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Original Article

Comparison of Resolvin D1 Levels in Patients with Aneurysmal Subarachnoid Haemorrhage with Those in Healthy Controls

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ABSTRACT

Objective: The literature points to the role of neuroinflammation in the aetiology of vasospasm, which is the leading cause of mortality and morbidity after aneurysmal subarachnoid haemorrhage. Neuroinflammation has been found to contribute to early and delayed brain injury, both of which are associated with poor clinical outcomes. Resolvin D1 is hypothesised to have a protective effect on neurons against apoptosis and has anti-inflammatory and pro-resolving effects on the neuroinflammation and vasospasm after aneurysmal subarachnoid haemorrhage. In this study, we aimed to investigate the serum resolvin D1 levels and its possible relationship with vasospasm and inflammatory markers, such as C-reactive protein, neutrophil and albumin in patients with aneurysmal subarachnoid haemorrhage.

Methods: Fifteen patients with spontaneous aneurysmal subarachnoid haemorrhage between June 2017 and May 2018 presenting at our institution were included in the study. Their data were compared with those of 17 healthy volunteers. Patients with aneurysmal subarachnoid haemorrhage were divided into two groups: the subarachnoid haemorrhage with vasospasm group (8 patients), which included patients with subarachnoid haemorrhage and angiographic vasospasm , and subarachnoid haemorrhage without vasospasm group (7 patients), which included patients with subarachnoid haemorrhage without angiographic vasospasm. Serial serum resolvin D1 measurements were taken on days 1, 4, 9 and 14 after subarachnoid haemorrhage.

Results: Resolvin D1 levels were statistically significantly higher on day 1 after subarachnoid haemorrhage in patients with angiographic vasospasm (p=0.021). Additionally, in the group with angiographic vasospasm, all the measured resolvin D1 values were also higher compared to other groups. The measurements of serum C-reactive protein and neutrophil levels were found to be statistically significantly higher on day 1 after subarachnoid haemorrhage in both groups compared to the control group.

Conclusion: Resolvin D1 levels tend to increase secondary to inflammation because of its neuroprotective and anti-inflammatory properties. Thus, high resolvin D1levels in the subarachnoid haemorrhage + vasospasm group indicated that inflammatory processes play a role in the aetiopathogenesis of angiographic vasospasm after aneurysmal subarachnoid haemorrhage. Consequently, resolvin D1 might be an important biomarker in the prediction of the angiographic vasospasm after aneurysmal subarachnoid haemorrhage.

INTRODUCTION

Subarachnoid haemorrhage (SAH), a type of stroke, is one of the most important causes of mortality and morbidity among stroke patients. The leading cause of spontaneous SAH is aneurysms with an incidence rate of 75%–85%. The worldwide incidence of aneurysmal SAH is 9–10 per 100,000 per year. A total of 10% of aneurysmal SAH cases die at the initial bleeding; 25% of these cases die within the first 24 hours. Approximately half of the cases die in the first 3 months after SAH, and morbidity is observed in half of the survivors.Cerebral vasospasm, a leading cause of mortality and morbidity after aneurysmal SAH, is the reversible narrowing of cerebral vessels against mechanical and physiological stimuli after aneurysm rupture. The pathogenesis of this complication has not yet been clearly elucidated and is affected by complex multifactorial events. The imbalance between lipid peroxides and endothelium-derived vasoconstrictor and vasodilator substances as well as the disruption of neuronal mechanisms

involved in the arachidonic acid cascade, inflammatory pathways, endothelial proliferation and apoptosis result in vasospasm.[1,2] Neuroinflammation plays an important role in the pathogenesis of SAH. Pro-inflammatory cytokines, such as interleukin 1 beta (IL-1β), interleukin 6 (IL-6) and tumour necrosis factor (TNF), as well as adhesion molecules, such as P- and S-selectins, reach high concentrations in serum and cerebrospinal fluid (CSF) in hours after SAH.[1,3,4] The inflammatory response has been shown to contribute to early and delayed brain injury as well as vasospasm. More than 75% of patients develop systemic inflammatory response syndrome (SIRS) characterised by increased systemic inflammatory cytokines. SIRS has also been associated with neurocognitive disorders that develop after subarachnoid haemorrhage.[5] Both cellular and molecular components involved in this inflammatory response. Pro-inflammatory cytokines, such as IL-1β, IL-6 and TNF, as well as adhesion molecules, such as P- and S-selectins, reach high concentrations in serum and CSF hours after SAH. Thus, the complement system is activated, erythrocyte lysis is accelerated, the release of spasmogens, including endothelin 1 (ET-1), increases first, free radicals appear, neurotransmitter and neuroendocrine system changes occur, resulting in neurodegeneration and neuronal apoptosis.[1,6–9] The resulting high inflammatory response is associated with hyperthermia, vascular spasm, early brain injury and poor neurological outcome.[10–13]

