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Comparative Review of the Correlation Between Electroneurography, Electromyography, Hematology Tests, or the Heart Rate Variability Test, with an Improvement in the Severity of Bell's Palsy Symptoms

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ABSTRACT

Background: In this retrospective study, we aimed to determine which diagnostic tests were associated with an improvement in Bell's palsy symptoms.
Methods: There were 30 patients who visited Kyung Hee University Korean Medicine Hospital from April 1, 2017 to February 29, 2020, and who received East-West collaboration treatment for Bell's palsy. The tests included electroneurography (ENoG), electromyography (EMG), hematology, and heart rate variability (HRV) results which were used to determine if any test correlated with improvement of Bell's palsy symptoms.
Results: The initial severity of symptoms did not correlate with the tests performed, with the exception of mean corpuscular hemoglobin concentration (p = 0.013). For both ENoG for oculi degeneration and mean EMG tests, the rate of nerve degeneration showed a significant negative correlation with the improvement of Bell's palsy symptoms. Amongst the HRV test indicators, the square root of the mean of the sum of the squares of differences between the adjacent normal R-R wave interval, the standard deviation of intervals, total power, very low frequency, and high frequency of the wave was negatively correlated with improvement of Bell's palsy symptoms. Similarly, glycosylated hemoglobin Type A1c (HbA1c) and erythrocyte sedimentation rate (ESR) showed a negative correlation with improvement of symptoms of Bell's palsy. With the exception of HbA1c and ESR, the remaining hematology test results showed no significant difference when comparing before and after treatment.
Conclusion: ENoG, EMG, HRV test, HbA1c, and ESR negatively correlated with improvements in Bell's palsy symptoms and may determine the prognosis of Bell's palsy.

Introduction

Bell's palsy is a paralysis or weakness of the muscle on one side of the face due to facial nerve damage. The most common symptoms in patients with Bell's palsy are facial palsy or asymmetry, which is sometimes accompanied by other symptoms such as otalgia, loss of taste, dry eye discomfort, tinnitus, hearing loss, and excessive tears. Facial palsy or asymmetry has a dramatic effect on a patient's appearance, psychological wellbeing, and quality of life. Therefore, being able to predict the prognosis of Bell's palsy in a patient using a particular diagnostic test, is valuable [1].

While prognostic evaluation is controversial, several tools have been proposed for management of treatment [2]. Electroneurography (ENoG) and electromyography (EMG) provide relatively accurate prognosis of Bell's palsy by measuring degeneration of affected nerve fibers [3-6].

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The heart rate variability (HRV) test which measures the variation in time interval between heart beats has been used for assessing the influence of the autonomic nervous system (ANS) [7]; changes in ANS have been studied to discern whether they affect the prognosis of Bell's palsy. In a study by Kim et al [8], the standard deviation of the R-R intervals (SDNN) was shown to have a significant correlation with mean axonal loss when measured using EMG, indicating its value was a prognostic factor; however, they reported the limitation that SDNN did not correlate with improvement in Bell's palsy symptoms.

In a study by Park et al [1], diabetes mellitus, and hypertension showed a correlation with improvement of Bell's palsy symptoms. Similarly, neutrophil to lymphocyte ratio and platelet to lymphocyte ratio have been reported to correlate with improvement of Bell's palsy symptoms [9,10]. Based on these findings, hematology tests including fasting blood sugar, HbA1c, erythrocyte sedimentation rate (ESR), and white blood cell differential counts were conducted on patients hospitalized for Bell's palsy.

Several studies have investigated ENoG, EMG, HRV, or hematology tests for Bell's palsy [1-5]. However, it is necessary to determine whether these findings are reasonably consistent because individual studies have reported various characteristics, and there has been no overall study of all these tests. In addition, there are few studies that have investigated whether the tests reflect improvement in severity of the initial symptoms.

Therefore, the aim of this study was to determine whether there were any correlations between ENoG, EMG, the hematology and the HRV test indicators, and improvement and initial severity of Bell's palsy symptoms.

