

Original Article

Evaluation of Neutrophil/Lymphocyte and Platelet/Lymphocyte Ratios in Sudden Sensorineural Hearing Loss and Relationship with Hyperbaric Oxygen Therapy

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OBJECTIVE: This study aimed to evaluate the prognostic value of neutrophil/lymphocyte (N/L) and platelet/lymphocyte (P/L) ratios in sudden sensorineural hearing loss (SSNHL) and investigate the effect of combined corticosteroid medical treatment and/or hyperbaric oxygen (HBO) therapy on these values.

METHODS: In this study, patients with SSNHL at our tertiary center were examined retrospectively. A total of 60 patients with SSNHL and 30 healthy individuals as the control group were included. The patient and control groups were compared in terms of N/L and P/L rates. Furthermore, 60 patients were divided into 2 equal groups (n=30) on the basis of whether they received HBO in addition to combined corticosteroid treatment.

RESULTS: The N/L and P/L rates were significantly higher in the patient groups than in the control group at the time of diagnosis and significantly decreased after treatment in the patient groups ($p < 0.05$). It was observed that HBO therapy lowered the N/L and P/L rates more than the HBO-free group, but the statistically significant decrease was only in N/L ratio ($p < 0.05$).

CONCLUSION: The N/L and P/L rates were higher in the patient groups than in the control group, and there was also a significant decrease in the 2 values after treatment. This was an important finding showing that SSNHL has a possible underlying inflammatory and vascular (ischemic) condition. We also found that the higher the P/L ratio, the lower the recovery rate from hearing loss. This finding suggests that the P/L ratio can be an important prognostic indicator in patients with SSNHL.

KEYWORDS: Sudden hearing loss, neutrophil lymphocyte ratio, platelet, hyperbaric oxygen therapy, inflammation

INTRODUCTION

Sudden sensorineural hearing loss (SSNHL) is described as hearing loss that occurs within 72 hours in the sensorineural component at ≥ 30 decibels (dB) and which affects at least 3 sequential frequencies; its incidence is reported to be 5-20/100,000. Accounting for nearly 1% of all cases of hearing loss, SSNHL can be treated medically, and this highlights the importance of emergency treatment ^[1].

In terms of using hyperbaric oxygen (HBO) for treating SSNHL, although some authors believe that HBO is effective in increasing the level of plasma oxygen in the blood flow to the inner ear ^[1,2], others believe that HBO is not effective for treating SSNHL and that different factors are effective in addition to the vascular etiologies in SSNHL ^[1,3]. Therefore, there exists a dilemma of whether HBO should be included in the treatment of SSNHL.

Recent hypotheses about the causes of SSNHL have focused on chronic inflammation ^[3,4]. Because the counts of white blood cells and their subtypes are common indicators of inflammation, whole blood count examination is routinely performed in patients with SSNHL ^[5]. The neutrophil/lymphocyte (N/L) ratio is a rapid and novel indicator of inflammation, because it is not expensive and can be checked on the whole blood count. Recent reports have indicated that in cases of inflammation, the N/L ratio is a better indicator of inflammation than the total leukocyte count ^[6,7].

The labyrinthine artery, an end artery, facilitates blood flow to the inner ear. This distal blood flow is weakly regulated and is mostly associated with normal plasma viscosity, platelet function, and locally regulated mechanisms ^[8]. The platelet/lymphocyte (P/L) ratio

is an important indicator of microcirculation disorders associated with ischemia and is determined in patients with peripheral arterial circulation diseases such as atherosclerosis ^[9].

In this study, we assessed the N/L and P/L ratios in patients with SSNHL who were treated with different treatment modalities and their effects on the recovery.

MATERIALS AND METHODS

In this study, we retrospectively analyzed patients diagnosed with SSNHL and hospitalized for treatment at our clinic. We examined the correlation of the N/L and P/L ratios with the presence of SSNHL by comparing these values in 60 patients with SSNHL and 30 healthy individuals with no otologic or circulatory problem for whom audiometric tests and blood analyses were performed during a routine check-up. The necessary ethics committee approval to conduct the study was obtained from the local ethics committee.

Moreover, the correlation between the changes in the N/L and P/L ratios and the stages of recovery in hearing, which were observed based on the pure tone audiometry (PTA) tests performed prior and subsequent to the treatment, was analyzed to reveal the prognostic importance of these values. All the audiological measurements were conducted using a calibrated clinical audiometer device (AC-40 Interacoustics®, Assens, Denmark).

