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Evaluation of serum ischaemia-modified albumin levels in patients with Bell's palsy

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Abstract

Objective. This prospective study aimed to evaluate the relationship between serum ischaemia-modified albumin levels and Bell's palsy severity.

Methods. The study included 30 patients diagnosed with Bell's palsy and 30 healthy individuals. The patients were separated into three disease severity groups (grades 2, 3 and 4) according to House–Brackmann classification. Blood samples were collected from all participants and the results compared between groups.

Results. Significant differences in serum ischaemia-modified albumin were found between the study and control groups ($p < 0.001$); values were significantly higher in the study group than in the control group.

Conclusion. The significantly higher levels of serum ischaemia-modified albumin in the study group suggest that Bell's palsy pathogenesis is associated with oxidative stress.

Main Article

Dr A E Göker takes responsibility for the integrity of the content of the paper

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Introduction

Bell's palsy, the idiopathic facial paralysis condition named by Scottish anatomist Sir Charles Bell, is an acute-onset mononeuropathy, in which a single nerve is affected.[1] It is characterised by the complete or partial loss of motion on one side of the face, often beginning with pain in the mastoid region.[2]

Oedema and ischaemia occurring at one or more segments of the facial nerve, caused by a viral infection or autoimmune reaction, is the most common hypothesis for Bell's palsy pathophysiology.[3,4] The activation of herpes simplex or herpes zoster virus is the most commonly hypothesised cause of viral infection.[5]

In recent years, reactive oxygen species due to vascular ischaemic damage have been the main focus in studies on patients with Bell's palsy. A number of studies have been conducted, with some indicating that ischaemia-modified albumin can be used as a biomarker of oxidative stress and ischaemia that occurs through hypoxia of the tissue.[6,7] Ischaemia-modified albumin is a well-known biomarker of ischaemia-based diseases, such as acute mesenteric ischaemia, cerebrovascular disease, acute pulmonary embolism and acute coronary syndrome.[8,9]

This study aimed to investigate the serum ischaemia-modified albumin level in patients with Bell's palsy, based on reports that it can be used as a biochemical marker given the elevated levels in ischaemic reactions. This study also investigated whether serum ischaemia-modified albumin values may be measured in facial nerve ischaemia, which is thought to be one of the aetiologies in Bell's palsy.

Materials and methods

Patients and study design

Thirty patients diagnosed with Bell's palsy were included in the study. The patients' ages were between 18 and 67 years. The study group was compared to a control group consisting of 30 healthy individuals. The Bell's palsy patients were separated into three disease severity groups (grades 2, 3 and 4) using the House–Brackmann classification system. There were no patients with Bell's palsy (House–Brackmann) grades 1 or 5.

Patients admitted to the emergency services of the University of Health Sciences, Okmeydani Training and Research Hospital, with tingling sensations on one side of the face and difficulties moving the facial muscles were referred to the ENT clinic. The House–Brackmann facial paralysis grading system was used to grade the Bell's palsy patients within the study group. Patients who presented to us within the first 8 hours after disease onset were included in the study. The voluntary control group comprised healthy individuals with no disease or drug use history.

The exclusion criteria were as follows: age under 18 years, acute or chronic systemic disease or infection, diabetes mellitus, hyperlipidaemia, hypertension, pregnancy and lactation, and previous diagnosis of Bell's palsy.

Table 1. Comparison of age, total protein, albumin and ischaemia-modified albumin levels between groups

Parameter	Study group*	Control group†	*p*
Age (mean ± SD; years)	43.3 ± 12.2	38.4 ± 8.1	0.074
Total protein (mean ± SD; g/dl)	6.9 ± 0.6	6.9 ± 0.4	0.763
Albumin (mean ± SD; g/dl)	4.2 ± 0.3	4.3 ± 0.3	0.072
Ischaemia-modified albumin (median (25–75 percentile); ng/ml)	24.8 (10.5–91.0)	6.0 (1.1–18.3)	<0.001‡

*$n = 30$; †$n = 30$. ‡Indicates $p < 0.05$ (Mann–Whitney U test). SD = standard deviation

The patients in the study group received the following treatments after the Bell's palsy diagnosis: prednisolone (1 mg/kg per day), proton pump inhibitors and vitamin B complex. Prednisolone was used in all patients with Bell's palsy of less than 72 hours' duration for whom there were no contraindications to steroid therapy. The dose used was 60 mg per day for 5 days, which was subsequently reduced by 10 mg per day (for a total treatment time of 10 days). No adverse events were reported.

