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Comparison between Neutrophil -Lymphocyte and Platelet-Lymphocyte Ratio to Predict Middle Ear Fluid Viscosity in Otitis Media with Effusion

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Abstract

Objectives: Serous otitis is one of the most common childhood illnesses due to exist of effusion in the middle ear. The reason of effusion is an increase negative pressure in the middle ear space. This effusion has different concentrations that vary from serous to mucus. The objective of our study was to compare the neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) in otitis media with effusion (OME) and the correlation of the effusion types in the middle ear with these ratios. Methods & Materials: This is a case-control study. Patients with OME that candidate for ventilation tube insertion were included in this study. Patients in the case group were divided into two groups of 64 cases, serous and mucus, according to the middle ear fluid viscosity, which were recorded by the surgeon after myringotomy. 64 healthy children, who applied for the routine examination and had blood count analysis, were included in the control group. In peripheral blood cells, the NLR and PLR are derived based on the absolute amount of lymphocyte and neutrophil and platelets. In this study, descriptive statistics were used to compare the mean of quantitative variables in 3 groups of ANOVA and to compare the qualitative variables, the x^2 test was used. The analysis was done with the SPSS v22.0 software program. Significant statistical level was 0.05. Results: The NLR levels of the serous OME groups were significantly higher than the mucoid (p= 0.047) and control groups (p= 0.002). No significant difference was observed between the mucoid and control groups (p= 0.326). The PLR levels of serous OME groups were significantly higher than the mucoid (p= 0.003) and control groups (p= 0.002). Similarly, a significant difference was observed between the mucoid and control groups (p= 0.391). Conclusion: Neutrophil/lymphocyte rate and PLR were a predictive value for the OME and could be used as a useful laboratory parameter to determine the viscosity of the middle ear fluid.

Keywords: Otitis Media with Effusion, Complete Blood Cell Count, Viscosity

Introduction

Otitis media is a relatively common disease in patients referring to otolaryngology and pediatrics' clinics which despite the advancement of medical knowledge is still one of the key issues of research (Tos, 1984; Abshirini et al., 2015). This disease, especially in early age, has been reported in 9% of the children, according to statistics. In 13-8% of cases, major hearing impairment occurs (Saki et al., 2009; Upadhya & Datar, 2014; Goldofsky, 1987). Although OME is encountered mostly at school age, it might be seen also in younger infants and if remain unrecognized it might be cause to delay in speaking and language learning, decrease in the school performance and might lead to the development of behavioral problems (Upadhya & Datar, 2014). The mechanism for the pathogenesis of OME is not clearly understood. However, bacterial infection, adenoid and tonsil hypertrophy, Eustachian tube dysfunction, allergy and immunologic factors are known as important factors in several studies (Saki et al., 2014; Sheikh et al., 2015; Nikakhlagh et al., 2002). Sinusitis and adenoid hypertrophy are also known to be involved in the disease process (Goldofsky, 1987; Sheikh et al., 2015). The mechanism of the effusion in the middle ear was explained with ''hydrops ex vacuo'' theory. According to this theory, the negative pressure in the middle ear caused by the Eustachian tube dysfunction provokes the fluid accumulation with properties of a transudate in the middle ear (Seo et al., 2015). The effusion is divided into different types, depending on viscosity, varies from serous to mucus (Sheikh et al., 2015, Seo et al., 2015). The fluid in otitis media with effusion is characterized by the presence of mucin glycoproteins (Saki et al., 2014). The mechanism, which affects the properties of the viscosity of the accumulated fluid in the middle is depends on the secretory function of the middle ear epithelium. In this liquid, it is clear that mucin, secretory IgA and lysozyme are higher than serum (Chung et al., 2002). Even though some studies have discovered that the bacteria in serous fluid are more than mucous (Seo et al., 2015, Saki et al., 2014). Total white blood cell counts and its subtypes are used as standard inflammatory markers. Neutrophils are activated by the tissue destruction release enzymes like myeloperoxidase, acid phosphatase, and elastase. The ratio of the leukocytes in the circulation changes during the inflammatory reaction. Neutrophilia is accompanied by relative lymphopenia. The neutrophil/lymphocyte rate (NLR) and the

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platelet/lymphocyte rate (PLR) were introduced as a simple marker of the inflammatory reaction (Sak et al., 2014). On the other hand, the effect NLR and PLR in OME and its role in the viscosity of middle ear fluid is not well defined (Seo et al., 2015). The aim of our study was to compare the NLR and PLR in OME and the correlation of the effusion types in the middle ear with these ratios.