In this study, mean values of PTA thresholds of 0.25 kHz, 0.5 kHz, 1 kHz, 2 kHz, and 4 kHz frequencies for all patients at initial diagnosis (pre-treatment) and 1 month after treatment (post-treatment) were considered as average hearing thresholds to evaluate hearing improvement according to the Sudden Deafness Research Committee of the Japanese Ministry of Health, Labour and Welfare in the 1984 classification ^[10, 11] as complete, marked, slight recovery, and no response. Hearing loss at the time of diagnosis was classified according to the average hearing thresholds as follows: 0-20 dB normal hearing, 21-40 dB mild hearing loss, 41-60 dB moderate hearing loss, 61-80 dB severe hearing loss, and >80 dB profound hearing loss.

This study included 60 patients with SSNHL and 30 healthy individuals. The group of patients with SSNHL was divided into

2 subgroups comprising 30 patients each. Group 1 included patients who received HBO in addition to the combined corticosteroid treatment, whereas group 2 included patients who received only the combined corticosteroid treatment owing to various reasons (claustrophobia, active respiratory tract infection, COPD, etc.).

In the combined corticosteroid treatment, all of the patients received oral methylprednisolone 1 mg/kg/day in 2 divided doses (maximum 60 mg/day) tapered every consecutive 3 days (60 mg/day for 3 days, 40 mg/day for 3 days, and 20 mg/day for 3 days) which is the routine treatment protocol followed for patients with idiopathic SSNHL at our clinic, and pentoxifylline at a dose of 300 mg 3 times a day, enoxaparin sodium 2x0.1 cc/kg, and dextran 40 at 1x1 (3 days). Vitamin B complex supplement were administered to all the patients. In addition to the routine combined medical corticosteroid treatment protocol followed for treating SSNHL in both patient groups, the HBO group (group 1) was administered 10 sessions of 2-hour HBO treatment at 2.5 ATA pressure. In terms of comorbidities, 9 patients (15%) had either diabetes mellitus (DM) or hypertension (HT), whereas 12 (20%) had both simultaneously.

In the whole blood counts of these 2 groups of patients who were administered the treatment, the N/L and P/L ratios were analyzed to determine whether HBO has any impact on these values. The pre-treatment N/L and P/L ratios of groups 1 and 2 were compared with those of the control group (group 3), which included healthy individuals without any hearing loss or systemic disease.

Statistical Analysis

The Shapiro-Wilk test or the Kolmogorov-Smirnov test was used to determine whether the values obtained were coherent with the normal distribution. To compare the 2 independent groups, the independent samples t-test (Student's t-test) was used for calculating means coherent with the normal distribution; the dependent samples paired t-test (paired samples t-test) was used for dependent groups. The data, which were not coherent with the normal distribution, were compared between the 2 groups. The Mann-Whitney U test was used for the independent groups, whereas the Wilcoxon test was used for the dependent groups. To compare multiple measurement results of the same group, repeated measures analysis of variance was performed for the data that were coherent with the normal distribution, and the Friedman test was performed for the data that were not coherent with the normal distribution. To calculate the group differences between the nominal values, the chi-square test was performed. To study the correlation between the numeric values, Spearman correlation analysis was performed for paired data groups that were coherent with the normal distribution, and Pearson correlation analysis was performed for the data groups that were not coherent with the normal distribution.

RESULTS

This study included 60 patients with SSNHL (45 men and 15 women) and 30 healthy individuals as control group (18 men and 12 women). The mean age of the patients was 50.0±15.9 years, whereas that of the control group was 46.3±10.4 years. There was no statistically significant difference between these 2 groups in terms of the male/female ratio (p=0.223) and mean age (p>0.05).

MAIN POINTS

- The increased N/L and P/L ratios in the patient group indicate an underlying inflammation and ischemia pathology of SSNHL.
- These ratios can easily be calculated via Complete Blood Count (CBC) which was cheap and easily applicable test.
- The higher the P/L ratio, the lower the recovery rate from hearing loss, and this finding suggests that the P/L ratio can be an important prognostic indicator in patients with SSNHL.
- P/L ratio is also an important indicator for microcirculatory disorders associated with ischemia that supports the vascular theory of SSNHL.
- N/L ratio significantly decreased after HBO therapy which reflects diminished inflammation that was caused by hypoxia.

Table 1. Comparison of neutrophil/lymphocyte and platelet/lymphocyte ratios measured for the first time (pre-treatment) between the patient and control groups

	SSNHL patients group (n=60)				Control group (n=30)				p*
	Mean	SD (±)	Min	Max	Mean	SD (±)	Min	Max	
First N/L ratio	4.1	3.8	0.25	16.7	1.8	0.5	1.0	2.9	<0.001 (pre-treatment)
First P/L ratio	141.4	71.4	44.3	385.7	117.1	29.9	64.9	205.8	0.027 (pre-treatment)

*t-test or Mann-Whitney U test was performed for the independent groups.

