The Journal of Laryngology & Otology (2013), ***127***, *972–976*.

doi:10.1017/S002221511300193X

MAIN ARTICLE

Impact of mean platelet volume on the occurrence and severity of sudden sensorineural hearing loss

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Abstract

Objective: We aimed to determine: (1) whether mean platelet volume was elevated in patients with sudden sensorineural hearing loss, compared with healthy controls; and (2) whether mean platelet volume level was related to hearing loss severity.

Materials and methods: The study included 31 patients with sudden sensorineural hearing loss and 31 age- and sex-matched, healthy controls. Peripheral venous blood samples were taken from subjects and mean platelet volume and levels of glucose, total cholesterol, high-density lipoprotein, low-density lipoprotein and triglyceride were measured.

Results: Mean platelet volume was significantly greater in the sudden sensorineural hearing loss group compared with the control group. However, there was no significant correlation between mean platelet volume level and hearing loss severity.

Conclusion: Mean platelet volume, a determinant of platelet activation, is elevated in patients with sudden sensorineural hearing loss. To our knowledge, this is the first report investigating mean platelet volume levels in such patients. Our findings indirectly support the hypothesis of vascular impairment as a pathogenetic factor in sudden sensorineural hearing loss.

Key words: Sensorineural Hearing Loss; Pathogenesis; Platelets; Morphology; Platelet Activation

Introduction

Sudden sensorineural hearing loss (SNHL) is defined as a hearing loss of 30 dB or more over 3 contiguous audiometric frequencies which develops over a period of a few hours to 3 days.[1] The pathogenesis of sudden SNHL is still unknown but several pathophysiological mechanisms have been proposed. These include viral infection and autoimmune and vascular disorders.[2]

Vascular disorders may cause sudden SNHL due to cochlear injury. Of particular note, a number of studies have reported an association between sudden SNHL and thrombosis.[3–6] Following the theory of thromboembolic aetiology, various studies have investigated rheological factors in the blood of patients with idiopathic sudden SNHL, and have reported that high plasma viscosity, elevated fibrinogen levels and reduced erythrocyte filterability are associated with sudden SNHL.[7,8]

Mean platelet volume is the most commonly used measure of platelet size, and is a potential marker of platelet reactivity.[9] Large platelets contain a greater number of dense granules and are enzymatically and metabolically more active, and thus have greater prothrombotic potential.[10] Previous studies have demonstrated increased mean platelet volume in patients with hypertension, unstable angina pectoris, myocardial infarction and cerebral stroke.[11–14] An increase in mean platelet volume may promote a prothrombic or hypercoagulable state, and this may be of relevance for the pathogenesis of sudden SNHL. However, no previous study has investigated the association between mean platelet volume and sudden SNHL.

The clinical picture of sudden SNHL is similar to that of other vascular diseases such as myocardial infarction and cerebral stroke; acute onset and unilateral symptoms reinforce the suggestion of underlying vascular occlusion.[1] Elevated serum mean platelet volume plays a role in the development of cardiovascular and cerebrovascular diseases such as myocardial infarction and cerebral stroke. Mean platelet volume may also be involved in the pathogenesis of sudden SNHL.

In this study, we aimed to determine whether mean platelet volume is elevated in patients with sudden SNHL compared with healthy controls. In addition,

Accepted for publication 23 January 2013 First published online 16 September 2013

we aimed to investigate whether the level of mean platelet volume is related to the severity of hearing loss.

Materials and methods

Study population

Thirty-one consecutive patients with a diagnosis of sudden SNHL were enrolled. All patients underwent complete history-taking, ENT examination and complete audiological evaluation. Sudden SNHL was defined as a hearing loss of 30 dB or more over 3 contiguous audiometric frequencies, which develops over a period of a few hours to 3 days. The diagnosis of sudden SNHL was made by an experienced audiologist by excluding other causes of sudden deafness such as inflammatory or traumatic factors.

For each case of sudden SNHL, a subject without hearing problems was identified as a matched control. Case and control subjects were matched for sex and ages (±two years). Control subjects were recruited from our hospital's ENT out-patient department. The control subjects had no history of sudden or chronic SNHL; these disorders were also excluded by pure tone audiometry.

The study population was investigated for evidence of any disease that constituted an exclusion criterion. Exclusion criteria for patients and control subjects were evidence of diabetes mellitus, hypercholesterolaemia, coronary artery disease, congestive heart failure, renal or hepatic dysfunction, arterial or venous thrombotic disease, haematological disease, cancer, thrombocytopenia (Fechtner syndrome), hypo- and hyperthyroidism, auto-immune disease, use of antithrombotic agents or serotonin reuptake inhibitor drugs, and chronic or systemic inflammatory diseases such as bronchial asthma, rheumatoid arthritis and psoriasis.