Methods & Materials

This study was conducted with the retrospective and case-control and data obtained from the hospital patient files. One hundred twenty-eight pediatric patients, who were diagnosed with otitis media with chronic effusion and had a ventilation tube inserted between March 2007 and September 2018, were included in the study. The laboratory tests of 64 healthy children, who applied to our hospital for a routine health examination and underwent blood count analysis, were included in the control group. Patients in the study group were distributed in 2 groups as serous and mucous groups according to the effusion viscosity evaluated according to the operation records of the patients. Sixty-four patients had serous, and 64 patients had mucous secretions. The inclusion criteria of the study were defined as the presence of effusion in otoscopy and presence of type-B tympanogram. Patients with acute infection, non-type-B tympanogram curve, and chronic disease were excluded from the study. Only patients, who had blood count analysis performed 1 day before the operation, were included in the study. Blood samples were obtained from patients during the initial application. Neutrophil/lymphocyte rate and PLR ratios were obtained by simply dividing the absolute neutrophil and absolute lymphocyte values. The neutrophil, lymphocyte, and platelet count was determined using the Sysmex 1000i analyzer (Sysmex, Kobe, Japan), as part of the routine blood count. The reference value for neutrophil, lymphocyte, and platelet in our laboratory is 1.63 to 6.96 #; 1.09 to 2.99 #; 155 to 366 10e3/uL respectively. Neutrophil, lymphocyte, and platelet counts in the blood count analyses were evaluated, and NLR and PLR were calculated with the help of this data. The study group was divided into 2 groups as serous and mucous groups according to the effusion viscosity evaluated macroscopically by the surgeon after the paracentesis, which was performed during the operation. The groups were compared statistically with the help of these results. Descriptive statistics were used to compare the mean of quantitative variables in 3 groups of ANOVA and to compare the qualitative variables, the x2 test was used. The analysis was done with the SPSS v22.0 software program. Significant statistical level was 0.05.

Results

A total of 128 patients, 64 (50%) males and 64 (50%) females, were included in the current study. The demographic values were primarily compared. The serous group included 64 subjects (33 M/31 F), and the mucoid group included 64 subjects (31 M/33 F). The control group included 64 (43.75%) M/36(56.25%) age-and sex-matched healthy subjects. There was no significant difference between the groups according to gender ($p = 0.2$). The mean age for the serous group was 6.88 ± 3.29, for the mucoid group was 5.46 ± 3.74, and for the control group was 6.32 ± 3.19 years. There was no significant difference between the groups according to age ($p = 0.393$). The comparison of the WBC, LYM, NEUT, PLT, NLR and PLR levels are shown in Table 1. The WBC counts were significantly higher in the mucoid OME groups compared to the controls ($p = 0.032$). In contrast, no significant difference was observed between the serous-mucoid OME groups ($p = 0.372$) and serous-control groups ($p = 0.2.43$). The LYM counts were significantly higher in the mucoid OME groups than the serous OME groups ($p = 0.002$). However, no significant difference was observed between the serous-control groups ($p = 0.184$) and mucoid-control groups ($p = 0.076$). The NEUT counts were significantly lower in the control groups compared to the serous and mucoid OME groups ($p = 0.002$). However, the serous and mucoid groups were not statistically significant ($p = 0.788$). The PLT counts were significantly lower in the mucoid groups than in the serous OME groups ($p = 0.003$). In contrast, no significant difference was observed between the serous- control groups ($p = 0.242$) and mucoid-control groups ($p = 0.308$). The NLR levels of the serous OME groups were significantly higher than for the mucoid ($p = 0.047$) and control groups ($p = 0.002$). No significant difference was observed between the mucoid and control groups ($p = 0.326$). The PLR levels of serous OME groups were significantly higher than the mucoid ($p = 0.003$) and control groups ($p = 0.002$). Similarly, a significant difference was observed between the mucoid and control groups ($p = 0.039$).

