Response of axonal regeneration in chronic Bell’s palsy to low intensity shockwave therapy: Randomized control trial

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Abstract

Background: Bell’s paralysis is an acute paralysis onset due to idiopathic facial nerve inflammation. It is the commonest cause of lower motor neuron facial paralysis with an annual rate of 15-30 per 100,000.

Objectives: Our aim of the study to detect the difference of axonal regeneration response in chronic Bell’s palsy to low intensity radial shock wave therapy and kabbat exercises.

Patients and methods: 60 chronic bell’s palsy patients (six months post injury) with age 35-60 years old randomly allocated to one of two groups; group A [Shock Wave (SW)] (n=30) treated with low intensity shock wave plus kabbat exercises and facial muscle exercise for six weeks. KE (kabbat exercise) group (n=30) treated with kabbat exercises plus sham treatment by a shock wave and facial muscle exercise for six weeks. Patients were assessed by electrophysiological study (Amplitude and degeneration index of facial nerve). The assessment was done before and after treatment.

Results: Degeneration index decrease significantly in the group A (p < 0.001), but not in the group B (p = 0.295). Amplitude of facial nerve was low at baseline, indicating sever axonal degeneration. After treatment, amplitude increased significantly in the two groups; however, the significance was higher in group A (SW) than group B (KE) (p < 0.001).

Conclusion: Low intensity shock wave therapy is safe and effective treatment of chronic bell’s palsy after 6 months from the onset.

Keywords: Chronic Bell’s Palsy; Extracorporeal Shockwave Therapy; Kabbat Exercises; Exercise Therapy; Nerve Conduction Study.

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Introduction
Acute onset of idiopathic facial muscles paralysis called Bell's palsy (BP). It is the most frequent reason for facial nerve paralysis in lower motor neurons (Gilden, 2004). Acute idiopathic peripheral facial palsy is a prevalent condition that affects 15–30 people out of every 100,000 people annually (Grogan, et al., 2001). BP most frequently affects people between the ages of 15 and 45; it is substantially less common in people under 15 and over 60 (Döner et al., 2000). Both sexes are affected equally (Rowlands et al., 2002). Approximately 85% of BP patients fully recover without medical assistance or physiotherapy within three weeks of the onset, whereas 15% of these instances do so between three and six months following the onset (Peitersen et al., 2002). About 25% of BP patients may have experience of persistently moderate-to-severe facial asymmetry, which can have devastating effects on patients’ psychological health and regularly reduces their quality of life. (Zhang et al., 2020).

A previous Cochrane analysis found a dearth of reliable data to back up the use of shock waves for improvement of BP in routine clinical practice (Teixeira et al., 2011). Only trials using electrostimulation and exercise fulfilled the minimum standard for methodological quality, according to their analysis of studies involving electrotherapy, workouts, biofeedback, manual therapy, and laser. All BP patients should exhibit some improvement after six months (Peitersen et al., 2002). Old age, hypertensive, diabetic patients with impairment of taste and complete facial weakness had bad prognosis (Gilden et al., 2004). A third of individuals may have experience of incomplete recovery. Post-paralytic hemifacial spasm, co-contracting muscles, synkinesis, and sweating while eating or working out are a few of the aftereffects. Crocodile tears, or the ipsilateral eye lacrimation during eating, and jaw-winking, or closing of the ipsilateral eyelid with opening of the jaw, are the two most prevalent abnormal regeneration patterns.

The pathophysiology of Bell’s palsy observed in post-mortem cases is vascular distension, inflammation and oedema with ischemia of the facial nerve with unknown cause. Numerous causes, such as viral, inflammatory, autoimmune, and vascular, have been suggested. The most likely cause, however, is thought to be the reactivation of the herpes simplex or herpes zoster virus from the geniculate ganglion. Despite advancements in neuroimaging, diagnosis of BP is primarily clinical (Zhanget al., 2020)

Axonal injuries typically experience Wallerian degeneration, an antegrade degeneration process that occurs distal to the site of the injury and is characterized by axonal discontinuity, myelin fragmentation, macrophage scavenging followed by Schwan cells activation, and axonal regrowth that can take up to 8 weeks to complete. (Burnett et al., 2004)
Physically, shockwaves have two effects: cavitation bubbles created in liquids and mechanical stress brought on by exposure to high peak pressure waves. The vaporization of the liquid produces these bubbles. As a result, when subjected to high pressure, these cavities collapse, resulting in localized damage and neovascularization (Young Academic Urologists Men's Health Group 2017). Other mechanisms, such as NO (Nitric Oxide) induction (Gotteet al., 2002), nerve regeneration, and stem cell proliferation, are also theorized (Sokolakis et al., 2019).