Our work was approved by the University of Health Sciences, Okmeydani Training and Research Hospital Ethics Committee, and designed in accordance with the Helsinki declaration.

Biochemical parameters

Patients with Bell's palsy underwent detailed examination. Haemogram and ischaemia-modified albumin level blood tests were performed within the first 8 hours of admission, prior to beginning prednisolone treatment. For these tests, blood samples were centrifuged at 4000 revolutions per minute for 10 minutes, after which time the samples were stored at −80°C until examination. The blood samples in the control group were studied in the same way.

Ischaemia-modified albumin levels were measured with a serum enzyme-linked immunosorbent assay testing kit (human ischaemia-modified albumin, catalogue number E-EL-H5422; Elabscience, Wuhan, China). The sandwich enzyme-linked immunosorbent assay method was used. The results were expressed in nanograms per millilitre (ng/ml).

The micro-enzyme-linked immunosorbent assay plate provided in this kit is pre-coated with an ischaemia-modified albumin-specific antibody. Standards or samples are added to appropriate wells of the micro-enzyme-linked immunosorbent assay plate and combined with the specific antibody. A specific biotin-fixing antibody for ischaemia-modified albumin and avidin-horseradish peroxidase conjugation is then added to each microplate and mixed thoroughly, and the microplates are incubated.

Free components are washed away, and the substrate solution is added to each of the wells. Only wells containing ischaemia-modified albumin, a biotinylated detection antibody and avidin-horseradish peroxidase conjugate appear blue. The enzyme-substrate reaction is terminated by the addition of a sulphuric acid solution, and the colour turns yellow.

The optical density is measured spectrophotometrically at a wavelength of 450 ± 2 nm. The optical density value is proportional to the ischaemia-modified albumin concentration. By comparing the samples' optical density values with the standard curve, the ischaemia-modified albumin concentrations of the samples are calculated. The co-efficients of intra- and inter-assay variation were 6.8 per cent ($n = 10$) and 7.6 per cent ($n = 10$), respectively.

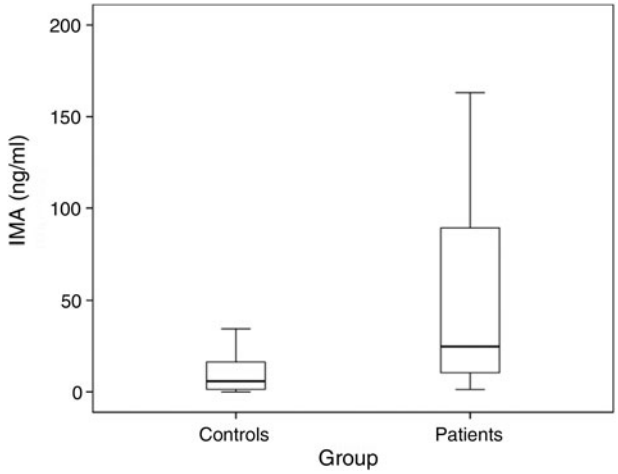

Fig. 1. Serum ischaemia-modified albumin (IMA) levels in Bell's palsy patients and healthy controls. Horizontal lines represent the mean value for each group.

Statistical analysis

Data analyses were performed using SPSS statistical software (version 17.0; SPSS, Chicago, Illinois, USA). The normal distribution of the data was assessed with the Shapiro–Wilk test. Among numerical variables, those with a normal distribution were expressed as means ± standard deviation, and those without normal distribution were shown as medians (interquartile range). Categorical variables were indicated by a number and percentage. The student's *t*-test was used to compare two groups of numerical variables with normal distributions, and the Mann–Whitney U test was used to compare two groups of numerical variables without normal distributions. In comparisons of three or more groups, the Kruskal–Wallis test was used. The correlation co-efficients were derived using Pearson's correlation test. A *p*-value of less than 0.05 was considered statistically significant.

