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Research Article

Circulating sphingosine-1-phosphate as a diagnostic biomarker for obstructive sleep apnea syndrome

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Abstract

Background

Obstructive sleep apnea syndrome (OSAS) is a major public health concern, which can predispose people to metabolic and cardiovascular diseases. It is an urgent problem in need of a reasonable biomarker in screening OSAS patients. The aim of this study is to determine the association between serum sphingosine-1-phosphate (S1P) concentrations with the presence and severity of OSAS.

Methods

The study included 111 obese subjects, who underwent nocturnal polysomnography (PSG) to assess eligibility for obesity surgery. Among them, 86 patients were diagnosed with OSAS, and the remaining 25 were enrolled as control cases. Serum S1P levels were detected with enzyme linked immunosorbent assay (ELISA). Demographic and clinical Information were collected and analyzed.

Results

There was a significant decrease in serum S1P in OSAS patients compared with control subjects. Among OSAS patients, serum S1P level progressively decreased with severity of OSAS. Linear regression analyses revealed the strong negative association between serum S1P level with apnea-hypopnea index (AHI), and positive association between S1P level with lowest saturation oxygen (LSaO2). Furthermore, Receiver operating characteristic (ROC) curve test demonstrated that serum S1P showed a better predictive capacity for OSAS compared to Epworth Sleepiness Scale (ESS) and STOP scores in OSAS screening.

Conclusion

Serum S1P was significantly lower in OSAS patients when compared with control subjects and was negatively correlated with the severity of OSAS. Furthermore, Serum S1P also has a reasonable specificity, sensitivity and positive predictive value in the diagnosis of OSAS. Thus, serum S1P can be a potential diagnostic biomarker for OSAS.

Keywords: Obstructive sleep apnea syndrome; Sphingosine-1-phosphate; Epworth Sleepiness Scale; Apnea-hypopnea index; Polysomnography

Abbreviations

OSAS: obstructive sleep apnea syndrome

S1P: sphingosine-1-phosphate

PSG: polysomnography

ELISA: enzyme linked immunosorbent assay

AHI: apnea-hypopnea index

LSaO2: lowest saturation oxygen

ROC: receiver operating characteristic

ESS: epworth sleepiness scale

AD: alzheimer's disease

AASM: american academy of sleep medicine

BMI: body mass index

WBC: white blood cells

RBC: red blood cells

PLT: platelet

HDL: high density lipoprotein

ALT: alanine aminotransferase

AST: aspartate aminotransferase

AUC: area under the curve

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IL-6: interleukin-6

IL-1β: interleukin-1β

TNF-α: tumor necrosis factor-α

Introduction

Obstructive sleep apnea syndrome (OSAS) is one of major public health challenges, affecting about 4% of the general population and 30-50% of the obese population [1, 2]. OSAS is characterized by intermittent hypoxia and airflow reduction, resulting from recurrent obstruction of upper airway during sleep [3, 4]. The diagnosis and severity classification of OSAS is verified by the apnea-hypopnea index (AHI) and lowest saturation oxygen (LSaO2) measured by overnight polysomnography (PSG) [5]. A large body evidence indicated that OSAS patients have much more risks of developing metabolic and cardiovascular diseases, such as hypertension, stroke, diabetes and metabolic syndrome, and that the severity of OSAS is associated with morbidity and mortality from these diseases [6,7]. Therefore, early diagnosis and medical intervention are the key to the treatment of OSAS patients. However, most OSAS patients have not been diagnosed in time because of the inconvenience and unavailability of PSG. It is of great interest to explore a reasonable biomarker in identifying diagnosis and severity classification of OSAS.

Sphingosine-1-phosphate (S1P) is well known as a pleiotropic lipid-signaling molecule [8]. S1P exerts its biological functions through activating a family of five G protein-coupled receptors (S1PR1–S1PR5) [8, 9]. Through binding with different receptor subtypes, S1P participates in several physiological and pathological processes, including inflammation [8], oxidative stress [10] and vascular endothelial function [11, 12], all of which play crucial roles in pathogenesis of OSAS. Thus, it is possible that S1P signaling is altered in OSAS patients, and S1P might possess biomarker potential in diagnosis and severity classification of OSAS. In this study, the experiment detected the serum S1P levels in OSAS patients, and explored the associations between serum S1P levels and OSAS severity. The experiment aimed to preliminarily evaluate the diagnostic value of serum S1P in OSAS patients.

