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OTOLOGY

Serum prolidase, malondialdehyde and catalase levels for the evaluation of oxidative stress in patients with peripheral vertigo

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Abstract

Purpose We aimed to evaluate oxidative stress in patients with peripheral vertigo by measuring serum prolidase, malondialdehyde (MDA) and catalase levels.

Methods A total of 30 patients (age: 60 <) with peripheral vertigo and 30 healthy subjects were recruited. Blood samples were collected from both groups and serum prolidase levels were measured using enzyme-linked immunosorbent assay (ELISA). MDA and catalase levels were measured by the spectrophotometric method.

Results The most common cause of vertigo was BPPV (53.3%), followed by Ménière's disease (16.6%), vestibular neuritis (13.3%), lateral semicircular canal fistula (3.3%), and idiopathic vertigo (13.3%). Mean serum prolidase activity and MDA levels were significantly higher in the vertigo patients than in the control subjects ($P < 0.05$); however, there was no statistically significant difference in mean serum catalase levels between the groups ($P > 0.05$).

Conclusion We concluded that serum prolidase and MDA levels may be used as markers of oxidative stress in patients with peripheral vertigo.

Keywords Oxidative stress · Peripheral vertigo · Prolidase · Malondialdehyde · Catalase

Introduction

Vertigo is the sensation of motion, either of the self or of surrounding objects. It is a general clinical symptom, and is usually defined as a rotational, spinning motion. The most commonly diagnosed vestibular disorders in patients with peripheral vertigo are benign paroxysmal positional vertigo (BPPV), Ménière's disease, vestibular neuritis, labyrinthitis, perilymph fistula and acoustic neuroma.

Oxygen excludes electrons from other molecules in the cell to make reactive oxygen species (ROS). ROS are controlled by a defense system that relies on the activity of enzymes and non-enzyme substances. Disequilibrium between ROS formation and the body's defense system against ROS is defined as oxidative stress [1]. Oxidation products are formed during inflammation and participate in tissue injury caused by inflammation. Prolidase is one of the sole enzymes capable of degrading dipeptides in which a proline or hydroxyproline residue is located at the C terminal position [2]. Prolidase has been found in diverse tissues, such as plasma, heart, thymus, brain and uterus [3]. Increased serum levels of prolidase have been

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associated with oxidative stress in several diseases such as mitral stenosis, helicobacter pylori infection and ovarian cancer [4, 5]. Malondialdehyde (MDA) and catalase levels have also been used in the evaluation of oxidative stress status in patients [6].

Although oxidative stress has been associated with peripheral vertigo [7–9], no study has yet reported the feasibility of using serum prolidase, catalase and MDA levels in the evaluation of oxidative stress in patients with peripheral vertigo. Therefore, we conducted this study, which to our knowledge is the first reported to date, to determine whether prolidase, catalase and MDA concentrations in serum are affected by peripheral vertigo and whether these play a role in the etiology of peripheral vertigo.

Materials and methods

Study design

Our consecutively selected study group consisted of 30 patients (age: 60 <) with a history of peripheral vertigo who presented to the Otolaryngology Department of Kutahya Saglik Bilimleri University Hospital, Kutahya, Turkey. All patients underwent detailed otorhinolaryngologic and neurologic examinations in addition to audiometric tests, to rule out any other pathology inducing vertigo. The audiograms of the patients were assessed, and patients with moderate or severe hearing loss were excluded from study due to the stress impact of hearing loss on these patients. Vertigo patients with neurological disorders, systemic diseases, malignancy or any inflammatory disease which could affect oxidative stress in the body, were also externalized from the study. In addition to the vertigo patients, we recruited age- and gender-matched healthy controls. Blood samples of the patients included in the study were taken during an acute vertigo crisis. As the control group, 30 healthy individuals, examined for check-up purposes, with no complaints in the head and neck region, and without any infection or other systemic diseases, were recruited.

