 2007. Neuromuscular electrical stimulation in neurorehabilitation. Muscle Nerve 35 (5), 562−590.

Sorce, L.R., Hamilton, S.M., Gauvreau, K., et al., 2009. Preventing corneal abrasions in critically ill children receiving neuromuscular blockade: a randomized, controlled trial. Pediatr. Crit. Care Med. : a J. Soc. Crit. Care Med. World Fed. Pediatr. Intensive Crit. Care Soc. 10 (2), 171−175.

Stew, B., Williams, H., 2013. Modern management of facial palsy: a review of current literature. Br. J. General Pract. : J. R. Coll. General Pract. 63 (607), 109−110.

Sullivan, F.M., Swan, I.R., Donnan, P.T., et al., 2007. Early treatment with prednisolone or acyclovir in Bell's palsy. N. Engl. J. Med. 357 (16), 1598−1607.

Terzis, J.K., Anesti, K., 2011. Developmental facial paralysis: a review. J. Plastic, Reconstr. Aesthet. Surg. : JPRAS 64 (10), 1318−1333.

Toros, S.Z., Karaca, C.T., Gunes, P., et al., 2013. Hyperbaric oxygen versus steroid in facial nerve injury: an experimental animal study. Am. J. Otolaryngol. 34 (5), 530−536.

Tsai, H.S., Chang, L.Y., Lu, C.Y., et al., 2009. Epidemiology and treatment of Bell's palsy in children in northern Taiwan. J. Microbiol. Immunol. Infect. = Wei mian yu gan ran za zhi 42 (4), 351−356.

Vrabec, J.T., Isaacson, B., Van Hook, J.W., 2007. Bell's palsy and pregnancy. Otolaryngol. Head Neck Surg. : Off. J. Am. Acad. Otolaryngol. Head Neck Surg. 137 (6), 858−861.

Whitley, R.J., Weiss, H., Gnann Jr., J.W., et al., 1996. Acyclovir with and without prednisone for the treatment of herpes zoster. A randomized, placebo-controlled trial. The national institute of allergy and infectious diseases collaborative antiviral study group. Ann. Intern. Med. 125 (5), 376−383.

Xu, S.B., Huang, B., Zhang, C.Y., et al., 2013. Effectiveness of strengthened stimulation during acupuncture for the treatment of Bell palsy: a randomized controlled trial. CMAJ : Can. Med. Assoc. J. = J. de l'Assoc. Med. Can. 185 (6), 473−479.

Yi, X., Jia, J., Deng, S., et al., 2013. A blink restoration system with contralateral EMG triggered stimulation and real-time artifact blanking. IEEE Trans. Biomed. Circuits Syst. 7 (2), 140−148.