Kabbat training includes the enhancement of the voluntary contraction of a paralyzed muscle by incorporate the muscle in diagonal pattern which subjected to resistance. This method is more efficient for facial muscles, since most of facial muscle fiber run in diagonal direction, due to the cross facial nerve innervations, the upper facial region is easily exposed to radiation. Upper, intermediate, and lower fulcra were three regional fulcra that were taken into account. The lower mimic-chewing-articulatory fulcrum is located along the horizontal axis, while the upper one (forehead and eyes) is connected to the intermediate one (nose) by a vertical axis. As a result, when the upper fulcrum is moved, the other two fulcra are likewise moved. Contralateral contractions and fundamental proprioceptive stimuli, such as stretching, maximum resistance, hand contact, and verbal input, are used to manipulate these three fulcra. The frontal, corrugators, and orbicularis oculi muscles in the upper fulcrum are contracted upwards or downwards, always in a vertical plane, according on the particular function that needs to be engaged. The common elevator muscle of the ala nasi and the upper lip are activated in the intermediate fulcrum as well employing traction movements, but this time in the opposite direction, along a vertical line. The rosarium and orbicularis oris muscles in a horizontal plane, and the mental muscle in a vertical plane, are used for the maneuvers for the lower fulcrum. (Barbara et al., 2003).

Patients and Methods
This randomized controlled trial included 60 patients with a confirmed diagnosis of chronic BP all patients provided written informed consent before inclusion in the study. Inclusion criteria were patients between 35-60 years of age with body mass index < 30 kg/m² and referred to the outpatient’s clinic in faculty of physical therapy south valley university with chronic BP lasting for at least six months. All patients had controlled DM confirmed by a recent measurement of the level of HbA1c. Patients with a history of facial paralysis post stroke, unstable medical or psychiatric disorders, and neurological diseases were excluded from the study.

Using the permuted block randomization method according to a computer-generated list prepared by an independent statistician not involved with subject recruitment, the patients were allocated into two equal groups. The sequence of allocation to either intervention was concealed and
performed by a person not involved in the testing or treatment of subjects in the study and kept in numbered and sealed envelopes. Patients in SW (Shock Wave) Group (n=30) were treated with Low intensity Extracorporeal Shock Wave (Li-ESWT) plus kabat exercises for six weeks. Patients kabat exercises Group (n=30) were treated with kabat exercise for facial muscles and sham therapy by a shock wave for six weeks. The sham treatment was conducted using a distinctively designed shock wave applicator. The sham shock wave applicator contained an element that blocked the delivery of shock waves.

Assessment: Electroneurography responses were recorded from surface electrodes placed over the frontalis and mentalis muscles and measured on the affected and unaffected sides in patients with chronic bell’s palsy using a bipolar surface stimulator placed over the stylomastoid foramen. The current intensity was increased to elicit compound muscle action potentials. The frontalis and mentalis muscles’ compound muscle action potentials (CMAP) were acquired in order to calculate the amplitude degeneration ratio, and the nasalis muscle’s CMAP was used to calculate the degeneration index using this equation: \[100 - (\text{ENoG amplitude affected/ unaffected side}) \times 100\]. The examination was done before and after treatment.

Treatment Protocol
1- Low-intensity extracorporeal shock wave
(2000 SWs, energy intensity of 0.09 mJ/mm²) was applied to two treatment points: one at stylomastoid foramen (500 SWs) and another point in front of ear by 1cm 1500 SWs. The shock waves were delivered through an applicator the facial nerve and its branches. The treatment consists six sessions, one session per week.

2- Kabat exercises and sham shock wave
During the first session, the physiotherapist explained the anatomy of the facial muscles and the function of the facial muscles. Then patient sit in front of mirror and physical therapist stand behind the patient and put one hand on the sound side to apply resistance and another hand on the affected side to apply manual traction and scratch in vertical direction for upper and intermediate parts of the face and in horizontal direction for lower part of the face, both hands act in diagonal direction. The sham treatment was conducted using a distinctively designed shock wave applicator. The sham shock wave applicator contained an element that blocked the delivery of shock waves.

Statistical analysis
IBM SPSS® Statistics version 26 (IBM® Corp., Armonk, NY, USA) was used for the statistical analysis. The right way to express numerical data was using the mean, standard deviation, or median and range. Using the Shapiro-Wilk test and the Kolmogorov-Smirnov test, data were examined for normality. Using an independent sample t-test, quantifiable data from the two groups were compared. It was decided whether to estimate the correlation between numerical variables using the Pearson
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Product-moment or Spearman-rho methods. All tests were two-tailed. A p-value of 0.05 or less was regarded as significant.