Blood preparation

In both the patient and control groups, blood samples were collected into evacuated tubes including a serum separator and clot activator (Vacuette®, Greiner Bio-One, Kremsmunster, Austria). Within 1 h of collection, the blood samples were centrifuged at 1500 × g for 15 min, to obtain serum samples. After centrifugation, serum samples were stored at − 80 °C until biochemical analysis.

Measurement of serum prolidase, malondialdehyde and catalase levels

Serum Xaa-Pro dipeptidase/prolidase (PEPD) levels were measured using enzyme-linked immunosorbent assay (ELISA), based on biotin double antibody sandwich technology, according to manufacturer's indications (Hangzhou Eastbiopharm Co Ltd, Hangzhou, China). The intra- and inter-assay coefficients of variation were < 10% and < 12%, respectively. Malondialdehyde (MDA) levels were detected using the thiobarbituric acid method, and the pink-colored complex was measured spectrophotometrically at 532 nm. The decomposition rate of the H_2O_2 substrate by the catalase enzyme was measured spectrometrically at 240 nm.

Ethical considerations

The study protocol was approved by the local ethics committee. Subjects were enrolled only after they provided written and oral informed consent.

Statistical analysis

Statistical analyses were performed using SPSS 21 (SPSS Inc, Chicago, IL, USA) software. Normality was assessed using a Shapiro–Wilk test and the results were presented as mean ± standard deviation. The independent-samples *t*-test and Kruskal–Wallis test were used to examine differences between groups, which were considered statistically significant if $P < 0.05$.

Results

For the vertigo group, the mean age of the patients was 47.0 ± 11.9 years; 65.51% of the patients were females and 34.49% were males. For controls, mean age was 44.3 ± 12.1 years; 62.96% of the subjects were females and 37.04% were males. There were no significant differences between the patients and control group in terms of age ($P = 0.410$) and gender ($P = 0.845$; Table 1).

The most common cause of vertigo was BPPV (53.3%), followed by Ménière's disease (16.6%), vestibular neuritis (13.3%), lateral semicircular canal fistula (3.3%), and idiopathic vertigo (13.3%). Mean serum prolidase activity and MDA levels were significantly higher in the vertigo patients than in the control subjects ($P < 0.05$; Fig. 1); however, there was no statistically significant difference in mean serum catalase levels between the groups ($P > 0.05$).

Table 1 Demographic data and mean serum levels of prolidase, malondialdehyde and catalase in peripheral vertigo and control groups

Variables	Patient group $n=30$	Control group $n=30$	P
Mean (±SD) age (years)	47.0 ± 11.9	44.3 ± 12.1	0.410
Sex (% female)	65.51	62.96	0.845
Prolidase	34.96 ± 24.46	20.71 ± 8.99	0.006
MDA	107.53 ± 44.79	66.28 ± 29.43	< 0.001
Catalase	0.19 ± 0.11	0.14 ± 0.01	0.083

SD standard deviation, *n* number of subjects, *MDA* malondialdehyde

$P < 0.05$ indicates significant difference

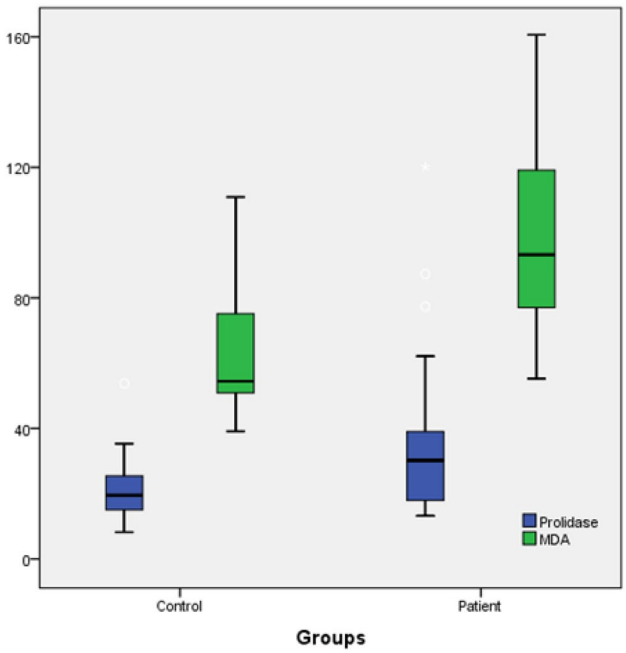

Fig. 1 Comparison of serum levels of prolidase and malondialdehyde between peripheral vertigo and control