SD: standard deviation (±); Min: minimum; Max: maximum; N/L: neutrophil/lymphocyte; P/L: platelet/lymphocyte; SSNHL, sudden sensorineural hearing loss; Bold p value: Indicate statistical significance.

Table 2. Comparison of neutrophil/lymphocyte and platelet/lymphocyte ratios measured for the first time (pre-treatment) and second time (post-treatment) in SSNHL patients (n=60)

	Mean	SD (±)	Min	Max	p*
First N/L ratio	4.1	3.8	0.25	16.7	0.001 (Pre-treatment)
Second N/L ratio	2.9	2.4	0.4	10.4	(Post-treatment)
First P/L ratio	141.4	71.4	44.3	385.7	<0.001 (Pre-treatment)
Second P/L ratio	115.6	57.8	12.4	280.1	(Post-treatment)

*t-test or Mann-Whitney U test was performed for the independent groups.

SD: standard deviation (±); Min: minimum; Max: maximum; N/L: neutrophil/lymphocyte; P/L: platelet/lymphocyte; SSNHL, sudden sensorineural hearing loss; Bold p value: Indicate statistical significance.

Table 3. Distribution of hearing loss degree and post-treatment hearing recovery (according to the Sudden Deafness Research Committee of the Japanese Ministry of Health, Labour and Welfare in 1984) of SSNHL patients

		N	%
First PTA average (pre-treatment)	Normal, 0–20 dB	-	0
	Mild HL, 21–40 dB	10	16.7
	Moderate HL, 41–60 dB	17	28.3
	Severe HL, 61–80 dB	23	38.3
	Profound HL, >80 dB	10	16.7
2. PTA average (post-treatment)	Slight recovery (10–29 dB gain)	14	23.3
	Marked recovery (>30 dB gain)	42	70.0
	Complete recovery (PTA≤20 dB, normal hearing)	4	6.7

PTA Average: Mean values of PTA thresholds of 0.25 kHz, 0.5 kHz, 1 kHz, 2 kHz, and 4 kHz frequencies.

PTA: pure tone audiometry; dB: decibels; HL: hearing loss; N: patient count; %: percentage of patients; SSNHL, sudden sensorineural hearing loss

The N/L ratio at the time of diagnosis in the groups 1 and 2, including patients with SSNHL, was found to be statistically significantly higher than that in the control group (4.1 ± 3.8 and 1.8 ± 0.5 ; $p < 0.001$, respectively). Similarly, the first P/L ratio measured at the time of diagnosis (pre-treatment) in the groups of patients with SSNHL was found to be statistically significantly higher than that in the control group (141.4 ± 71.3 and 117.1 ± 29.9 ; $p < 0.05$, respectively) (Table 1).

The second N/L ratio (post-treatment) in the patients with SSNHL measured after treatment (2.9 ± 2.4) was found to be significantly lower than the first N/L ratio (pre-treatment) (4.1 ± 3.8) ($p = 0.001$). Similarly, the second P/L ratio (post-treatment) measured after treatment was also found to be statistically significantly reduced compared

with the first P/L ratio (pre-treatment) (141 ± 71.4 and 115.6 ± 57.8 ; $p < 0.001$) (Table 2).

A comparison of the average PTA test results at the time of diagnosis and after the treatment in all the patients revealed that the recovery observed with the second measurement was statistically significantly higher than that observed with the first measurement (62 ± 21 dB and 44 ± 22 dB respectively; $p = 0.004$).

In a total of 32 patients (32/60; 53.3%), there was hearing loss in the left ear, and in 28 patients (46.7%), there was hearing loss in the right ear. According to the first average PTA test (pre-treatment), 16.7% patients had mild hearing loss, 28.3% had moderate hearing loss, 38.3% had severe hearing loss, and 16.7% had profound hearing loss; in addition, 4 of these patients recovered completely, 42 (70%) recovered markedly, and 14 (23.3%) recovered slightly following treatment (Table 3).

There was statistically no significant difference between the subgroups of patients (with and without HBO treatment) in terms of age, time of diagnosis, and number of comorbidities ($p > 0.05$). Furthermore, there was statistically no significant difference between the patients who were administered HBO treatment and those who were not administered HBO treatment with respect to the degrees of hearing loss assessed by the first PTA and the stages of recovery assessed by the second PTA after the treatment ($p > 0.05$).

The evaluation of the changes in the N/L and P/L ratios before (first measurement) and after treatment (second measurement) between the patients who were administered HBO treatment and those who were not revealed that the additional administration of HBO reduced these values further, but this decrease was not statistically significant ($p > 0.05$).