Docosahexaenoic acid (DHA), the longest chain polyunsaturated fatty acid of the omega-3 family, and its metabolites are essential for the maturation and regulation of the nervous system. DHA and its metabolites also promote synaptogenesis and neurogenesis, stimulate gene expression and neuronal activity, inhibit the release of major inflammatory cytokines like TNF, IL-1 and IL-6, and act as neuroprotective agents.[14] Resolvin D1 (RvD1) is a derivative of DHA, an omega-3 fatty acid. RvD1 is an endogenous chemical mediator that has a potent anti-inflammatory effect and is involved in the resolution of inflammation.[15] It has two specific receptors on polymorphonuclear leukocytes (PMNL), namely lipoxin A4 receptor/formyl-peptide receptor 2 (ALX/FPR2) and G protein-dependent receptor 32 (GPR32). Moreover, RvD1 stimulates phagocytosis and increases clearance via its receptors on macrophages. It also promotes its anti-inflammatory effect through its two specific receptors.[16] Further, RvD1 exerts a protective effect by reducing neutrophil migration in tissue damage secondary to ischemia-reperfusion.[17] In an experimental animal model of autoimmune encephalitis, daily oral administration of RvD1 has been shown to suppress autoreactive T cells and reduce disease progression by stimulating the M2 phenotype of monocytes/macrophages and microglial cells.[18]

The primary aim of this study was to evaluate the serum RvD1 levels for a few days in patients with aneurysmal SAH, to compare these values with the control group, and to reveal the possible associations between RvD1 with vasospasm. The secondary aim of the study was to identify the possible associations between RvD1 levels and inflammatory markers [C-reactive protein (CRP), neutrophil and albumin]. Therefore, this study may contribute to identifying the possible role of RvD1 in neuroinflammation and vasospasm after aneurysmal SAH.

MATERIALS AND METHODS

Patients treated for aneurysmal SAH in our department between June 2017 and May 2018 were included in the study. The control group included healthy volunteers. All patients and/or their first-degree relatives as well as healthy volunteers provided informed consent to participate in the study. The study was approved by the University of Health Sciences Kartal Dr. Lütfi Kırdar City Hospital Ethics Committee, with reference number 2017/514/202/26.

Thirteen female and six male patients with aneurysmal SAH who met the inclusion and exclusion criteria were included in the study. As 1 female and 3 male patients died within the first four days, they were excluded from the study. Blood samples were obtained on days 1, 4, 9 and 14 after the SAH. Thirteen female and four male healthy volunteers not receiving any medical treatment were included in the study. The patients' history was obtained, they underwent neurological examinations as well as brain computed tomography (CT), CT angiography and cerebral angiography, and a definitive diagnosis was made accordingly. A form questioning sociodemographic information was filled by the clinician; and through this form information about personal and family history, comorbidities, medications and habits were obtained. At the time of admission, the patients were classified according to scoring systems including Hunt and Hess Scale, Fisher Scale and World Federation of Neurosurgical Societies (WFNS) grading system. Angiographies was performed on day 3 or 4 after SAH by an experienced neuroradiologist, and the patients were divided into groups according to the presence (8 patients) or absence (7 patients) of radiological vasospasm. Blood samples were obtained from the patients in 10 cc biochemistry tubes after at least 8 hours of fasting, and these blood samples were centrifuged at 4000 g for 5 minutes. Next, the separated serum samples were transferred to sterile Eppendorf tubes, and delivered to an external laboratory at +4°C and stored in a deep freezer at −80°C. These serum samples were used to examine the RvD1 levels. In addition, post-discharge laboratory test results of the patients and the control group evaluated retrospectively. Statistical evaluations and analyses were performed according to the results obtained.

