Original Article

The importance of serum paraoxonase, arylesterase and ischemia modified albumin levels in evaluation of patients with Bell palsy

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ABSTRACT

Objectives: This study aims to evaluate the possible roles of paraoxonase (PON), arylesterase (ARE), ischemia-modified albumin (IMA) and albumin-adjusted IMA levels in patients with Bell palsy.

Patients and Methods: Thirty patients with Bell palsy and 30 healthy control subjects were included in the study. Serum PON, ARE, IMA, albumin-adjusted IMA and lipid profiles were measured.

Results: Paraoxonase and ARE levels of the patient group were significantly lower than controls ($p<0.001$, $p<0.001$, respectively) and IMA, albumin-adjusted IMA levels were significantly higher than controls ($p<0.001$, $p=0.002$, respectively).

Conclusion: This study suggests that oxidative stress may have a role in the pathophysiology of Bell palsy.

Keywords: Arylesterase; Bell palsy; ischemia-modified albumin; oxidative stress; paraoxonase.

The most common type of peripheral facial paralysis is idiopathic facial paralysis or Bell palsy (BP), which accounts for 60-70% of all facial paralyses.[1] Bell palsy is an idiopathic, acute, unilateral paralysis of the facial nerve.[2] The incidence is 15-40/100,000. It is seen most frequently between the ages of 15-40 with equal frequency among men and women.[1] The cause of BP is not fully known, but vascular ischemia, autoimmune diseases, genetic and viral inflammation have been proposed.[3]

Oxidative stress involves an imbalance between the production of free radicals and the ability of the body to neutralize their harmful effects by antioxidant mechanisms.[4] Paraoxonase 1 (PON1) is an enzyme with a glycoprotein structure having both PON and arylesterase (ARE) activity.[5] Paraoxonase 1 is an antioxidant enzyme linked to plasma high-density lipoprotein (HDL) and it has shown to protect low-density lipoprotein (LDL) from oxidation by free radicals and to reduce oxidative stress.[6]

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Systemic markers of oxidative stress include ischemia-modified albumin (IMA).[7] When tissue ischemia occurs, the circulating albumin is structurally altered. As a result of this change, the cobalt binding property of albumin decreases and it cannot bind with this metal. This newly formed albumin is called IMA.[8]

To our knowledge, there are no studies conducted to date on BP that evaluate levels of PON, ARE and IMA. Therefore, we aimed to investigate the combined relationship of PON, ARE and IMA concentrations in the evaluation of patients diagnosed with BP.

PATIENTS AND METHODS

This study was a collaboration between Ankara Numune Training and Research Hospital Medical Biochemical clinic and Otorhinolaryngology clinic. It was performed prospectively in November 2017. Thirty adult BP patients and 30 adult controls without any systemic disease were included in this study. The diagnoses of the patients were made by an otolaryngologist.

Blood samples were collected from all participants after overnight fasting. All samples were centrifuged at 1200 g for 15 minutes and separated sera were stored at -80°C until the time of analysis. Serum total cholesterol, high density lipoprotein (HDL) cholesterol, Low density lipoprotein (LDL) cholestrol, triglycerides (TG) and albumin were analyzed by routine biochemical procedures. Measurements were performed by using Beckmann Coulter AU5800 (Beckmann Coulter Inc., Brea, CA, USA) analyzer. Paraoxonase 1 and ARE activity were measured by photometric assay. Paraoxonase 1 and ARE activities were expressed as U/L.[9,10] Paraoxonase and ARE kit (Rel Assay Diagnostics, Turkey) measurements were performed using Beckmann Coulter AU 680 (Beckmann Coulter, Inc., Brea, CA, USA) analyzer. Ischemia-modified albümin was measured by a colorimetric assay developed by Bar-Or et al.[11] based on measurement of unbound cobalt after incubation with patient serum. Ischemia-modified albumin was measured by using a spectrophotometer (Metertech Inc., Nangang, Taipei, Taiwan). The results were reported as absorbance unit (ABSU). All tests were performed on the same day. Albumin-adjusted IMA was calculated according to the following formula: (Individual

Table 1. Mean ages, gender distribution, PON, ARE, IMA, albumin, HDL, LDL, cholesterol, TG, albumin-adjusted IMA levels of patient and control groups