This study complied with the Declaration of Helsinki, and was approved by the Ethics Committee and the Institutional Review Board of Erciyes University Medical School (which supervised research activities in the Kayseri area).

Audiological testing and classification

All patients underwent pure tone audiometry (at the frequencies 125, 250, 500, 1000, 2000, 4000 and 8000 Hz, in accordance with the International Organization for Standardization) and impedance audiometry. The pure tone average was calculated as the average hearing threshold at the frequencies 500, 1000, 2000 and 4000 Hz. We used the following scale to categorise the degree of hearing loss: mild, 21 dB or greater but less than 41 dB; moderate, 41 dB or greater but less than 71 dB; severe, 71 dB or greater but less than 91 dB; and profound, greater than 91 dB hearing loss.

Biochemical measurements

Blood samples, anticoagulated with tripotassium ethylene diamine triacetic acid, were drawn from the antecubital vein immediately after the diagnosis of sudden SNHL. Analyses were performed immediately after phlebotomy in order to prevent *in vitro* platelet activation. Mean platelet volume and other haematological parameters were measured using a Beckman Coulter LH 780 Haematology Analyzer (Brea, California, USA). Expected mean platelet volume values in our laboratory ranged from 6 to 11 femtolitres (fl).

For biochemical parameters, blood samples were drawn from the antecubital vein in the morning after a 20-minute rest following a fasting period of 12 hours. Levels of glucose, total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL) and triglycerides were determined by standard methods.

Statistical analysis

The SPSS statistical software program (SPSS, version 16.0 for windows; SPSS Inc, Chicago, Illinois, USA) was used to perform all statistical calculations. Quantitative variables were expressed as mean ± standard deviation (SD), and categorical variables were expressed as percentages. All parameters were tested for conformity to a normal distribution using the Kolmogorov–Smirnov test. Parametric tests were applied to parameters with a normal distribution, while non-parametric tests were used for parameters with a non-normal distribution. The independent samples *t*-test was used for statistical comparison of data with a normal distribution. The Mann–Whitney U test was applied to compare data without a normal distribution, between the groups. The chi-square test was used to compare categorical parameters between the groups. Spearman's correlation coefficient was used to evaluate the association between mean platelet volume and severity of hearing loss. Differences were considered statistically significant at a p value of less than 0.05.

Results

The sudden SNHL group comprised 31 patients: 17 (54.8 per cent) males and 14 (45.2 per cent) females, with a mean age of 37.45 ± 15.70 years. The control group comprised 31 healthy subjects: 16 (51.6 per cent) males and 15 (48.4 per cent) females, with a mean age of 35.77 ± 14.93 years. There was no significant difference between the two groups regarding age or gender distribution. The characteristics for the two groups are presented in Table I.

Regarding laboratory characteristics, the mean values for platelet count and levels of haemoglobin, total cholesterol, triglyceride, HDL and LDL were similar between the groups. However, mean platelet volume was significantly greater in the sudden SNHL group compared with the control group (9.01 ± 1.24 fl *vs* 8.21 ± 0.76 fl, respectively ($p < 0.05$); median mean platelet volume, 8.90 *vs* 8.10 fl; first quartile mean platelet volume, 8.00 *vs* 7.70 fl; third quartile mean platelet volume, 9.90 *vs* 8.80 fl; minimum mean platelet volume, 6.60 *vs* 6.50 fl; maximum mean platelet volume, 11.30 *vs* 9.70 fl) (Figure 1). The sudden SNHL

https://doi.org/10.1017/S002221511300193X Published online by Cambridge University Press

TABLE I
SUBJECTS' DEMOGRAPHIC AND LABORATORY CHARACTERISTICS

Parameter	Group		*p*
	SSNHL*	Controls*	
Age (years)	37.45 ± 15.70	35.77 ± 14.93	0.683
Gender (M/F; *n*)	17/14	16/15	0.799
Hb (g/dl)	14.22 ± 1.71	14.41 ± 1.64	0.434
WBC count ($\times 10^3$/μl)	10.15 ± 3.87	7.51 ± 2.06	0.002*
Platelet count ($\times 10^3$/μl)	258.03 ± 58.28	249.06 ± 61.96	0.647
PCT (%)	0.23 ± 0.06	0.20 ± 0.04	0.028*
PDW (%)	16.29 ± 1.10	14.65 ± 2.13	0.001*
MPV (fl)	9.01 ± 1.24	8.21 ± 0.76	0.016*
Glucose (mg/dl)	123.67 ± 52.67	95.26 ± 16.69	0.012*
Total chol (mg/dl)	179.04 ± 45.53	169.03 ± 33.47	0.422
LDL-chol (mg/dl)	105.25 ± 36.67	98.84 ± 24.62	0.524
HDL-chol (mg/dl)	47.57 ± 13.06	44.47 ± 10.07	0.628
Triglyceride (mg/dl)	146.08 ± 98.38	130.48 ± 88.47	0.552