Inclusion criteria: 1) Patients with aneurysmal subarachnoid haemorrhage diagnosed with imaging techniques were included in the experimental group, and healthy volunteers were included in the control group b) Cases who provided informed written consent for participation were included in the study. Exclusion criteria: a) alcohol/substance-use disorder; b) the presence of acute infection or chronic inflammatory diseases, such as chronic lung dis-

ease, kidney disease, chronic hepatitis, thyroid disease or rheumatoid arthritis, or a history of active cancer; c) the presence of a psychiatric illness; d) the presence of on-going infection and allergy.

The examination and calculation of RvD1

The Human Resolvin D1 ELISA Kit (Human RvD1 ELISA kit, SUNRED, 201-12-9313) was used. The RvD1 measurement from serum samples obtained from the patients was carried out in accordance with the colorimetric measurement principle and the manufacturer's recommendation. In summary, the method was based on the principle of in vitro quantitative measurement of the RvD1 level in human serum in an experimental setting using a colorimetric spectrophotometer. A total of 77 human serum samples were analysed in this study. The post-reaction colorimetric colour change (absorbance value) was measured with a spectrophotometer (ELISA reader) using 450 nm filters in accordance with the manufacturer's recommendations, and the results were analysed as follows: a) a standard graph was obtained with the optical density of the standards for verification of the study and determination of the Resolvin levels of the human serum samples; b) samples were analysed according to the standard curve (Fig. 1) obtained and the formula provided by the manufacturer; c) The Resolvin results of the tested human serum samples were calculated in ng/ml; d) the patient outcome range is specified as 0.15 ng/ml–30 ng/ml as recommended by the manufacturer (Fig. 2).

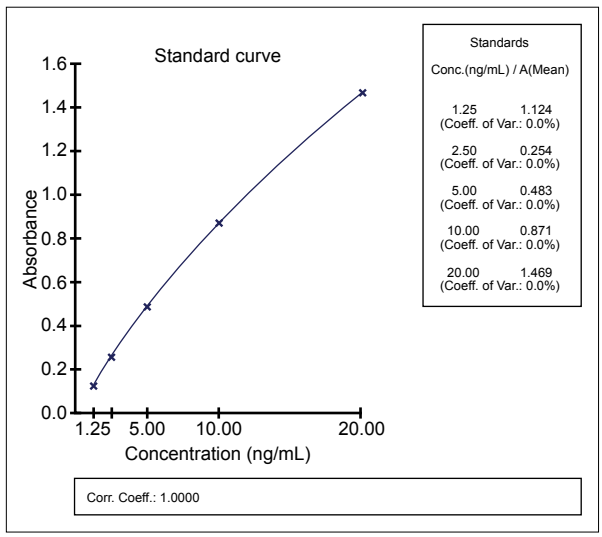

Figure 1. Standard plot of Resolvin D1.

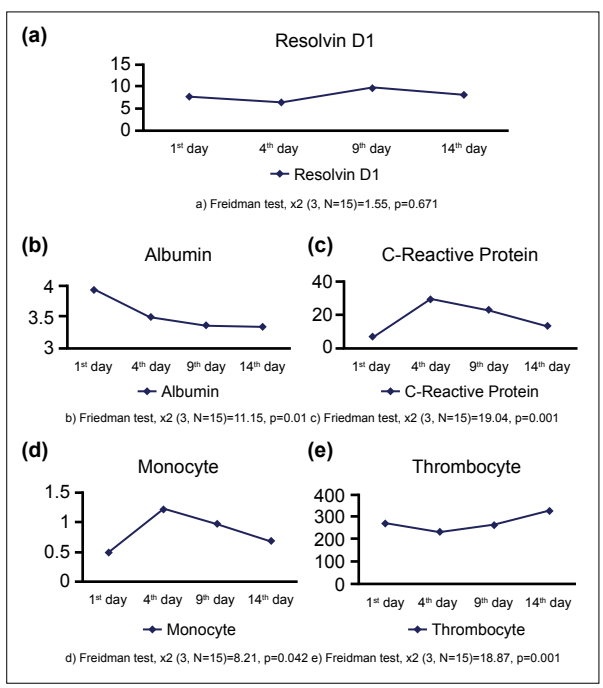

Figure 2. Statistically significant levels of **(a)** Resolvin D1, **(b)** Albumin, **(c)** C-reactive protein, **(d)** Monocyte and **(e)** Platelets.