Discussion

Otitis media with effusion or serous otitis media is currently one of the most common diseases in children (Saki et al., 2014). In this disease, people suffer from hearing loss due to fluid in the middle ear (Goldofsky, 1987; Park et al., 2004). The presence of fluid and microbial contamination in the middle ear in some cases associated with serious complications. Due to the fact that the disease occurs in children in the age of speech, and in the event of chronic disease, serious complications such as hearing impairment, adhesion and tear of the eardrum, ossicular problems, educational and learning problems, and even behavioral problems are expected (Abshirini et al., 2015). Ventilation tube insertion is the most common pediatric surgical procedure in many industrialized countries (Hörmann, 1987, Sun et al., 2018). The pathophysiologic mechanisms of persistent OME are not well understood. Dysfunction of the Eustachian tube is an important factor, but there is increasing interest in the role of persistent bacterial infection and chronic inflammation in this Process (17, Boztepe et al., 2015). In a study focused on the relation of OME and inflammation, the levels of interleukin-1-beta, interleukin-2, and tumor

necrosis factor-alpha were higher in the children with OME than in the children of the control group (Elbistanli et al., 2017, Lin et al., 2001). Hormann postulated a staged course for the pathogenesis of ME effusion as follows. First, a serous effusion develops inside the tympanum because of a high inflammation level. Then, an increase in the viscosity of the OME occurs because of active water absorption by the middle ear mucosa (Hörmann, 1987). Effusions vary in their composition, but they primarily consist of mucins. Mucins consist of glycoproteins, and they are important components of the mucociliary clearance process from the middle ear cavity through the Eustachian tube into the nasopharynx. According to viscosity measurements for middle ear effusion, the level of mucin in mucoid effusions was significantly higher than for serous effusion (Lin et al., 2001; Kum et al., 2015). Impairment of the mucociliary clearance system, resulting from the viscosity of the effusion, interferes with the drainage of middle ear effusions into the nasopharynx and results in chronic OME. For this situation, medical treatment has been a great disappointment and surgical removal of the effusions and insertion of a ventilation tube are highly recommended (Atan et al., 2016; Seo et al., 2014). Therefore, it is important to determine the composition of middle ear effusions and predicting the character of the effusion preoperatively could help the surgeon decide on whether to use surgical or medical treatment (Liu et al, 2011; Bucak et al., 2014). Neutrophil/lymphocyte rate and PLR values are inflammatory parameters defined in recent years and correlate with the severity of the inflammation (Bucak et al., 2014; Turkmen et al., 2013; Boztepe et al., 2015). Atan et al conducted a study with 77 patients and showed that NLR and PLR were high in OME (Atan et al., 2016). Middle ear effusions into five groups (serous, seropurulent, purulent, mucopurulent, and mucoid) on the basis of histologic and biochemical studies (Hörmann, 1987; Park et al., 2004; Atan et al., 2016; Seo et al., 2014; Liu et al, 2011; Bucak et al., 2014; Turkmen et al., 2013). However, in our study, we classified effusions macroscopically in OME into 2 main groups as serous and mucous. We classify thick and sticky fluids as mucous and light and easy-to-flow fluids as serous in our study, the NLR and PLR were higher in the patients with serous effusion compared with the patients with mucous effusion and control group. These findings showed that in patients of low viscosity, a more prominent inflammation developed. In concordance with our study, Boztepe et al, conducted a study with 81 patients and reported that NLR was significantly increased in the serous middle ear effusions and calculated NLR value of less than 1.38 may show mucoid effusion and if the PLR value is less than 97.96, the effusion is mucoid (Boztepe et al., 2015). We did not detect any difference between the mucous effusion group and the control group in respect of NLR and PLR that similar to Boztepe and Suphi studies (Boztepe et al., 2015, Elbistanli et al., 2017). Neutrophil/lymphocyte rate and PLR can be used a supportive parameters along with the otoscopic examination in the estimation of the properties of the middle ear effusions.

Conclusion

Neutrophil/lymphocyte rate and PLR were a predictive value for the OME and could be used as a useful laboratory parameter to determine the viscosity of the middle ear fluid.

Conflict of interest statement

No potential conflict of interest relevant to this article was reported.

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Table 1- Differences between the three groups.

variables	Serous(64)	Mucoid(64)	Control(64)	p*
WBC+	7.94±2.2	8.42±1.90	7.43±1.84	0.021
lymphocyte+	3.24±1.12	3.91±.98	2.37±0.59	0.003
neutrophil#	4.89(2.14-9.72)	4.38(3.39-6.81)	3.75(2.42-6.27)	0.024
PLT+	358±89	279±39	318±71	0.002
NLR#	1.92(1.03-4.7)	1.67(1.02-2.68	1.18(0.77-2.96)	<0.001
PLR#	147.29(61.20-228.7	94.71(42.31-102.24)	102.37(49.64-192.52	<0.001

+ One-way ANOVA.

Kruskal Wallis parametric test. The results are presented as the Mean SD and Median (Min–Max). The Sheffe test was performed after ANOVA, and the Bonferroni–Dunn

Test was performed after the Kruskal Wallis test.

P* < 0.05 was accepted as the significance level.