	Bell palsy group (n=30)				Control group (n=30)				
	n	Mean±SD	Median	Min-Max	n	Mean±SD	Median	Min-Max	*p**
Age (year)		33.6±8.3				31.1±6.4			0.189
Gender									0.609
Male	14				16				
Female	16				14				
PON (U/L)			71.10	30-162			109.47	38-189	<0.001
ARE (U/L)		1131.6±255.2				1412.1±264.2			<0.001
IMA (ABSU)		0.6±0.1				0.5±0.1			<0.001
Albumin (g/dL)		4.9±0.5				4.1±0.3			<0.001
HDL (mg/dL)		54.3±9.1				49.2±9.5			0.035
LDL (mg/dL)		157.2±46.7				90.8±19.1			<0.001
Cholesterol (mg/dL)		260.7±54.4				159.4±26.2			<0.001
TG (mg/dL)			255.10	79-636			107.6	40-326	<0.001
Albumin-adjusted IMA (ABSU)		0.6±0.1				0.5±0.1			0.002

PON: Paraoxonase; ARE: Arylesterase; IMA: Ischemia modified albumin; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; SD: Standard deviation; Min: Minimum; Max: Maximum; ABSU: Absorbans unit; * Student t test and Mann-Whitney U tests.

serum albumin concentration/median albumin concentration of the population) × IMA value.[12]

This study was conducted at Ankara Numune Teaching and Research Hospital with approval of the local Ethics Committee (E-17-1632). Informed consent for participation in the study was obtained from all participants. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Statistical analysis

Data were analyzed with PASW version 18.0 for Windows (SPSS Inc., Chicago, IL, USA). Distributions of the groups were analyzed using the Kolmogorov-Smirnov test. Numerical variables were expressed as mean ± standard deviation or median (minimum-maximum) values. Additionally, parametric variables were compared using the Student t-test, whereas non-parametric continuous variables were compared with the Mann-Whitney U test. A *p* value of less than 0.05 was considered significant.

RESULTS

Thirty patients with BP (14 males, 16 females; aged 33.6±8.2 years; range 20 to 49 years) and 30 controls (16 males, 14 females; aged 31.1±6.4 years; range 20 to 47 years) were included in this study. Differences between age and sex were not statistically significant (p>0.05).

Paraoxonase, ARE, IMA, albumin, HDL, LDL, cholestrol, TG, albumin-adjusted IMA levels of patient and control groups are listed in Table 1.

Paraoxonase and ARE levels in the patient group were significantly lower than those in the control group (p<0.001). Paraoxonase and ARE levels of control and patient groups are shown in Figures 1 and 2 respectively.

Patient group IMA and albumin-adjusted IMA levels were significantly higher than control group levels (p<0.001, p=0.002, respectively). Ischemia-modified albumin and albumin-adjusted IMA levels of control and patient groups are shown in a Box-Whisker plot in Figure 3, Figure 4, respectively.

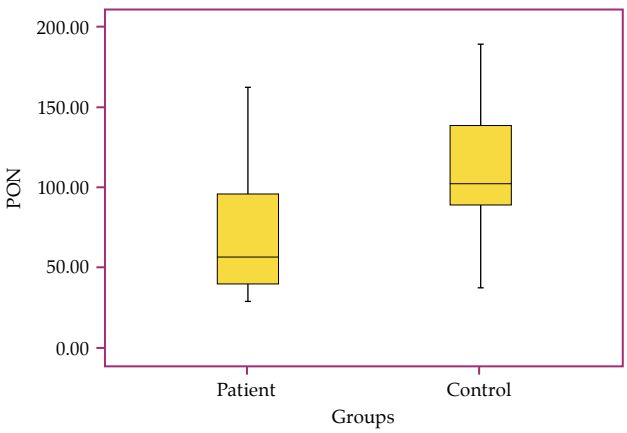

Figure 1. Box and whisker plot showing the distribution of serum PON levels in patient and control groups.
PON: Paraoxonase.

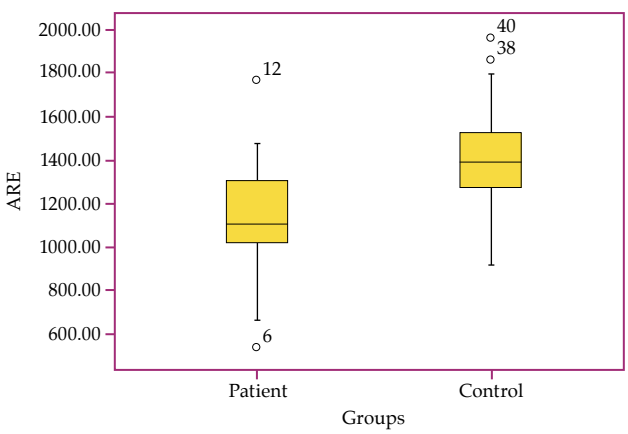

Figure 2. Box and whisker plot showing the distribution of serum ARE levels in patient and control groups.
ARE: Arylesterase.