**Table 1: Baseline characteristics of the two studied groups**

<table>
<thead>
<tr>
<th>Variables</th>
<th>SW Group n=30</th>
<th>KE Group n=30</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>40.6±5.5</td>
<td>40.5±5.7</td>
<td>0.993</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>75.5±9.0</td>
<td>75.4±8.9</td>
<td>0.937</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>168±4</td>
<td>168±3</td>
<td>0.355</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>25.2±2.5</td>
<td>25.3±2.5</td>
<td>0.827</td>
</tr>
<tr>
<td>Duration of BP (Months)</td>
<td>4.8±1.1</td>
<td>4.7±1.3</td>
<td>0.634</td>
</tr>
</tbody>
</table>

SW (shock wave), KE (Kabat Exercise)

At baseline measurement, there were no significant differences in the degeneration index and the amplitude between the two groups but there is high significance difference after treatment, favoring to SW group (Table 2,3).

**Table 2. The degeneration index of facial nerve recorded from nasalis muscle**

<table>
<thead>
<tr>
<th>Variables</th>
<th>SW Group n=30</th>
<th>KE Group n=30</th>
<th>p-value**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Degeneration index of facial nerve</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>from nasalis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>75%±2%</td>
<td>75%±3%</td>
<td>0.295</td>
</tr>
<tr>
<td>After treatment</td>
<td>30%±3%</td>
<td>70%±3%</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

SW (shock wave), KE (Kabat Exercise); (*) Statistically significant

**Table 3. The amplitude of facial nerve recorded from nasalis muscle.**

<table>
<thead>
<tr>
<th>Variables</th>
<th>SW Group n=30</th>
<th>KE Group n=30</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amplitude of facial nerve from nasiles</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>0.6±0.1</td>
<td>0.6±0.1</td>
<td>0.999</td>
</tr>
<tr>
<td>After treatment</td>
<td>1.6±0.2</td>
<td>0.7±0.1</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

SW (shock wave), KE (Kabat Exercise); (*) Statistically significant

**Discussion**

This study demonstrated the positive effect of Li-ESWT on axonal regeneration in patients with axonal degeneration caused by chronic bell’s palsy. The mode of action of low intensity shock wave is still hypothetical. In-vitro shock wave therapy has been shown to speed up the proliferation of Schwann cells and their expression of regenerative phenotype-associated...
markers including glial fibrillary acidic protein and c-Jun (Schuh et al., 2016). In the early stages of regeneration, single-ESW-treated participants had considerably better motor performance and larger nerve fiber counts than controls, according to Hausner et al. (2012). However, after three months, these differences were no longer statistically significant. Instead of an increased absolute number of sprouts crossing the nerve gap, these transient gains may instead be the result of quicker axonal regrowth and subsequently earlier muscular reinnervation.

Early ESWT treatment raised the expression of neurotrophin-3 in the spinal cord, and daily treatment promoted macrophage and Schwann cell activity, which influence the survival and regeneration of neurons in rats after sciatic nerve injury. (Lee et al., 2015)

Hausner et al. found that low-energy ESWT significantly improved nerve regeneration, conduction velocity, and amplitude. Although radial extracorporeal shock wave therapy for nerve damage has received much research, it has not yet been used for trigeminal neuralgia. After two months of rESWT, the patient was successfully treated without any visible side effects, indicating a potential new conservative treatment for trigeminal neuralgia.

After an acute ischemic stroke, extracorporeal shock wave therapy in rats improved neurological function and decreased the size of the cerebral infarct through possible mechanisms that included enriching angiogenesis, preserving neuron cells, and reducing inflammation, cell apoptosis, and oxidative stress. (Yuen et al., 2015)

The effect of ESWT on peripheral nerves has recently attracted a lot of attention. Extracorporeal shock wave therapy significantly decreased diabetic neuropathy in a murine experimental setting by decreasing the mRNA expressions of inflammatory (MMP-9, TNF-, and iNOS), oxidative stress (NOX-1 and NOX-2), and apoptosis-related genes (Bax and caspase 3), and increasing the mRNA expressions of antioxidants (HO-1 and NQO1). According to in vitro studies, All ESWT restored the higher protein expressions of oxidative stress, inflammation, apoptosis, and DNA damage indicators in schwannoma cells treated with a cytotoxic substance (Yuen et al., 2015).

In patients with carpal tunnel syndrome, the most prevalent peripheral entrapment neuropathy that includes compression of the median nerve in the carpal tunnel, RESWT (Radial Extra-corporeal Shock Wave Therapy) is safe and most efficieint for reducing pain and disability and enhancing the sensory nerve conduction velocity of the median nerve. (Raissi et al., 2017).

**Conclusion**

In conclusion, Li-ESWT seems to be a reliable and secure noninvasive treatment for axonal degeneration in patients suffer from chronic bell’s palsy. after a 6-weeks course of treatment, facial function improved significantly. Li-ESWT improved
nerve conduction amplitude of facial nerve branches. The rational outcome of increased facial function in these people is a higher quality of life. Li-ESWT must demonstrate its efficacy in larger studies with longer follow-up in order to be authorized for the treatment of chronic bell's palsy.

References