Statistical analysis

This is a prospective study. SPSS 22.0 was used for statistical analysis. During the statistical analysis of the findings, the frequencies were expressed as percentages for categorical variables and as mean±standard deviation for continuous variables. The Shapiro–Wilk test was used to test conformity to the normal distribution, and non-parametric tests were used as the continuous variables did not fit normal distribution. Kruskal–Wallis and Mann–Whitney U tests were used to reveal the mean differences between independent samples, and the Friedman and Wilcoxon tests were used to determine the mean differences between repeated measurements. The statistical significance level was accepted as $p<0.05$ (Table 1).

RESULTS

The study group consisted of 12 female and 3 male patients with aneurysmal SAH, and the control group included 13 female and 4 male healthy volunteers. The mean age of patients with aneurysmal SAH was 51.4±12.8 years, and the mean age of the control group was 38.3±10.6 years. The patients were divided into groups according to the Hunt and Hess Scale, Fisher Scale and WFNS grading system, and the details are shown in the table below (Table 2).

Table 1. Comparison of the mean values of Resolvin D1 levels according to vasospasm status

	Radiological vasospasm	Mean Resolvin D1 level	p-value
Resolvin D1 (day 1)	+	10.50	0.021*
	–	5.14	
Resolvin D1 (day 4)	+	9.25	0.247
	–	6.57	
Resolvin D1 (day 9)	+	10.00	0.064
	–	5.71	
Resolvin D1 (day 14)	+	8.63	0.563
	–	7.29	

*Mann–Whitney U test was applied.

Table 2. Grouping of patients according to grading systems

Grade	Fisher	Hunt and Hess	WFNS
1	0	3 (20%)	5 (33.3%)
2	1 (6.7%)	7 (46.7%)	7 (46.7%)
3	12 (80%)	5 (33.3%)	3 (20%)
4	2 (13.3%)	0	0
5	•	0	0

• Fisher scale consists of 4 grades. WFNS: World Federation of Neurosurgical Societies.

Blood samples were obtained on days 1, 4, 9 and 14 after aneurysmal SAH. Only a single blood sample was obtained from the control group. The change within the days was analysed by evaluating the serum samples and comparing the results, and a statistically significant difference was found in albumin, monocytes, CRP and platelet (PLT) values. RvD1 levels and laboratory tests showing significant differences are presented in the graphics below.

When the serum albumin levels obtained on days 1, 4, 9 and 14 after SAH in the patient group were compared using the Friedman test, a statistically significant difference was found between the values obtained on the specified days. A Wilcoxon test was performed when comparing two measurement results in dependent samples to determine the significance of the measurement day. In the comparison made according to the rating scale scores, statistically significant differences were observed between measurements obtained on days 1 and 4 (p=0.011), days 1 and 9 (p=0.003) as well as days 1 and 14 (p=0.002). Albumin levels were compared in the groups with and without vasospasm, but no statistically significant difference was found; however, the group with vasospasm was found to have lower albumin levels than the group without it on all days. There was a significant difference in CRP levels between those measured on days 1 and 4 (p=0.005). Further, there was a significant difference in monocyte levels between those measured on days 1 and 4 (p=0.041) as well as on days 1 and 9 (p=0.027). Platelet values were found to be different on days 1 and 4 (p=0.003), 1 and 14 (p=0.011), 4 and 14 (p=0.002) and 9 and 14 (p=0.02), and platelet values increased gradually.

All parameters of the serum samples were compared between the experimental and control groups, and statistically significant differences were found in RvD1 (p=0.001), albumin (p=0.01), leukocyte (p=0.002), lymphocyte (p=0.001) and neutrophil (p=0.001) values.

The mean neutrophil value In the group with vasospasm, was found to be statistically significantly higher on day 1 after SAH compared to the group without vasospasm (p=0.008). In addition, the measurements of leucocytes on days 1 (p=0.015) and 4 (p=0.028) and PLT on days 1 (p=0.049), 4 (p=0.013) and 9 (p=0.028) were also found to be significant.