The patients who were administered HBO treatment were included in a separate group (group 1), and the results of the first (pre-treatment) and second (post-treatment) average PTA results in addition to the N/L and P/L ratios were compared. According to this comparison, there was a statistically significant improvement in the average PTA test results after the treatment in the patients who were administered HBO treatment ($p < 0.001$) and a statistically significant decrease in their N/L ratios after the treatment ($p = 0.009$); however, there was no significant change in their P/L ratios after the treatment ($p = 0.125$) (Table 4).

In the patients who were not administered HBO treatment (group 2), the second (post-treatment) average PTA test results presented a significant improvement compared with the first (pre-treatment)

Table 4. Comparison of hearing recovery and the first (pre-treatment) and second (post-treatment) neutrophil/lymphocyte and platelet/lymphocyte ratios in patients who were administered HBO treatment (group 1)

	Group given HBO (group 1) (n=30)		p*
	First M (Mean±SD)	Second M (Mean±SD)	
Av. PTA, dB	66±22	46±25	<0.001
N/L ratio	3.8±3.5	2.6±2.0	<0.05
P/L ratio	132±70	116±59	0.125

Av. PTA: Average pure tone audiometry (mean values of PTA thresholds of 0.25 kHz, 0.5 kHz, 1 kHz, 2 kHz, and 4 kHz frequencies).

*Wilcoxon test was performed.

SD: standard deviation (±); HBO: hyperbaric oxygen; dB: decibels; N/L: neutrophil/lymphocyte; P/L: platelet/lymphocyte; M: Mean values; Bold p value: Indicate statistical significance.

average PTA test results ($p<0.001$), whereas there was a statistically significant decrease in the P/L ratios after the treatment ($p=0.002$) (Table 5). However, there was no significant difference between the first and second measurements of the N/L ratio in patients who were not administered HBO treatment ($p=0.125$).

The correlation between the results from and the difference in the first and second average PTA test results and the first and second N/L and P/L ratios were studied. Therefore, there was a single correlation between the average PTA and blood test results, and there was a moderately negative correlation between the first P/L ratios and dB difference as assessed by PTA tests after treatment ($r=-0.378$; $p=0.003$). It was observed that as the P/L ratios increased, the recovery of hearing loss decreased. In addition, there was no significant correlation between the average values of the pre- and post-treatment hearing tests and the N/L and P/L ratios ($p>0.05$).

The blood test results significantly correlated with each other as did the PTA test results. The first and second N/L and P/L ratios were compared and were found to be statistically significantly correlated. Moreover, the average values of the first and second audiometry tests and their differences were found to be significantly positively correlated ($p<0.05$).

DISCUSSION

SSNHL, presenting with total or partial loss of hearing, is described as a sensorineural hearing loss with unknown pathogenesis, with a rarely determined etiology, occurring suddenly ≤ 72 hours at 3 sequential frequencies at ≥ 30 dBs, and is an otologic emergency [1].

The incidence of SSNHL is higher in individuals aged 45–60 years compared with other age groups. The mean age at which individuals develop SSNHL is 43–53 years according to studies on 7,500 patients in Europe, Japan, and the United States [12–14]. In this study, the mean age of the patients with SSNHL was 50.0 (± 15.9) years, which was consistent with that reported in the literature.

The etiology of SSNHL still remains uncertain, and only a small portion (about 10%) of causative factors could be established [11]. The proposed etiologic factors are mainly based on the following 3 theories: viral hypothesis, vascular theory, and immunological theory [15]. The viral hypothesis states that direct viral infection from hematogenous and other routes, reactivation of a latent virus, and triggering

of an indirect immune-mediated mechanism are responsible factors for viral infection of inner ear structures and the cochlear nerve that leads to SSNHL. Thromboembolic or vasospastic vascular occlusion is responsible for SSNHL per the vascular theory. The immunological theory postulates that SSNHL could be because of cross-reaction of inner ear antigens and structures with circulating antibodies and/or immune complexes and a direct attack of activated T-cells. Moreover, etiologic transition between these propounded theories has also been possible, such as immune-mediated antibody response to inner ear antigens triggered by viral infections, autoantibodies against phospholipids (anti-PL) causing thrombotic phenomena (vascular compromise) in phospholipid syndrome, and antibodies against endothelial cells (anti-EC) causing vascular endothelial destruction and vasculitis [16–18].

In patients with SSNHL, common measures as bed rest, salt-free diet, limited-intake of alcohol, limited smoking, and abstaining from stress are the starting point for treatment. The treatment of patients with SSNHL is controversial. The objective of the combined treatment model is to benefit from each medication's (corticosteroids, anti-viral agents, vitamin B complex, vasodilators, etc.) possible limited effects or possibly from the synergic impact generated by the combined use of these [1, 19].