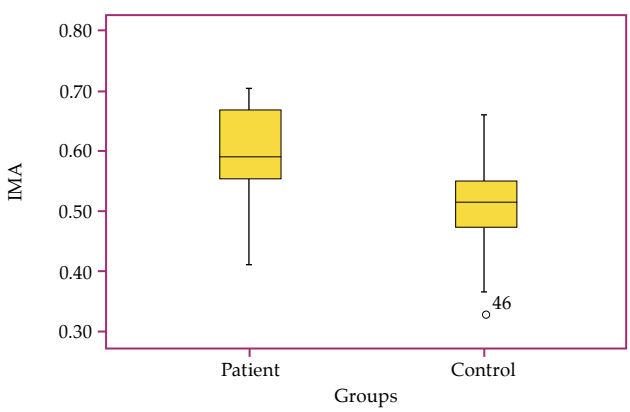

Figure 3. Box and whisker plot showing the distribution of serum IMA levels in patient and control groups.
IMA: Ischemia modified albumin.

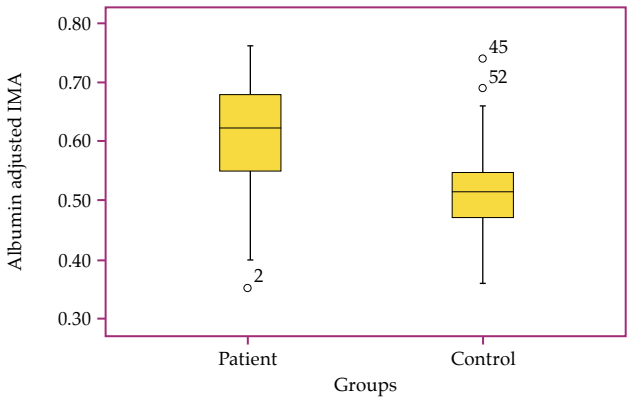

Figure 4. Box and whisker plot showing the distribution of serum albumin adjusted IMA levels in patient and control groups.

IMA: Ischemia modified albumin.

Albumin, HDL, LDL, cholestrol, and TG levels of patients were significantly higher than controls ($p<0.001$, $p=0.035$, $p<0.001$, $p<0.001$, $p<0.001$, respectively).

DISCUSSION

Bell palsy is an idiopathic, acute peripheral facial nerve paralysis (PFP) usually affecting only one side of the face. The cause of BP is unclear, but viral infections, vascular ischemia and autoimmune disorders have all been postulated as possible mechanisms.[3]

Oxidative stress is defined as the accumulation of reactive oxygen species in the body when the antioxidant capacity is not enough. One of the most common side effects of oxidative stress is DNA damage and endothelial dysfunction, which may underlie various diseases.[13]

Paraoxonase 1 is an antioxidant and anti-inflammatory enzyme associated with HDL. Paraoxonase 1 has PON and ARE activities. The enzyme prevents oxidation of serum lipoproteins and its activity is sensitive to oxidative stress. An oxidative medium causes a decrease in the enzyme activity of PON.[14,15] Our data showed that serum PON and ARE activities were significantly lower in patients with BP compared with controls.

The mechanism of the observed decrease in serum PON and ARE activities in BP patients remains unclear. This decrease could be related to enhanced lipid peroxidation, since an increased number of lipid and protein oxidation products and decreased number of antioxidant enzymes has been reported to affect the expression and activities of PON1.[9,16] It was also seen that LDL, TG and total cholesterol levels in the patient group were significantly higher than in the control group. This may also support the fact that higher levels of lipids cause an increase in oxidative stress. The mean age of the patient group was 33, and the patients were known not to have any cardiovascular risks for an increased lipid profile, so this increase in blood lipid levels may be evaluated in conjunction with decreased PON activity in BP patients as markers of oxidative stress.

Excess of ROS may produce a chemical modification of serum albumin resulting in increased IMA. For this reason, IMA appears to serve as an effective oxidative stress biomarker. Serum IMA levels have a close relationship with oxidative balance. An inadequate antioxidant level may lead to increased IMA levels.[17,18] Our results showed that IMA and albumin-adjusted IMA in the patient group were significantly higher than the control group which also supports our findings of increased oxidative stress in BP patients.

The present study is novel in that it investigates serum PON, ARE, IMA and albumin-adjusted IMA levels and lipid profile in patients with BP.

A major limitation of our study is its cross-sectional design. The data were obtained from only a single center, and patient selection bias was not completely avoided. This can be considered a pioneer study for larger-scale clinical trials that may be planned in the future.

In conclusion, the decrease in PON1 and ARE activity and the increase in IMA and albumin-adjusted IMA levels in patients with BP suggest that oxidative stress may play a role in the pathophysiology of BP.

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Declaration of conflicting interests

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