Materials and Methods

Patient selection

This was a retrospective study based on a review of medical records of patients who visited Kyung Hee University Hospital, Gangdong, from April 1, 2017 to February 29, 2020, who received East-West collaboration treatment (EWCT) for Bell's palsy. All patients were selected within 8 days of the onset of unilateral acute Bell's palsy and were hospitalized for more than 10 days, followed by outpatient treatment for at least 2 months. Patients below a House-Brackmann Grade 3 and those with acute or chronic otitis media, trauma, tumor, Ramsay-Hunt syndrome, congenital facial palsy, or history of autonomic neuropathy were excluded from the study population.

Patients received EWCT at the Facial Palsy Center of Kyung Hee University Hospital, Gangdong (Fig. 1). During hospitalization, patients were treated with high dose oral corticosteroid, antivirals, physical therapy, daily electroacupuncture, pharmacopuncture, moxibustion, and herbal medicines. Outpatients were treated using electroacupuncture, pharmacopuncture, and herbal medicine at every visit.

Due to the retrospective nature of this study approval by the Institutional Review Board was waivered.

Methods

Clinical evaluation

A total of 30 patients with acute unilateral Bell's palsy within 8 days of onset were selected for this retrospective study. The initial severity of facial palsy was measured using the House-Brackmann grade scale (HBGS) to detect the most severe grade of Bell's palsy in the acute stage. Recovery rate was measured using the normalized HBGS improvement index of Bell's palsy [(initial HBGS - last HBGS)/ initial HBGS × 100 (%)] at the end of the course of treatment. The House-Brackmann grade was used to evaluate paralysis to be correlated with prognosis [11].

Electrical testing

Thirty patients with acute unilateral Bell's palsy were evaluated with ENoG within 3-9 days of onset. ENoG was performed on the healthy side first and then on the affected side (on the nasalis and orbicularis oculi muscles). EMG was performed within 12-16 days of onset of Bell's palsy. EMG was performed by stimulation of the facial nerve terminal branches (zygomatic, temporal, and buccal) followed by the recording of the compound muscle action potentials (CMAP) from the facial muscles supplied by these branches. Facial nerve degeneration rate was calculated using the following equation: 1-affected/unaffected amplitude of CMAP recorded in the frontalis muscle or orbicularis muscle (peak to peak of the CMAP) × 100%.

HRV testing

The HRV test was conducted by attaching the McPulse (Meridian Co., Ltd., Seoul, Korea) sensor device to the patient who had not consumed a caffeinated drink, smoked within 2 hours, and had rested 5 minutes prior to the test.

Hematology tests

All patients had blood collected at their admission to hospital. A complete blood count, white blood cell differential count, liver function test and HbA1c, ESR, serum glucose, cholesterol, and albumin levels were conducted to determine the underlying history of the patients.

Statistical analysis

Descriptive statistics about age, outpatient treatment number,

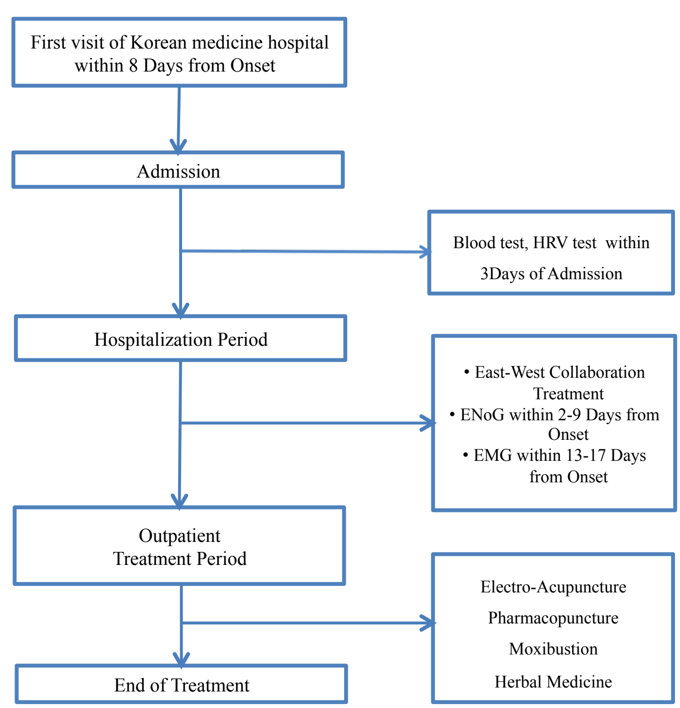

Fig 1. Flow chart of East-West collaboration treatment.
EMG, electromyography; ENoG, electroneurography; HRV, heart rate variability.

duration from onset of Bell's palsy to initial treatment, length of hospitalization, period of dosing with herbal medicine, and total treatment period were reported as a minimal value, maximal value, mean value, and standard deviation.