The medical agents used by various healthcare centers for patients with SSNHL are mostly focused on suppressing inflammation and autoimmune damage, thus reducing edema and regulating microcirculation. Recently, the immunological and the vascular theories have been found as stronger etiologic factors in patients with SSNHL [15, 20]. The available data for the viral hypothesis as a causative mechanism are limited [15]. In addition, the presence of antibodies to heat shock protein 70 (anti-HSP70) and phospholipids (anti-PL) were found in 40% and 33% of patients with SSNHL, respectively [15, 21]. Corticosteroids (the most potent anti-inflammatory medications) given through the intravenous, oral, and intratympanic routes was found to be the only proven drug improving hearing loss in patients with SSNHL. Other treatments, including HBO, antivirals, and plasma volume expanders has controversial benefits. All these findings support the immunological theory as a more common possible etiologic factor [1, 22–24].

The effects of corticosteroids, owing to their anti-inflammatory properties, on the inner ear are as follows: reduced lymphocyte, eosinophil, and basophil counts; inhibition of macrophage function; decreased release of inflammatory mediators, such as prostaglandin (PG), leukotriene (LT), and platelet activating factor; reduced secretion and release of cytokines; reduced complement impact; and reduced capillary permeability [23–24]. It is believed that corticosteroid treatment is responsible for reduced inflammation of the labyrinth, increased cochlear blood flow, and the protection of cochlea from ischemia [24, 25].

In this study, the combined corticosteroid treatment, which is the routine treatment protocol for SSNHL, was administered to all the patients. The comparison of the audiometry test results at the time of diagnosis and after treatment revealed that there was a statistically significant improvement in favor of the PTA test results after treatment. Patients with SSNHL have increased counts of neutrophils and levels of interleukin-6 (IL-6), and tumor necrosis factor (TNF), and this

increase is associated with the severity and prognosis of the disease [26]. In a study by Masuda et al. [26], it was reported that polymorphisms in IL-6 results was an increased risk for SSNHL; however, the inflammatory mechanisms of and treatment mechanisms for SSNHL, such as corticosteroid and HBO treatments, were yet to be clarified.

There is an intention to include HBO treatment in addition to the corticosteroid treatment for patients with SSNHL, although its efficacy is yet to be confirmed [1]. The patients included in this study were divided into 2 groups of 30 patients each, and these groups were homogenous in terms of age, sex, duration of starting treatment, and severity of hearing loss. The statistical analyses revealed that administering HBO and a combined corticosteroid treatment had a positive impact on the recovery of hearing loss; however, this impact was not statistically significant ($p>0.05$).

Clinical trials and basic research indicate that HBO treatment, as the only treatment or as an adjuvant treatment, was beneficial in terms of acute inflammatory response or in the inflammatory process that emerges secondary to ischemia [27]. In their study, Yu et al. [28] revealed that HBO treatment diminished the inflammatory response observed in cases of acute pancreatitis by inhibiting IL-2, IL-6, and TNF- α expression. The results of a study conducted by Wilson et al. [29] on animals also revealed that HBO treatment diminished joint inflammation and soothed mechanical hyperalgesia. HBO treatment also suppressed immunity response to antigen, reduced leucocytes in circulation, and increased the lifespan of an allograft owing to the immunological changes it caused [30]. It is unfortunate that the number of studies on the effect of HBO on the inflammatory response in SSNHL is extremely low [31].

The N/L ratio is a potential indicator in determining inflammation. The neutrophil count reflects the non-specific inflammatory process that is the first line of defense, whereas the lymphocyte count is associated with the regulating and protective components of inflammation. Therefore, the N/L ratio is a valuable index of inflammatory processes [32, 33].

A study by Ulu et al. [34] reported that the first N/L ratio was significantly higher in patients with SSNHL than in healthy individuals and that the N/L ratio was statistically significantly high in patients who barely responded to treatment in a group of patients with SSNHL. According to the results of this study, the first N/L and P/L ratios were statistically significantly higher in patients with SSNHL than in the healthy individuals (group 1, $p=0.001$; group 2, $p<0.001$). P/L ratio is also an important indicator for microcirculatory disorders associated with ischemia and is examined in patients with peripheral arterial circulation diseases such as atherosclerosis [9]. Increase of these markers suggest that both of inflammatory and vascular (ischemic) factors are intertwined with each other in varying degrees. There was a statistically significant decrease in the N/L and P/L ratios following treatment in all patients with SSNHL.