Data represent means ± standard deviations unless otherwise specified. *n = 31. SSNHL = sudden sensorineural hearing loss; M = males; F = females; HB = haemoglobin; WBC = white blood cell; PCT = platelet crit; PDW = platelet distribution width; MPV = mean platelet volume; chol = cholesterol; LDL = low-density lipoprotein; HDL = high-density lipoprotein

group was also found to have elevated results, compared with the control group, for white blood cell count (10.15 ± 3.87 g/dl *vs* 7.51 ± 2.06 g/dl, respectively), platelet crit (0.23 ± 0.06 per cent *vs* 0.20 ± 0.04 per cent), platelet distribution width (16.29 ± 1.10 per cent *vs* 14.65 ± 2.13 per cent) and serum glucose level (121.13 ± 56.56 mg/dl *vs* 95.26 ± 16.69 mg/dl).

Sudden SNHL was unilateral in all patients, affecting the right ear in 16 patients (51.6 per cent) and the left in 15 patients (48.4 per cent). The condition was profound in 8 patients (25.8 per cent), severe in 8 (25.8 per cent), moderate in 14 (45.2 per cent) and mild in 1 (3.2 per cent). There was no significant correlation between the level of mean platelet volume and the severity of hearing loss ($p > 0.05$).

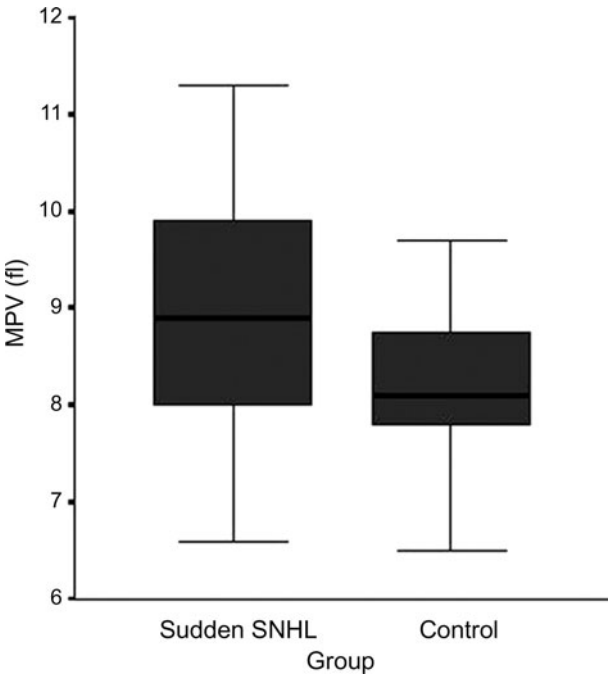

FIG. 1
Comparison of mean platelet volume (MPV) in sudden sensorineural hearing loss (SNHL) and control groups. Bar = median; box = 1st and 3rd quartiles; whiskers = minimum and maximum

Discussion

The pathogenesis of sudden SNHL is still unknown, although vascular impairment or circulatory disturbance are the most common mechanisms hypothesised to explain its occurrence. It has been proposed that thrombosis or vasospasm of the internal auditory artery, or of its subdivisions, leads to impaired perfusion of the cochlea (a vascular region supplied by a terminal capillary bed).[15] Alterations in the microcirculation of the cochlea may be a cause of sudden SNHL.

There are a number of studies which report a relationship between cardiovascular and thromboembolic risk factors and sudden SNHL, supporting the vascular occlusion hypothesis. Diabetes mellitus and hypercholesterolaemia are well-established risk factors for atherosclerosis and are associated with vascular occlusion of large arteries in the coronary, cerebral and peripheral regions.[16–18] It is conceivable that these conditions play a similar role in the impairment of cochlear perfusion.[19] Case-control studies evaluating the presence of cardiovascular and thromboembolic risk factors in patients with sudden SNHL are rare. Several authors have found higher mean cholesterol concentrations in patients with sudden SNHL, compared with controls, and hypercholesterolaemia is known to be an independent risk factor for sudden SNHL.[6,19,20] Lin *et al.* found a higher prevalence of hypertension, diabetes mellitus and hyperlipidaemia in sudden SNHL patients compared with controls.[21] Aimoni *et al.* demonstrated that diabetes mellitus, hypercholesterolaemia and high levels of other cardiovascular risk factors are associated with elevated risk of sudden SNHL.[22] However, other authors have failed to find an association between

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diabetes mellitus, hypertension and hyperlipidaemia and sudden SNHL risk.[23,24] In our study, although we excluded patients with diabetes mellitus and hypercholesterolaemia, the sudden SNHL patients had significantly higher serum glucose levels. However, high glucose concentration and elevated white blood cell count may also be associated with the stress of hearing loss experienced by these patients.[25,26]