DISCUSSION

The main finding of the study is that the day 1 serum RvD1 levels in patients with aneurysmal SAH were found to be statistically significantly lower than in the control group. In the patient group, the highest RvD1 value was measured on day 9 and the lowest on day 4. Statistically significant differences were found in RvD1 values of the patients on day 4. Comparison of RvD1 levels on days 1, 4, 9 and 14 in patients with and without radiological vasospasm revealed that RvD1 levels on day 1 were statistically significantly higher in the group with vasospasm (Fig. 3). No significant correlation was found between day 1 levels of RvD1 and Fisher, Hunt-Hess and WFNS scales. CRP, another inflammatory marker, demonstrated a statistically significant progressive increase in its serum values from day 1 to day 4 after SAH in the patient group, and there was a slow decrease in its values from day 4 to day 9 and 14. Comparing the serum CRP levels between patients with and without radiological vasospasm, no statistically significant differences was found, but mean CRP values were higher in the group with vasospasm; these findings were similar to the findings of RvD1 levels. On the other hand, albumin, a negative acute phase reactant, was found to be statistically significantly lower in the patient group on the day 1 of measurement compared to the control group, and this value showed a statistically significant decrease within days in the patient group.

A previous study showed that the release of free radicals and lipid peroxidation are associated with vasospasm.[13] Polin et al.[19] and Nakayama et al.[20] showed that the blockade of E-selectin, a cell adhesion molecule, reduces SAH-induced vasospasm in an animal model. Moreover, Aihara et al.[21] and Oshiro et al.[22] showed a similar association for ICAM-1 and determined that Anti-ICAM-1 monoclonal antibodies can block vasospasm in an animal model. Consistent with these studies showing the role of inflammatory processes in vasospasm, the statistically significantly higher RvD1 measurements in our study on day 1 in the group with radiological vasospasm compared to the group without it indicates that inflammation may be one of the factors responsible for the development of vasospasm.

In a study by Hong et al.[23] DHA, resolvin and neuroprotectin, synthesised from DHA by lipoxygenases, were shown to help resolve inflammation. Titos et al.[24] showed

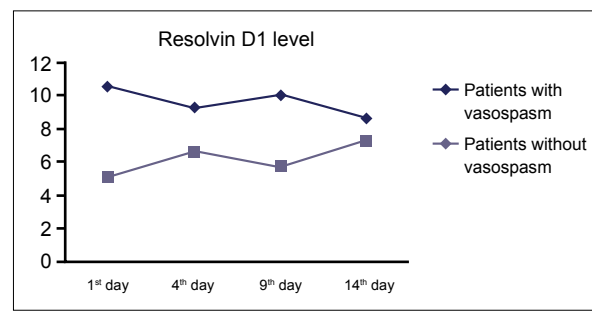

Figure 3. Graphical variation of Resolvin D1 levels according to the presence of radiological vasospasm.

that DHA and RvD1 play a key role in the polymerisation of macrophages to the M2 phenotype in animal experiments, thereby reducing the production of pro-inflammatory cytokines and increasing the production of anti-inflammatory cytokines. Moreover, DHA and RvD1 induce phagocytosis by stimulating macrophages and reduce reactive oxygen species. In our study, monocyte and CRP levels were found to be higher on days 4 and 9 compared with those on day 1; the CRP levels were highest on day 4 and then decreased in parallel. These findings suggest that pro-inflammatory processes increased up to day 4 in the patient group with aneurysmal SAH and that the increase in the RvD1 level detected on day 9 might be an effort to maintain a balance at the pro-inflammatory process in favour of the anti-inflammatory process. In an animal model study conducted by Luo et al.,[25] the effect of RvD1 on the aetiopathogenesis of experimental autoimmune neuritis was investigated, and the effects of endogenous and exogenous RvD1 were examined. The study found that RvD1, its synthesising enzyme (12/15 LOX) and its receptors (ALX/FPR2) were greatly increased at the beginning of the recovery phase. In addition, it was observed that the resolution of inflammation was adversely affected by the pharmacological blockade of RvD1, and inflammation was regulated with exogenous RvD1 following therapeutic treatment. It has been emphasised that RvD1 is a critical molecule in the resolution of inflammation, and its potential to be a therapeutic target in human neuropathies has been demonstrated. While the groups with and without radiological vasospasm were compared in our study, RvD1 elevation was detected on day 1 in the group with radiological vasospasm. Considering that the development of vasospasm began on day 3, this finding may be an important marker of the development of vasospasm.In our study, day 1 neutrophil values were found to be statistically significantly higher in the patient group compared to the control group, and the day 1 neutrophil values were found to be statistically significantly higher in the patient group with radiological vasospasm compared to those i without radiological vasospasm in the patient group. This finding supports the relationship between neuroinflammation and vasospasm after SAH. The fact that neutrophil values were found to be significantly higher in the patient group with vasospasm, similar to the RvD1 levels findings, suggests that both can be used as markers of vasospasm.