The N/L and P/L ratios are indicators for inflammation that have been described here and can be assessed in the peripheral blood [35]. Thrombocytes have an important role in atherosclerosis. Gary et al. [36] emphasized that an increased P/L ratio was a critical risk factor in ischemia. Ciccone et al. [37] maintained that SSNHL was closely

associated with vascular endothelial dysfunction and that increased N/L and P/L ratios were also associated with hearing loss. In this study, the P/L ratio and dB difference between the first average PTA test results before and after treatment were statistically significantly negatively correlated ($p=0.003$; $r=-0.378$). Therefore, higher the P/L ratio, lower the recovery rate from hearing loss. This finding suggests that the P/L ratio can be an important prognostic indicator in patients with SSNHL, and this is the first study to evaluate this correlation. Because this ratio has a close relationship with ischemia, this finding suggests that higher the P/L ratio (and possibly more severe ischemia), hearing improvement is less likely.

A separate comparison revealed that the N/L ratios in the patients who were administered HBO treatment in addition to the corticosteroid treatment were statistically significantly lower than those in the other patient group ($p=0.009$). Although HBO treatment reduced the N/L ratio, no improvement was observed in the results of the PTA test results at the same ratio. Furthermore, though administering HBO treatment improved the hearing levels of the patients, this improvement was not statistically significant. This is considered to be consistent with the uncertainty related to the efficacy of HBO treatment in patients with SSNHL.

There are contradictory results from numerous studies with respect to the efficacy of HBO treatment. A study demonstrated HBO treatment administered along with the conventional treatment significantly improved the results in treating SSNHL [38]. In contrast, in a study by Satar et al. [39], 37 patients with SSNHL were administered medical treatment along with HBO, and another group of 17 patients were administered only medical treatment; and their results were compared. The conclusion from this comparison emphasized that administering HBO treatment in addition to the medical treatment did not have any additional benefit.

However, in this study, the comparison between the complete blood counts obtained before and after HBO treatment revealed that the N/L and P/L ratios were decreased, and this was statistically significant only with respect to the N/L ratio ($p=0.009$). This indicates that inflammation is important in the pathophysiology of SSNHL and that HBO treats inflammation and plays a role in microcirculation. To the best of our knowledge, this is the first study examining the effect of HBO treatment on the N/L and P/L ratios in patients with SSNHL. The limitations of this study are its retrospective nature and the small sample size of the groups.

CONCLUSION

Although there are positive views that advocate addition of HBO to the steroid treatment in patients with SSNHL, there are also doubts about its efficacy. To determine the underlying pathophysiology of SSNHL and the mechanism of action of HBO treatment on the pathophysiology of the disease, studies [3-9] have been conducted on the N/L and P/L ratios, which are the inflammation and ischemia indicators that have recently been described. The reduced N/L and P/L ratios in the patient group indicated an underlying inflammation and ischemia pathology. Adding HBO to the treatment reduced the N/L ratio significantly after the treatment. This indicates that HBO treatment acts by diminishing inflammation. Moreover, the first P/L ratio (indicator of ischemia), which was high, was found to be inversely

proportional to the improvement observed in the patients with SSNHL. This negative correlation indicates that the P/L ratio can be an important prognostic indicator for SSNHL. There is need for new homogenous studies on larger groups of patients in the literature so that the prognostic importance of these indicators that have only been described with respect to treating SSNHL can be further highlighted.

Ethics Committee Approval: Ethics committee approval was received for this study from the Ethics Committee of Istanbul Medeniyet University Göztepe Training and Research Hospital (2017/0329).