Methods

Subjects

This research was a retrospective study based on prospective data collection. All 111 patients were consecutively enrolled from Department of General Surgery, the Second Hospital of Anhui Medical University from September 2018 to June 2022. All patients in the study underwent nocturnal PSG to assess eligibility for obesity surgery. The exclusion criteria included that: Previous diagnosis of OSAS; Age was less than 18 years; Central sleep apnea accounted for more than 5 per hour; Total sleep time was less than 5h; Patients who had incomplete information. Fasting blood samples were collected from patients on admission after written informed consent completed. Clinical characteristics and demographic information were extracted from the electronic patient record system. This study was approved by the Research Ethics Committee of the Second Hospital of Anhui Medical University.

PSG monitoring

PSG monitoring was performed in all patients with a polygraph system (Embla S4500, USA). PSG recordings were analyzed and scored according to the standard method by the American Academy of Sleep Medicine (AASM) in 2007. Apnoea was defined as a ≥ 90% decrease in airflow for at least 10s, and hypopnoea was defined as a ≥ 30% decrease in airflow for at least 10s with at least a 4% decrease in oxygen desaturation. The Apnoea-hypopnoea index (AHI), the most common index used in diagnosis and severity classification of OSAS, was defined as the average number of apnoea and hypopnea per hour of sleep. The patients with AHI ≥ 5 were diagnosed as having OSAS. Then OSAS patients can be classified into 3 groups based on AHI: mild OSAS (AHI ≥ 5 and <15), moderate OSAS (AHI ≥ 15 and < 30) and severe OSAS (AHI ≥ 30). Patients with AHI <5 were included in the control group.

Enzyme-linked immunosorbent assay (ELISA)

Serum samples were collected from participants and centrifugated at a speed of 3,000 rpm at 4°C. S1P in serum were measured through ELISA kits. All detections were conducted according to the manufacturer's protocol.

Statistical analysis

Statistical analyses were performed using SPSS 18.0 software. Categorical variables were reported as counts or percentages and compared by the chi-square test or Fisher's exact test. Continuous data were reported as means ± SEM or medians with interquartile ranges. Student's t-test or nonparametric test was used to assess differences between two groups. Differences between multiple groups were assessed by one-way ANOVA with Tukey's post hoc tests. The correlations of serum S1P and clinical characters were analyzed with Spearman and Pearson correlation analyses. The respective associations between serum S1P and AHI, LSaO2 were estimated through linear regression analysis. A value of $P < 0.05$ was considered statistically significant.

Results

Demographic and clinical Information

86 OSAS patients and 25 control subjects were included in this study. The demographic and clinical information of the study subjects were expressed in Table 1. There was no difference in age, gender, body mass index (BMI), and systolic and diastolic pressures between OSAS patients and control cases. Fasting blood samples were collected on admission for blood routine and biochemical indices. The results showed that the counts of white blood cells (WBCs), blood glucose and uric acid were elevated in OSAS patients. There was no difference in the counts of red blood cells (RBCs) and platelet, albumin, high density lipoprotein (HDL), cholesterol, triglyceride, alanine aminotransferase (ALT), aspartate aminotransferase (AST), urea nitrogen and creatinine between the two groups. In addition, OSAS patients displayed higher AHI and lower LSaO2.

Serum S1P level in OSAS patients and control subjects

Serum S1P level were significantly lower in OSAS patients compared to control subjects (Figure 1A). Among OSAS patients, serum S1P level progressively decreased with severity of OSAS. As shown in Figure 1B, significant serum S1P level decrease was observed in both moderate and severe group compared to mild group.