As an additional extension of the thromboembolism theory of sudden SNHL, disturbances of rheological factors in the blood of patients suffering from sudden SNHL and genetic thrombophilic polymorphisms have been investigated. High plasma viscosity, high plasma fibrinogen levels and reduced erythrocyte filterability have been reported to be associated with sudden SNHL.[7,8] Several studies have investigated elevated plasma homocysteine and plasminogen activator inhibitor-1 levels in patients with sudden SNHL, and have found hyperhomocysteinaemia to be an independent risk factor for sudden SNHL.[1,6,19] Other studies have assessed the association between sudden SNHL and genetic polymorphisms thought to act as prothrombotic risk factors, mainly factor V Leiden and prothrombin G2021A variants; however, anticoagulant deficiencies and thrombophilic polymorphisms have not been observed to play a role in the pathogenesis of sudden SNHL.[1,4,24,27,28] Rudack *et al.* reported an association between an inherited risk factor, GPIaC807T, and negative outcomes of sudden SNHL.[24]

To gain further insight into the mechanisms linking thromboembolism and sudden SNHL, we investigated the association between mean platelet volume and sudden SNHL. Mean platelet volume is a well-known indicator of platelet activation: platelets of larger volume are enzymatically and metabolically more active than those of smaller volume. Platelets with more granules and adhesion receptors are larger, i.e. have increased volume. An increase in mean platelet volume indicates the presence of activated platelets.[29] Increased platelet activation plays an important role in the development of atherosclerosis.[11] As previously established, most vascular complications depend on endothelial damage, which initiates thrombosis. Increased platelet activation contributes to the process of thrombus formation. Elevated mean platelet volume levels may promote a prothrombic or hypercoagulable state, which could be relevant to the pathogenesis of sudden SNHL.

The clinical picture of sudden SNHL is similar to that of other vascular disease such as myocardial infarction and cerebral stroke, with an acute onset and unilateral symptoms, and this picture reinforces the theory of an underlying vascular occlusion.[1] Various authors have studied the relationship between mean platelet volume and cardiovascular and cerebrovascular disease. Kaya *et al.* and Nadar *et al.* found that mean platelet volume was elevated in hypertensive patients.[12,30] Endler *et al.* reported that patients with pre-existing coronary artery disease and increased mean platelet volume were at higher risk of myocardial infarction.[13] Bath *et al.* found an association between mean platelet volume and stroke in patients with a history of cerebrovascular disease.[14] To our best knowledge, the present study is the first to show an association between mean platelet volume and sudden SNHL. We found that mean platelet volume was significantly greater in the sudden SNHL group compared with controls. We believe that mean platelet volume may be involved in the pathogenesis of sudden SNHL, because elevated serum mean platelet volume plays a role in cardiovascular and cerebrovascular diseases such as myocardial infarction and cerebral stroke.

Fechtner syndrome is a rare autosomal dominant platelet disorder thought to be a variant of Alport syndrome. It is characterised by macrothrombocytopenia, leukocyte inclusions, SNHL, nephropathy and ocular abnormalities.[31] Fechtner syndrome should be kept in mind in patients with high mean platelet volume levels and sensorineural hearing loss. In our study, no patient had ocular anomalies, thrombocytopenia or renal function abnormalities.

- **A relationship between thrombosis and sudden sensorineural hearing loss (SNHL) has been proposed**
- **Mean platelet volume is a marker of potential platelet reactivity**
- **This study investigated the association between mean platelet volume and sudden SNHL**
- **Mean platelet volume was significantly greater in sudden SNHL patients**
- **Mean platelet volume level did not correlate with sudden SNHL severity**
- **Our findings support the vascular impairment theory of sudden SNHL pathogenesis**

Our study had some limitations. Firstly, the small size of our patient sample represents an important limitation. Secondly, our patients did not receive prospective clinical follow up. Thirdly, the effect of sudden SNHL treatment on mean platelet volume levels was not investigated. However, this study was designed solely to investigate the association between mean platelet volume levels and sudden SNHL.

Conclusion

These results suggest that mean platelet volume, a determinant of platelet activation, is elevated in patients with sudden SNHL. To our best knowledge, this is the first study investigating mean platelet volume levels in patients with sudden SNHL. Our findings indirectly support the hypothesis of vascular impairment in the pathogenesis of sudden SNHL. Further experimental

https://doi.org/10.1017/S002221511300193X Published online by Cambridge University Press

and clinical research, on a larger number of individuals, will lead to a better understanding of the role of thromboembolic factors, including mean platelet volume, in sudden SNHL.

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Dr M Sagit takes responsibility for the integrity of the content of the paper
Competing interests: None declared

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