In a study by Prüss et al.,[26] patients with multiple sclerosis were divided into two groups as less active and highly active according to the severity of the disease, and the levels of lipid mediators RvD1, neuroprotectin D1, prostaglandinE2 (PGE2), Lipoxin A4 (LXA4) and 15-Hydroxyeicosatetraenoic acid (15-HETE) were measured in the CSF and serum of the patients. The researchers found a significant correlation between the severity of the disease and the CSF levels of RvD1. This is an remarkable outcome in terms of revealing the association between RvD1 and disease severity. Supporting this outcome, RvD1 levels found to be higher in the group with vasospasm on all measurement days in our study.

A previous psychiatric study investigated the role of RvD1 in inflammation based on the role of inflammatory processes in the aetiology of bipolar disorder (BPD). Comparing the serum RvD1 levels of patients diagnosed with BPD in manic-depressive-euthymic episodes were compared with healthy individuals, it was found that patients with manic and depressive episodes were statistically significantly higher than the healthy control group. The highest serum RvD1 concentrations were found in the manic group, followed by the depressive and euthymic group, whereas the lowest concentration was found in the healthy group.[27] Parallel to the high RvD1 values in the acute stages of the disease, the first-day measurements, which were found to be significantly higher in the group with radiological vasospasm in our study, as well as the high RvD1 values throughout all measurement days, suggest that RvD1 may be a marker of the possible severe course of the vasospasm and accordingly, the disease.

Kacira et al.[28] measured serum and CSF CRP levels were measured on days 3, 5 and 7 after aneurysmal SAH; the study results stated that both serum and CSF CRP levels increased during the first three days and continued to increase until the day 7. Similarly, in our study, it was found that serum CRP values increased progressively from day 1 to day 4 and decreased slowly from day 4 to day 9. However, a statistically significant difference was found between the measurement value on day 1 and day 2. Although there was no statistically significant difference in the measurements between patients with and without radiological vasospasm, the mean CRP values were found to be higher in the group with vasospasm on all measurement days. In our opinion, these findings confirm the presence of neuroinflammation after aneurysmal SAH.

In their study, Kapoor et al.[29] have investigated the relationship between the percentage decrease in serum albumin levels neurological outcomes in patients to evaluate the inflammatory-mediated catabolic process after aneurysmal SAH; low albumin levels were associated with the development of new neurological deficits, high mortality and poor long-term prognosis. Similarly, in our study, the serum albumin level measured on day 1 in the patient group was found to be significantly lower than control group, and it showed a significant decrease within days in the patient group. The increase in inflammatory markers and decrease in albumin levels, both of which were detected after aneurysmal SAH in our study, supports the findings that a catabolic process occurs along with the inflammatory process due to aneurysmal SAH.

Limitations of study

Since the inflammatory process was investigated in our study, careful selection of the patient group and exclusion of those with acute infection or chronic disease to eliminate possible confounders of inflammatory processes were the strengths of our study; however, the small number of patients included in the study is the limitation of the study. In addition, the mortality rate of the disease and the

death of some patients during the study period caused a decrease in the number of patients included in the study. In the light of all these data, studies on a large population in which RvD1 and inflammatory cytokines can be investigated are needed to determine the role of RvD1 in the aetiopathogenesis of neuroinflammation and vasospasm after aneurysmal SAH.