The initial HBGS of Bell's palsy was defined as when paralysis was the most severe, and Pearson's correlation analysis was conducted to analyze relationships between therapeutic variation, ENOG, EMG, hematology tests, and HRV test, and initial HBGS of Bell's palsy.

The degree of improvement was defined as the normalized HBGS improvement index (NHII) of Bell's palsy [NHII, (initial HBGS - final HBGS)/initial HBGS × 100 (%)]. Differences in the treatment period among patients may affect the improvement of paralysis therefore, partial correlations of ENoG, EMG, hematology tests, HRV test, and NHII with total treatment period as a covariate were analyzed.

Statistical analyses were performed using SPSS statistics Version 18.0 (IBM Co., Armonk, NY, USA). A value of $p < 0.05$ was considered statistically significant [12].

Results

Patient characteristics

The 30 Bell's palsy patients selected for this retrospective study comprised of 27 females and 3 males. Of these, 20 patients were affected on the right side and 10 on the left. The mean age and standard deviation was 50.87 ± 14.36 years. The mean ± standard deviation of number of outpatient treatments, duration from onset of symptoms to initial treatment of Bell's palsy, length of hospitalization, period of dosing with herbal medicine, and total treatment period (days) were 44.53 ± 36.01, 2.73 ± 2.11, 20.83 ± 7.31, 33.53 ± 11.05, 327.57 ± 267.84 , respectively (Table 1).

Clinical analysis of age and therapeutic variation

Age and therapeutic variation did not correlate with the initial HBGS. However, a significant negative correlation between length of hospitalization, and period of dosing with herbal medicine using the normalized improvement index of Bell's palsy was observed ($p < 0.05$; Table 2).

Table 1. Characteristics of Patients with Bell's Palsy ($n = 30$).

	Min-value	Max-value	Mean-value	SD
Age (y)	15	72	50.87	14.36
Outpatient treatments (No.)	5	139	44.53	36.02
Duration from onset to initial treatment (d)	0	8	2.73	2.17
Length of hospitalization (d)	10	38	20.83	7.32
Herbal medicine dosing (d)	12	66	33.53	11.05
Total treatment period (d)	65	942	327.57	267.84

Max, maximum; min, minimum.

Table 2. Age and Therapeutic Variation Effect on the Initial HBGS and Improvement of Bell's Palsy Symptoms.

		Initial HBGS	Normalized HBGS improvement index
Age	Pearson correlation	0.228	0.192
	p	0.225	0.317
No. outpatient treatments	Pearson correlation	0.295	0.081
	p	0.114	0.675
Duration from onset to initial treatment	Pearson correlation	0.281	0.153
	p	0.132	0.428
Length of hospitalization	Pearson correlation	-0.098	-0.623**
	p	0.607	< 0.001
Herbal medicine dosing	Pearson correlation	0.151	-0.437*
	p	0.426	0.018

* Correlation is significant at the $p < 0.05$ level (2-tailed).
** Correlation is significant at the $p < 0.01$ level (2-tailed).
HBGS, House-Brackmaan grade scale.

Correlations between clinical evaluation, electroneurography, and electromyography

Correlations between ENoG, EMG, and the initial HBGS showed no statistical significance; however, there was a significant correlation of NHII with both ENoG oculi degeneration and mean degeneration as detected by EMG ($p < 0.05$; Table 3). High degeneration of oculi detected using ENoG, and high degeneration of the temporal branch and buccal branch detected using EMG were related to a low improvement of Bell's palsy symptoms.

Correlations between clinical evaluation, hematology tests, and HRV test

Hematology test results are summarized in Table 4. Mean corpuscular hemoglobin concentration showed a statistically significant correlation with the initial HBGS, while HbA1c and ESR showed statistically significant correlations with NHII ($p < 0.05$). Other hematology test results showed no significant correlation ($p > 0.05$). The HRV test indicator results are summarized in Table 5. There were no correlations between HRV test indicator

Table 3. Correlations of Nerve Degeneration Detected by ENoG and EMG with the Initial HBGS and Normalized HBGS Improvement Index.