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REFERENCES

- Chandrasekhar SS, Tsai Do BS, Schwartz SR, Bontempo LJ, Faucett EA, Finestone SA, et al. Clinical Practice Guideline: Sudden Hearing Loss (Update). *Otolaryngol Head Neck Surg* 2019; 161: S1-S45. [\[Crossref\]](#)
- Holy R, Navara M, Dosel P, Fundova P, Prazenica P, Hahn A. Hyperbaric oxygen therapy in idiopathic sudden sensorineural hearing loss (ISSNHL) in association with combined treatment. *Undersea Hyperb Med* 2011; 38: 137-42.
- Korpinar S, Alkan Z, Yigit O, Gor AP, Toklu AS, Cakir B, et al. Factors influencing the outcome of idiopathic sudden sensorineural hearing loss treated with hyperbaric oxygen therapy. *Eur Arch Otorhinolaryngol* 2011; 268: 41-7. [\[Crossref\]](#)
- Masuda M, Kanzaki S, Minami S, Kikuchi J, Kanzaki J, Sato H, et al. Correlations of inflammatory biomarkers with the onset and prognosis of idiopathic sudden sensorineural hearing loss. *Otol Neurotol* 2012; 33: 1142-50. [\[Crossref\]](#)
- Elkind MS. Inflammatory markers and stroke. *Curr Cardiol Rep* 2009; 11: 12-20. [\[Crossref\]](#)
- Guthrie GJ, Charles KA, Roxburgh CS, Horgan PG, McMillan DC, Clarke SJ. The systemic inflammation-based neutrophil-lymphocyte ratio: experience in patients with cancer. *Crit Rev Oncol Hematol* 2013; 88: 218-30. [\[Crossref\]](#)
- Balta S, Demirkol S, Arslan Z, Demir M, Ozturk C. The neutrophil lymphocyte ratio in patients with ST segment elevation myocardial infarction. *Eur Rev Med Pharmacol Sci* 2014; 18: 141.
- Rudack C, Langer C, Stoll W, Rust S, Walter M. Vascular risk factors in sudden hearing loss. *Thromb Haemost* 2006; 95: 454-61. [\[Crossref\]](#)
- Kwon HC, Kim SH, Oh SY, Lee S, Lee JH, Choi HJ, et al. Clinical significance of preoperative neutrophil-lymphocyte versus platelet-lymphocyte ratio in patients with operable colorectal cancer. *Biomarkers* 2012; 17: 216-22. [\[Crossref\]](#)
- Nakagawa T, Kumakawa K, Usami S, Hato N, Tabuchi K, Takahashi M, et al. A randomized controlled clinical trial of topical insulin-like growth factor-1 therapy for sudden deafness refractory to systemic corticosteroid treatment. *BMC Med* 2014; 12: 219. [\[Crossref\]](#)
- Penido NO, Cruz OL, Zanon A, Inoue DP. Classification and hearing evolution of patients with sudden sensorineural hearing loss. *Braz J Med Biol Res* 2009; 42: 712-6. [\[Crossref\]](#)
- Byl FM Jr. Sudden hearing loss: eight years' experience and suggested prognostic table. *Laryngoscope* 1984; 94: 647-61. [\[Crossref\]](#)
- Shaia FT, Sheehy JL. Sudden sensori-neural hearing impairment: a report of 1,220 cases. *Laryngoscope* 1976; 86: 389-98. [\[Crossref\]](#)
- Megighian D, Bolzan M, Barion U, Nicolai P. Epidemiological considerations in sudden hearing loss: a study of 183 cases. *Arch Otorhinolaryngol* 1986; 243: 250-3. [\[Crossref\]](#)
- Greco A, Fusconi M, Gallo A, Marinelli C, Macri GF, De Vincentiis M. Sudden sensorineural hearing loss: an autoimmune disease? *Autoimmun Rev* 2011; 10: 756-61. [\[Crossref\]](#)
- Shoenfeld Y, Blank M, Cervera R, Font J, Raschi E, Meroni PL. *Ann Rheum Dis* 2006; 65: 2-6.
- Naarendorp M, Spiera H. Sudden sensorineural hearing loss in patients with systemic lupus erythematosus or lupus-like syndromes and antiphospholipid antibodies. *J Rheumatol* 1998; 25: 589-92.
- Ottaviani F, Cadoni G, Marinelli L, Fetoni AR, De Santis A, Romito A, et al. Anti-endothelial autoantibodies in patients with sudden hearing loss. *Laryngoscope* 1999; 109: 1084-7. [\[Crossref\]](#)
- Conlin AE, Parnes LS. Treatment of sudden sensorineural hearing loss: II. A Meta-analysis. *Arch Otolaryngol Head Neck Surg* 2007; 133: 582-6. [\[Crossref\]](#)
- Fusconi M, Chistolini A, de Virgilio A, Greco A, Massaro F, Turchetta R, et al. Sudden sensorineural hearing loss: a vascular cause? Analysis of prothrombotic risk factors in head and neck. *Int J Audiol* 2012; 51: 800-5. [\[Crossref\]](#)
- García Berrocal JR, Ramírez-Camacho R, Arellano B, Vargas JA. Validity of the Western blot immunoassay for heat shock protein-70 in associated and isolated immunorelated inner ear disease. *Laryngoscope* 2002; 112: 304-9. [\[Crossref\]](#)
- Rauch SD. Intratympanic steroids for sensorineural hearing loss. *Otolaryngol Clin North Am* 2004; 37: 1061-74. [\[Crossref\]](#)
- Nagura M, Iwasaki S, Wu R, Mizuta K, Umemura K, Hoshino T. Effects of corticosteroid, contrast medium and ATP on focal microcirculatory disorders of the cochlea. *Eur J Pharmacol* 1999; 366: 47-53. [\[Crossref\]](#)
- Tabuchi K, Oikawa K, Uemaetomari I, Tsuji S, Wada T, Hara A. Glucocorticoids and dehydroepiandrosterone sulfate ameliorate ischemia-induced injury of the cochlea. *Hear Res* 2003; 180: 51-6. [\[Crossref\]](#)
- Haynes DS, O'Malley M, Cohen S, Watford K, Labadie RF. Intratympanic dexamethasone for sudden sensorineural hearing loss after failure of systemic therapy. *Laryngoscope* 2007; 117: 3-15. [\[Crossref\]](#)
- Masuda M, Kanzaki S, Minami S, Kikuchi J, Kanzaki J, Sato H, Ogawa K. Correlations of inflammatory biomarkers with the onset and prognosis of idiopathic sudden sensorineural hearing loss. *Otol Neurotol* 2012; 33: 1142-50. [\[Crossref\]](#)
- Lee YS, Chio CC, Chang CP, Wang LC, Chiang PM, Niu KC, et al. Long course hyperbaric oxygen stimulates neurogenesis and attenuates inflammation after ischemic stroke. *Mediators Inflamm* 2013; 2013: 512978. [\[Crossref\]](#)
- Yu X, Li YG, He XW, Li XR, Din BN, Gan Y, et al. Hyperbaric oxygen reduces inflammatory response in acute pancreatitis by inhibiting NF-kappaB activation. *Eur Surg Res* 2009; 42: 130-5. [\[Crossref\]](#)
- Wilson HD, Wilson JR, Fuchs PN. Hyperbaric oxygen treatment decreases inflammation and mechanical hypersensitivity in an animal model of inflammatory pain. *Brain Res* 2006; 1098: 126-8. [\[Crossref\]](#)
- Erdmann D, Roth AC, Hussmann J, Lyons SF, Mody NJ, Kucan JO, et al. Skin allograft rejection and hyperbaric oxygen treatment in immune-histoincompatible mice. *Undersea Hyperb Med* 1995; 22: 395-9.
- Li H, Zhao D, Diao M, Yang C, Zhang Y, Lv Y, et al. Hyperbaric Oxygen Treatments Attenuate the Neutrophil-to-Lymphocyte Ratio in Patients with Idiopathic Sudden Sensorineural Hearing Loss. *Otolaryngol Head Neck Surg* 2015; 153: 606-12. [\[Crossref\]](#)