Results

Our study included 60 participants: 29 (48 per cent) were male and 31 (52 per cent) were female. The mean age was 40.33 ± 10.58 years, and there was no statistically significant difference in age between the study and control groups ($p = 0.074$). In terms of disease severity within the study group, 10 patients (33 per cent) were grade 2, 10 (33 per cent) were grade 3, and 10 (33 per cent) were grade 4.

The mean serum ischaemia-modified albumin value was 24.8 ng/ml (range, 10.5–91.0 ng/ml) in the study group and 6.0 ng/ml (range, 1.1–18.3 ng/ml) in the control group (Table 1). The mean serum ischaemia-modified albumin level was significantly higher in the study group than in the control group ($p < 0.001$) (Table 1 and Figure 1). There were no significant differences between the study and control

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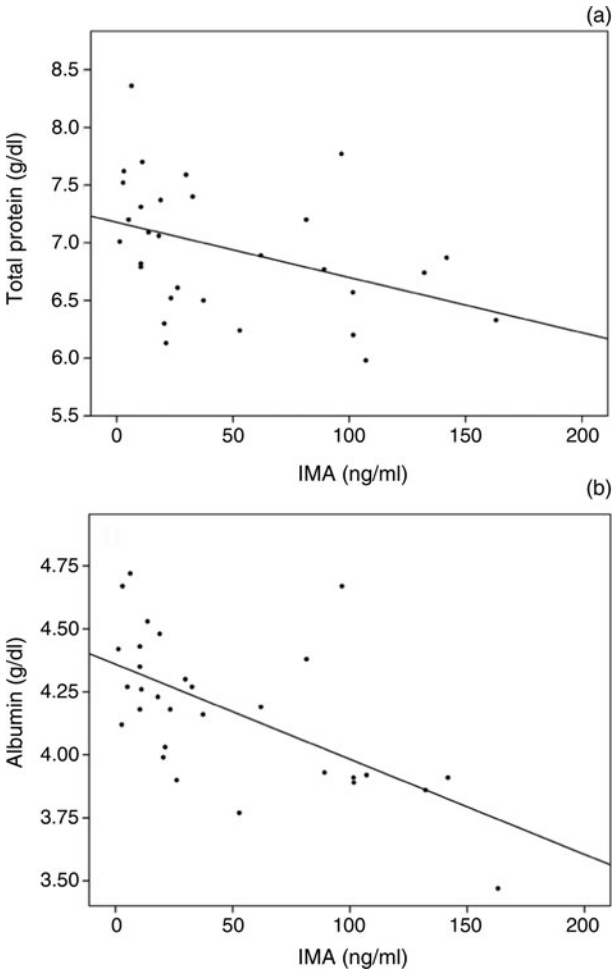

Fig. 2. Graphs showing significant inverse correlations between ischaemia-modified albumin (IMA) and: (a) total protein ($r = -0.488$, $p = 0.006$), and (b) albumin ($r = -0.619$, $p < 0.001$).

groups in serum total protein or albumin levels ($p = 0.763$ and $p = 0.072$, respectively) (Table 1).

In the study group, we found a significant correlation between serum ischaemia-modified albumin levels and values for total protein and albumin (Figures 2a and 2b, respectively). There was no statistically significant relationship between patient age and serum ischaemia-modified albumin ($r = -0.014$, $p > 0.05$), and there was no statistically significant difference in serum ischaemia-modified albumin values between male and female patients ($p = 0.611$). In the study group, there was no significant relationship between serum ischaemia-modified albumin values and the severity of Bell's palsy ($p = 0.818$) (Table 2).

Table 2. Ischaemia-modified albumin levels according to gender and Bell's palsy severity*

Parameter	Ischaemia-modified albumin (mean (range); ng/ml)	*p*
Gender		0.611
– Male	29.9 (10.5–101.6)	
– Female	23.4 (10.5–62.0)	
Disease severity		0.818
– Grade 2	17.1 (8.6–107.9)	
– Grade 3	29.4 (20.4–68.8)	
– Grade 4	24.4 (9.4–101.6)	