		Initial HBGS	Normalized HBGS improvement index
ENoG detection of nasalis nerve degeneration	Pearson correlation	0.234	-0.333
	p	0.213	0.078
ENoG detection of oculi nerve degeneration	Pearson correlation	0.103	-0.381*
	p	0.587	0.042
EMG detection of temporal branch nerve degeneration	Pearson correlation	0.105	-0.392*
	p	0.582	0.036
EMG detection of buccal branch nerve degeneration	Pearson correlation	0.272	-0.236
	p	0.146	0.217
EMG detection of zygomatic branch nerve degeneration	Pearson correlation	0.356	-0.414*
	p	0.054	0.025
Mean EMG	Pearson correlation	0.280	-0.408*
	p	0.134	0.028

* Correlation is significant at the $p < 0.05$ level (2-tailed).
** Correlation is significant at the $p < 0.01$ level (2-tailed).
EMG, electromyography; ENOG, electroneurography; HBGS, House-Brackmaan grade scale.

Table 4. Correlations Between the Hematology Tests, the Initial HBGS, and Normalized HBGS Improvement Index.

		Initial HBGS	Normalized HBGS improvement index
HBA1c	Pearson correlation	-0.160	-0.643*
	p	0.467	0.010
WBC	Pearson correlation	0.182	-0.046
	p	0.335	0.870
RBC	Pearson correlation	-0.222	-0.390
	p	0.239	0.151
Hb	Pearson correlation	0.111	0.151
	p	0.558	0.492
Hct	Pearson correlation	-0.046	0.097
	p	0.810	0.730
MCV	Pearson correlation	0.180	0.453
	p	0.340	0.090
MCH	Pearson correlation	0.302	0.434
	p	0.105	0.106

Table 4. (Continued).

		Initial HBGS	Normalized HBGS improvement index
MCHC	Pearson correlation	0.448*	0.321
	p	0.013	0.243
PLT	Pearson correlation	0.104	-0.075
	p	0.584	0.790
MPV	Pearson correlation	-0.012	-0.435
	p	0.951	0.105
ESR	Pearson correlation	0.089	-0.519*
	p	0.639	0.047
ANC	Pearson correlation	0.082	-0.073
	p	0.666	0.795
Neutrophil segment	Pearson correlation	-0.166	-0.172
	p	0.380	0.539
Lymphocyte	Pearson correlation	0.176	0.121
	p	0.352	0.668
Monocyte	Pearson correlation	-0.017	0.384
	p	0.928	0.157
Eosinophil	Pearson correlation	0.132	-0.004
	p	0.488	0.988
Basophil	Pearson correlation	0.360	0.110
	p	0.051	0.697
Serum glucose	Pearson correlation	-0.009	-0.494
	p	0.964	0.062
Protein	Pearson correlation	0.103	-0.393
	p	0.588	0.147
Albumin	Pearson correlation	-0.153	-0.152
	p	0.421	0.589
Cholesterol	Pearson correlation	-0.001	-0.302
	p	0.994	0.274
Total bilirubin	Pearson correlation	0.253	0.183
	p	0.177	0.513
AST	Pearson correlation	0.193	0.282
	p	0.307	0.308
ALT	Pearson correlation	0.322	0.261
	p	0.082	0.348
ALP	Pearson correlation	0.141	-0.128
	p	0.458	0.649
GGT	Pearson correlation	0.109	0.244
	p	0.648	0.381

* Correlation is significant at the $p < 0.05$ level (2-tailed).
** Correlation is significant at the $p < 0.01$ level (2-tailed).
ALP, alkaline phosphatase; ALT, alanine transaminase; ANC, absolute neutrophil count; AST, aspartate aminotransferase; ESR, erythrocyte sedimentation rate; GGT, gamma-glutamyl transferase; Hb, hemoglobin; HbA1c, hemoglobin Type A1c; HBGS, House-Brackmaan grade scale; Hct, hematocrit; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; MCV, mean corpuscular volume; MPV, mean platelet volume; PLT, platelet count test; RBC, red blood cell; WBC, white blood cell

Table 5. Correlations Between the HRV Tests, and the Initial HBGS, and Normalized HBGS Improvement Index.