CONCLUSION

This is the first study to examine RvD1 levels in patients with aneurysmal SAH. Serum RvD1 levels of patients diagnosed with aneurysmal SAH with and without radiological vasospasm were measured on the day 1, 4, 9 and 14 after SAH. The levels of RvD1 on day 1 were found to be statistically significantly higher in the group with vasospasm than the group without vasospasm. It was concluded that RvD1 was a significant marker in showing the radiological vasospasm that occurs during the course of SAH.

Ethics Committee Approval

This study approved by the Kartal Dr. Lutfi Kirdar City Hospital Clinical Research Ethics Committee (Date: 26.05.2021, Decision No: 2017/514/202/26).

Informed Consent

Prospective study.

Peer-review

Internally peer-reviewed.

Authorship Contributions

Concept: B.C.K., E.A., T.H.; Design: B.C.K., T.H.; Supervision: B.C.K., T.H.; Fundings: B.C.K., E.A., T.H.; Materials: B.C.K., E.A., T.H.; Data: B.C.K., E.A.; Analysis: B.C.K., E.A., T.H.; Literature search: B.C.K., E.A.; Writing: B.C.K., E.A.; Critical revision: B.C.K., E.A., T.H.

Conflict of Interest

None declared.

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Anevizmal Subaraknoid Kanamalı Hastalarda Resolvin D1 Düzeylerinin Sağlıklı Kontrollerdekilerle Karşılaştırılması

Amaç: Literatür, anevrizmal subaraknoid kanamadan sonra önde gelen mortalite ve morbidite nedeni olan vazospazmın etiyolojisinde nöroinflamasyonun rolüne işaret etmektedir. Resolvin D1'in nöronlar üzerinde apoptoza karşı koruyucu bir etkiye sahip olduğu ve anevrizmal subaraknoid kanamadan sonra nöroinflamasyon ve vazospazm üzerinde anti-inflamatuar etkisi olduğu varsayılmaktadır. Bu çalışmada, anevrizmal subaraknoid kanamalı hastalarda serum resolvin D1 düzeylerini ve bunun vazospazm ve C-reaktif protein, nötrofil ve albümin gibi inflamatuar belirteçlerle olası ilişkisini araştırmayı amaçladık.

Gereç ve Yöntem: Spontan anevrizmal subaraknoid kanaması olan 15 hastanın verileri, 17 sağlıklı gönüllünün verileriyle karşılaştırıldı. Anevrizmal subaraknoid kanamalı hastalar iki gruba ayrıldı: anjiyografik vazospazm olan subaraknoid kanama grubu (8 hasta) ve anjiografik vazospazm olmayan subaraknoid kanama grubu (7 hasta). Subaraknoid kanamadan sonra 1, 4, 9 ve 14. günlerde seri serum resolvin D1 ölçümleri alındı.

Bulgular: Resolvin D1 seviyeleri, anjiyografik vazospazmı olan hastalarda subaraknoid kanamadan sonraki birinci günde istatistiksel olarak anlamlı derecede yüksekti (p=0.021). Ayrıca anjiyografik vazospazmı olan grupta da ölçülen tüm resolvin D1 değerleri diğer gruplara göre daha yüksekti. Serum C-reaktif protein ve nötrofil düzeylerinin ölçümleri, kontrol grubuna kıyasla her iki grupta da subaraknoid kanamadan sonraki birinci günde istatistiksel olarak anlamlı derecede yüksek bulundu.

Sonuç: Resolvin D1 seviyeleri, nöroprotektif ve antiinflamatuar özelliklerinden dolayı inflamasyona sekonder yükselme eğilimindedir. Böylece subaraknoid kanama + vazospazm grubunda yüksek resolvin D1 seviyeleri, anevrizmal subaraknoid kanama sonrası anjiyografik vazospazmın etyopatogenezinde inflamatuar süreçlerin rol oynadığını göstermiştir. Sonuç olarak, resolvin D1, anevrizmal subaraknoid kanama sonrası anjiyografik vazospazmın tahmininde önemli bir biyobelirteç olabilir.

Anahtar Sözcükler: Nöroenflamasyon; resolvin D1; subaraknoid kanama; vazospazm.