Discussion

There are various causes of vertigo, which can be described as peripheral or central depending on its origin. While central causes of vertigo originate from the brain or spinal cord, peripheral vertigo originates from the inner ear. There are many causes of peripheral vertigo and [10] gives the most common ones as BPPV (52.5%), Ménière's disease (14.6%) and sudden idiopathic hearing loss (2.9%). Less common causes are benign paroxysmal vertigo of childhood (0.7%), labyrinthitis (0.7%) and vestibular schwannoma (0.3%). Our study found the most common causes of peripheral vertigo were BPPV, Ménière's disease and vestibular neuritis.

Oxidative stress in plasma and tissues of the human body is well known as the major cause of advancing decline in functional cellular capability. Oxidative stress is established as the primary factor in biological aging in all organisms and cellular degeneration, and there is increasing focus in the literature on the responsibility of oxidative stress for a diverse range of pathological conditions affecting the human body [9].

Increasing evidence suggests that oxidative stress is involved in the advancement of endolymphatic hydrops and that the sensorineural hearing loss seen in advanced stages of Ménière's disease may be ascribed to cellular damage and apoptotic cell death [11]. Calabrase et al. [8] investigated oxidative stress, redox homeostasis and cellular stress response in patients with Ménière's disease and found that in these patients finite augmentations in markers of cellular stress response and oxidative stress in peripheral blood exist. Their study also explored the hypothesis that alterations in the redox status of glutathione, the major endogenous antioxidant, associated with abnormal expression and activity of carbonic anhydrase, can be ascribed to increase oxidative stress and to degradation of systemic redox homeostasis. This was possibly related to changes in vulnerable neurons, such as spiral ganglion neurons, and consequent cellular degeneration. Raponi et al. [9] claimed that using a high-powered antioxidant medicine, Gluta-Tios (Omega Industries), to treat vertigo symptoms, particularly in Ménière's patients, significantly prevented vertigo attacks.

Tsai et al. [7] investigated the relationship between BPPV, Parkinson's disease (PD) and oxidative stress. BPPV patient blood samples were searched for SIRT1 axis gene expression, and a PD cell model of 6-hydroxydopamine (6-OHDA)-treated PC-12 cells was used to elucidate potential in vitro and in vivo mechanisms of degeneration in PD and BPPV. They found that BPPV is independently related to an augmented hazard of PD. This result may be related to oxidative stress-mediated prevention of SIRT1 expression levels.

The deleterious influences of ROS are moderated by diverse cellular defense systems consisting of enzymatic (catalase, glutathione peroxidase, superoxide dismutase, etc.) and non-enzymatic (vitamins E, C, glutathione, etc.) constituents [12]. Catalase is an important constituent of the antioxidant defense system and affects the amount of free radicals in cells. We found no statistically significant

difference in catalase levels between the two groups in our study. MDA is the main aldehyde end product of lipid peroxidation of membrane polyunsaturated fatty acids by free radicals and its presence is a marker of oxidative stress [13]. Serum MDA levels were considerable higher in the patient group compared with the control subjects in our study.

Serum prolidase level has been explored extensively in research as a marker of oxidative stress in various diseases such as cancer, psychological disorders, eye diseases, nephropathy and metabolic syndromes [14–17]. Gecit et al. [14] investigated total antioxidant status (TAS), MDA and nitric oxide (NO) levels in patients with bladder cancer for their association with prolidase activity. They found that serum prolidase activity, NO levels and MDA levels were considerably higher in patients with bladder cancer than in controls, while TAS levels were significantly lower. In another study, increased serum prolidase activity was associated with hepatocellular carcinoma [15]. Kokacya et al. claimed that increased prolidase activity is associated with etiopathogenesis of major depressive disorders [17]. In addition to these associations between disease and prolidase activity, our study contributes to the established literature by providing a novel demonstration of the association between increased serum prolidase activity and peripheral vertigo.