		Initial HBGS	Normalized HBGS improvement index
LF norm	Pearson correlation	0.100	0.224
	p	0.600	0.243
HF norm	Pearson correlation	-0.130	-0.224
	p	0.492	0.242
LF/HF ratio	Pearson correlation	0.182	0.212
	p	0.335	0.270
SRD	Pearson correlation	0.131	0.345
	p	0.490	0.067
Total power	Pearson correlation	-0.253	-0.465*
	p	0.177	0.011
VLF	Pearson correlation	-0.340	-0.522**
	p	0.066	0.004
LF	Pearson correlation	-0.169	-0.305
	p	0.372	0.108
HF	Pearson correlation	-0.116	-0.435*
	p	0.540	0.018
Mean HRT (bpm)	Pearson correlation	-0.211	-0.321
	p	0.263	0.089
SDNN	Pearson correlation	-0.269	-0.398*
	p	0.150	0.033
RMSSD	Pearson correlation	-0.109	-0.408*
	p	0.566	0.028
PSI	Pearson correlation	0.099	0.186
	p	0.602	0.333
ApEn	Pearson correlation	0.082	-0.158
	p	0.667	0.412

* Correlation is significant at the $p < 0.05$ level (2-tailed).
** Correlation is significant at the $p < 0.01$ level (2-tailed).
ApEn, approximate entropy; HF, high frequency; HRT, heart rate; LF, low frequency; VLF, very low frequency; PSI, pound force per square inch; RMSSD, square root of the mean of the sum of the squares of differences between adjacent normal R-R intervals; SDNN, standard deviation of R-R intervals; VLF, very low frequency.

results and the initial HBGS. However, SDNN, the square root of the mean of the sum of the squares of differences between the adjacent normal R-R wave interval (RMSSD), total power, very low frequency (VLF) and high frequency (HF) waves showed statistically significant correlations with the normalized HBGS improvement index ($p < 0.05$).

Discussion

Bell's palsy is the most common cause of unilateral facial palsy, but its pathologic cause and prognostic evaluation are controversial [12]. Many studies have reported the prognostic value of ENoG and EMG for Bell's palsy, and these 2 tests have been actively used in clinical practice [3-6]. In a study by Kim et al [8], the HRV test showed the possibility as a prognostic factor, but it had a limitation in that results were not related to the improvement in Bell's palsy symptoms. In a study by Park et al [1], age, season of onset, hypertension, diabetes, fasting blood sugar, and the number of treatments were related to the prognosis of Bell's palsy.

Nevertheless, these studies are not sufficient to confirm a reasonably consistent conclusion. To provide further information, this study was designed to identify the prognostic values of ENoG, EMG, HRV, and hematology tests in Bell's palsy prognoses. In addition, any correlation between the initial grade of severity and test results was analyzed to identify whether 1 particular test used was more related to the initial severity, or improvement of Bell's palsy symptoms.

In this study, degeneration detected by using ENoG and EMG did not show significant correlation with initial symptoms but did show statistically significant negative correlations with improvement of Bell's palsy (Table 3). This result indicated that the ENoG and EMG results are related to improvement in symptoms rather than the initial severity of Bell's palsy. In addition, since there was no significant correlation in degeneration of nasalis nerve using ENoG or in that of the zygomaticus branch nerve using EMG, a comprehensive rather than single reading of ENoG and EMG are required for an accurate prognosis.

The HRV test did not correlate with the initial severity, while several values (RMSSD, SDNN, TP, VLF, HF) showed a correlation with the improvement rate of Bell's palsy symptoms (Table 5). Therefore, it appears that the HRV test may be related to improvement of Bell's palsy rather than to initial severity. In a study by Leal [13], the sympathetic nerve system (SNS) was reported to be responsible for the "fight or flight" response to threatening situations, and diverse stimuli such as stressors, cytokines, and infection triggered the SNS to release catecholamine, enhance host defenses to eliminate pathogens, and promote healing after tissue injury. This early reaction of the SNS induces functional alterations in the immune system and ultimately allows a smooth recovery in the state of inflammation. However, in situations where there is constant hyperactivity of the PNS, the SNS response decreases, which can adversely affect recovery, suggesting that parasympathetic hyperactivity could decrease the improvement in Bell's palsy symptoms.