32. Frisina ST, Mapes F, Kim S, Frisina DR, Frisina RD. Characterization of hearing loss in aged type II diabetics. *Hear Res* 2006; 211: 103-13. [\[Crossref\]](#)
33. Soardo G, Donnini D, Domenis L, Catena C, De Silvestri D, Cappello D, et al. Oxidative stress is activated by free fatty acids in cultured human hepatocytes. *Metab Syndr Relat Disord* 2011; 9: 397-401. [\[Crossref\]](#)
34. Ulu S, Ulu MS, Bucak A, Ahsen A, Yucedag F, Aycicek A. Neutrophil-to-lymphocyte ratio as a new, quick, and reliable indicator for predicting diagnosis and prognosis of idiopathic sudden sensorineural hearing loss. *Otol Neurotol* 2013; 34: 1400-4. [\[Crossref\]](#)
35. Imtiaz F, Shafique K, Mirza SS, Ayoob Z, Vart P, Rao S. Neutrophil lymphocyte ratio as a measure of systemic inflammation in prevalent chronic diseases in Asian population. *Int Arch Med* 2012; 5: 2. [\[Crossref\]](#)
36. Gary T, Pichler M, Belaj K, Hafner F, Gerger A, Froehlich H, et al. Platelet-to-lymphocyte ratio: a novel marker for critical limb ischemia in peripheral arterial occlusive disease patients. *PLoS One* 2013; 8: e67688. [\[Crossref\]](#)
37. Ciccone MM, Cortese F, Pinto M, Di Teo C, Fornarelli F, Gesualdo M, et al. Endothelial function and cardiovascular risk in patients with idiopathic sudden sensorineural hearing loss. *Atherosclerosis* 2012; 225: 511-6. [\[Crossref\]](#)
38. Topuz E, Yigit O, Cinar U, Seven H. Should hyperbaric oxygen be added to treatment in idiopathic sudden sensorineural hearing loss? *Eur Arch Otorhinolaryngol* 2004; 261: 393-6. [\[Crossref\]](#)
39. Satar B, Hidir Y, Yetiser S. Effectiveness of hyperbaric oxygen therapy in idiopathic sudden hearing loss. *J Laryngol Otol* 2006; 120: 665-9. [\[Crossref\]](#)