Conclusion

In conclusion, serum prolidase and MDA levels may be used as markers of oxidative stress in patients with peripheral vertigo. Although we did not find a statistically significant difference between the groups for serum catalase levels, further research into the benefit of antioxidant use in the treatment of peripheral vertigo is needed.

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Compliance with ethical standards

Conflict of interest There is no financial or personal relationship with other people or organizations that could inappropriately influence (bias) the authors' actions.

Ethical approval All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants recruited in the study.

References

1. Goodyear-Bruch C, Pierce JD (2002) Oxidative stress in critically ill patients. Am J Crit Care 11:543–551
2. Endo F, Matsuda I (1991) Molecular basis of prolidase (peptidase D) deficiency. Mol Biol Med 8:117–127
3. Zanaboni G, Dyne KM, Rossi A et al (1994) Prolidase deficiency: biochemical study of erythrocyte and skin fibroblast prolidase activity in Italian patients. Haematologica 79:13–18
4. Rabus M, Demirbag R, Yildiz A et al (2008) Association of prolidase activity, oxidative parameters, and presence of atrial fibrillation inpatients with mitral stenosis. Arch Med Res 39:519–524
5. Camuzoglu H, Arioz DT, Toy H et al (2009) Assessment of preoperative serum prolidase activity in epithelial ovarian cancer. Eur J Obstet Gynecol Reprod Biol 147:97–100
6. Yüksel S, Yiğit AA (2015) Malondialdehyde and nitric oxide levels and catalase, superoxide dismutase, and glutathione peroxidase levels in maternal blood during different trimesters of pregnancy and in the cord blood of newborns. Turk J Med Sci 45:454–459
7. Tsai KL, Cheng YY, Leu HB et al (2015) Investigation the role of Sirt1modulated oxidative stress in relation to benign paroxysmal positional vertigo and Parkison's disease. Neurobiol Aging 36:2607–2616
8. Calabrase V, Cornelius C, Maiolino L et al (2010) Oxidative stress, redox homeostasis and cellular stress response in Ménière's disease: role of vitagens. Neurochem Res 35:2208–2217
9. Raponi G, Alpini D, Volonte S et al (2003) The role of free radicals and plasmatic antioxidant in Meniere's syndrome. Int Tinnitus J 9:104–108
10. Orji F (2014) The influence of psychological factors in Meniere's disease. Ann Med Health Sci Res 4:3–7
11. Labbe D, Teranishia M, Hessa A et al (2005) Activation of caspase-3 is associated with oxidative stress in the hydropic guinea pig cochlea. Hear Resarch 202:21–27
12. Mates JM, Perez-Gomez C, de Castro IN (1999) Antioxidant enzymes and human diseases. Clin Biochem 32:595–603
13. Marnett LJ (2000) Oxyradicals and DNA damage. Carcinogenesis 21:361–370
14. Gecit I, Aslan M, Gunes M et al (2012) Serum prolidase activity, oxidative stress, and nitric oxide levels in patients with bladder cancer. J Cancer Res Clin Oncol 138:739–743
15. Ilikhan SU, Bilici M, Sahin H et al (2015) Assessment of the correlation between serum prolidase and alpha-fetoprotein levels in patients with hepatocellular carcinoma. World J Gastroenterol 21:6999–7007
16. Yıldırım Y, Kaya A, Kar T et al (2015) Prolidase Enzyme Activity in Conjunctiva and Pterygium Tissues. Med Sci Monit 21:3275–3278
17. Kokacya MH, Bahceci B, Bahceci I et al (2014) Prolidase activity and oxidative stress in patients with major depressive disorder. Psychiatr Danub 26:314–318