Among the HRV indicators, RMSSD, SDNN, TP, and HF showed a significant negative correlation with improvement of Bell's palsy symptoms (Table 5); except for TP, these components increase when the PNS is hyperactive [14,15]. Thus, it appears that hyperactivity of the PNS can slow the improvement of Bell's palsy symptoms by decreasing activity of the SNS when in a state of inflammation.

Conversely, in the aforementioned study by Kim et al [8], there was no significant correlation between the indicators of the HRV test and improvement of Bell's palsy symptoms. Nevertheless, the authors defined improvement of paralysis as the difference between HBGS at the 1st examination and the HBGS in the 2nd week. This is an insufficient period of time to measure the degree of improvement of paralysis, considering that Wallerian degeneration of nerve axons occurs for about 7 days [16]. Therefore, to compensate for these limitations, this study was conducted on patients who were followed for at least 2 months so that a clearer conclusion could be obtained.

In this study, HbA1c statistically significantly correlated with normalized HBGS improvement index but not with initial HBGS of severity. This result suggested that HbA1c is related to improvement of symptoms of Bell's palsy rather than the initial severity. The relationship between HbA1c and improvement rate showed a negative correlation, indicating that hyperglycemia can adversely affect improvement of Bell's palsy symptoms. Therefore, strict blood sugar management is needed to increase the improvement rate of Bell's palsy symptoms.

The ESR is associated with systematic illnesses and measures the rate at which erythrocytes settle in the plasma of an anticoagulated blood specimen over a specified period of time (usually 60 minutes) in millimeters (mm)/hour [17]. There are few reports where ESR tests are used in Bell's palsy, and the prognostic value for Bell's palsy for inflammation markers such as neutrophil to lymphocyte ratios and platelet to lymphocyte ratios has been reported [9,10]. In this study, ESR was not associated with the initial severity of Bell's palsy symptoms, but ESR was adversely affected with the improvement of symptoms (Table 4), which suggests that the more severe the inflammatory reaction, the lower is the improvement; in clinical practice, this should be considered to expedite recovery.

This study was conducted to confirm prognostic values and determine whether the initial HBGS of severity of Bell's palsy was reflected and drew the following conclusions. Initial severity did not correlate with results from the tests performed, and ENoG, EMG, the HRV test, HbA1c, and ESR significantly negatively correlated with predicting Bell's palsy symptom improvement. Therefore, while it is reasonable to use these tests as a tool for prognosis, they should not be used to determine symptom severity.

ENOGs and EMG have shown prognostic value for Bell's palsy in many studies, and the results of this study support this finding. Furthermore, this study determined that the level of inflammation as measured using ESR, hyperglycemia, and parasympathetic hyperactivity have a prognostic value. Therefore, it seems that the use of HRV and hematology tests in addition to the existing electrical tests will be helpful in determining the prognosis of Bell's palsy.

However, in the course of this study, there were limitations. Firstly, individualized treatments, such as variations in acupuncture treatment and in herbal medicine, reduced the level of control. Secondly, the subjective opinions of researchers were reflected in their use of the HB grading system. Therefore, further study with an improved design should be conducted. In addition, even though acupuncture stimulation modulates the ANS by changing the somatosensory reflex and the flow of extravascular fluid [17], it appeared that the response to treatment for patients with Bell's palsy was poor when the PNS was hyperactive. Moreover, it was difficult to evaluate the effect of a single treatment because patients received complex EWCT. Despite these treatments, parasympathetic hyperactivity showed an adverse effect on the improvement of Bell's palsy symptoms, so it is necessary to investigate the mechanism of the adverse effect of hyperactive PNS on treatments individually used.

Conclusion

In this study, we investigated 30 patients diagnosed with Bell's palsy and analyzed the results of ENoG, EMG, the HRV test, and the hematology tests to identify the relationship of initial severity of symptoms and improvement of symptoms of Bell's palsy; ENoG, EMG, HRV test, HbA1c, and ESR showed statistically significant negative correlations in predicting improvement in Bell's palsy symptoms. We suggest that use of HRV test indicators and hematology tests in addition to the currently used electrical test, as these may be helpful in determining the prognosis of Bell's palsy.

Conflicts of Interest

The authors have no conflicts of interest to declare. None of the authors have any personal, financial, or institutional interest in any of the materials or devices described in this article. We identified no conflicts of interests.

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