*In the study group

Discussion

Although the causes of Bell's palsy have been shown to include autoimmunity, viral infections and ischaemic conditions, the exact aetiology remains unknown.[10] Many studies have suggested that the re-activation of latent human herpes viruses (herpes simplex virus 1, varicella-zoster virus, Epstein–Barr virus and human herpesvirus 6) in the geniculate ganglion results in Bell's palsy.[11] Decompression operations on the facial nerve have shown the effect of facial nerve compression into the intratemporal canal where transient or permanent damage has occurred.[2,11,12] However, the utility of decompression operations is controversial.[2] The labyrinthine segment of the facial nerve is the narrowest, and this segment is highly sensitive to ischaemia caused by acute inflammation and oedema.[2] Although the cause of this inflammation is not known precisely, viral infections and autoimmunity have been hypothesised.[3,11] Iritani *et al.* have shown experimentally that secondary facial paralysis develops in vascular embolisation in intratemporal facial nerve sections.[13]

Ischaemia-modified albumin, ischaemia and ischaemia-reperfusion injury are caused by oxidative stress, resulting in modification of the N-terminal region of the albumin of reactive oxygen species.[14] In 2003, ischaemia-modified albumin was approved by the Food and Drug Administration as a diagnostic marker for acute myocardial infarction, and it is used in laboratory testing in emergency situations.[14] In a study of 538 patients by Collinson *et al.*, ischaemia-modified albumin values were found to have 100 per cent sensitivity and 34.5 per cent specificity for the diagnosis of acute myocardial infarction with a troponin measurement.[4]

Significantly elevated serum ischaemia-modified albumin values, lower than those in acute cardiac ischaemia, have been reported in many pathologies, including acute stroke, pulmonary embolism, polytrauma and end-stage renal failure.[15] In a study on patients with prostate hypertrophy, serum ischaemia-modified albumin levels were significantly higher in the study group than in the control group.[16] High levels of ischaemia-modified albumin have also been reported in: patients diagnosed with stomach cancer, children with neuroblastoma and sarcoma, and patients with bladder and colorectal cancer.[7,17,18]

Recent studies have suggested that increased free oxygen radicals in the serum may play a role in the development of Bell's palsy. Terzi *et al.* compared the oxidative stress index, total antioxidant status and total oxidant status values (used to evaluate free oxygen radicals) in patients with Bell's palsy.[10] They found that total oxidant status and oxidative stress index values were significantly higher in these patients. In a similar study, Babademez *et al.* investigated the relationship between the oxidative stress marker thiol–disulphide homeostasis and Bell's palsy.[19] They reported that the mean serum levels of native and total thiol were significantly lower in the Bell's palsy patients than in the control group, and they found higher levels of disulphide in the study group than in the healthy control group.

To our knowledge, this is the first study to show the relationship between Bell's palsy and serum ischaemia-modified albumin values. We found that serum ischaemia-modified albumin values were significantly higher in Bell's palsy patients

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than in healthy volunteers (Table 1 and Figure 1). These results suggest that ischaemia may play a role in the aetiopathogenesis of Bell's palsy.

The House–Brackmann classification system is widely used to determine the severity and prognosis of Bell's palsy.[20] However, no significant associations between disease severity according to House–Brackmann classification and serum oxidative stress marker values have been reported.[19] In our study, there was also no correlation between House–Brackmann grades and serum ischaemia-modified albumin levels (Table 2).

Greco *et al.* reported that ischaemia in one or more segments of the facial nerve was correlated with Bell's palsy.[3] The high ischaemia-modified albumin values in this study support the hypothesis of ischaemia occurring in Bell's palsy. However, ischaemia-modified albumin values were not correlated with ischaemia severity, in line with reports by Güldoğan *et al.*[8]

- This is the first study to investigate the relationship between serum ischaemia-modified albumin and Bell's palsy
- Serum ischaemia-modified albumin levels were higher in patients with Bell's palsy than in healthy controls
- The results support the idea that ischaemia occurs in Bell's palsy
- No relationship was found between ischaemia severity and disease prognosis

This study, which had a level of evidence of 1b, found no correlation between the patients' prognosis and ischaemia-modified albumin values, but this relationship should be further investigated with prospective randomised studies that comprise larger patient groups.

Study limitations

Our work has limitations that must be addressed in further studies. It is unclear whether there is a causal relationship between the elevated serum ischaemia-modified albumin levels and Bell's palsy. Another limiting factor is the small number of patients.

Competing interests. None declared

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