Variables	OSAS (86)	Control (25)	P
Age (years)	33.22± 0.82	30.00 ± 1.5	0.06
Male (%)	40 (46.51)	6 (24.0)	0.06
BMI	40.71 (35.14,44.88)	39.03 (35.80,43.18)	0.49
Systolic pressure (mmHg)	135.70 (122.00,146.00)	129.80 (124.80,134.30)	0.22
Diastolic pressure (mmHg)	81.21 (73.00,90.25)	78.09 (69.75,87.00)	0.31
WBC (109/L)	9.62 ± 0.33	8.2 ± 0.35	0.0049
RBC (1012/L)	4.91 ± 0.08	4.81 ± 0.09	0.4859
PLT (1012/L)	288.0 ± 9.11	284.7 ±20.12	0.8647
Albumin (mg/L)	40.75 ± 0.525	41.73 ± 0.70	0.308
Blood glucose (mmol/L)	5.90 (5.19,6.63)	4.94 (4.64,5.62)	0.0029
HDL	0.98 (0.83,1.17)	1.07 (0.90,1.23)	0.22
Cholesterol (mmol/L)	4.45 (3.92,5.06)	4.29 (3.65,4.83)	0.53
Triglyceride (mmol/L)	2.36 ± 0.36	1.75 ± 0.45	0.35
ALT (U/L)	45.79 ± 4.80	42.45 ± 8.80	0.73
AST (U/L)	30.85 ± 2.99	27.60 ± 3.82	0.55
Urea nitrogen (mmol/L)	5.05 ± 0.19	5.12 ± 0.35	0.86
Creatinine (mmol/L)	54.10 ± 1.34	52.75 ± 2.69	0.62
Uric acid (mmol/L)	444.9 ± 11.20	391.4 ± 21.39	0.02
AHI	24.15 (8.60,33.73)	1.36 (0.15,2.3)	<0.0001
LSaO2 (%)	71.16 (62.50,81.25)	81.63 (74.00,88.75)	0.0004

Table 1: Demographic and clinical Information of the study subjects.

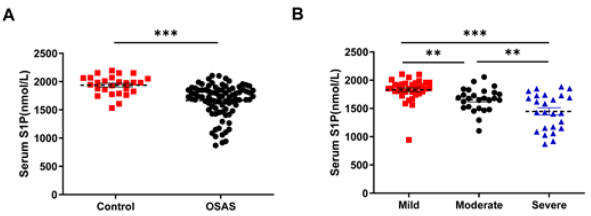

Figure 1: The levels of S1P in OSAS patients and control subjects. A, serum S1P levels in OSAS patients and control cases. B, serum S1P levels in OSAS patients with different severity. All data were expressed as mean± SEM. **P < 0.01, ***P < 0.001.

Associations between serum S1P level and PSG parameters

AHI and LSaO2 were the most common used PSG parameters in OSAS diagnosis and severity classification. The associations of serum S1P levels with AHI and LSaO2 were analyzed with linear regression analysis in OSAS patients. As shown in Table 2, univariable linear regression analyses showed strong negative association between serum S1P level with AHI (β=-0.586, 95%CI: -9.496, -5.112), and positive association between S1P level with LSaO2 (β=0.553, 95%CI: 7.439, 14.664). Multivariable linear regression analysis revealed serum S1P was negatively associated with AHI (β=-0.380, 95%CI: -7.395,-2.071) and positively associated with LSaO2 (β=0.272, 95%CI: 1.148, 9.733).

Variables	Univariable (β, 95% CI)	P	Multivariable (β, 95% CI)*	P
AHI	-0.586 (-9.496,-5.112)	<0.001	-0.380 (-7.395, -2.071)	0.001
LSaO2 (%)	0.553 (7.439,14.664)	<0.001	0.272 (1.148,9.733)	0.014

Table 2: Associations between serum S1P level with PSG parameters among OSAS patients.

*Adjusted for age and sex.

Receiver operating characteristic curves and cutoff point analysis for serum S1P

Receiver operating characteristic (ROC) area under the curve (AUC) were used to evaluate the diagnostic value of serum S1P level in OSAS. As shown in Figure 2, the AUC of serum S1P for OSAS was 0.808 (95% CI: 0.714, 0.902). The optimal cutoff value of serum S1P was 1856.00 nmol/L, followed with 73.08% sensitivity and 77.91% specificity. Moreover, Epworth Sleepiness Scale (ESS) and STOP scores were commonly used screening tools for OSAS. The AUC of ESS and STOP for OSAS were 0.697 (95% CI: 0.585, 0.810), 0.706 (95% CI: 0.599, 0.811), respectively.

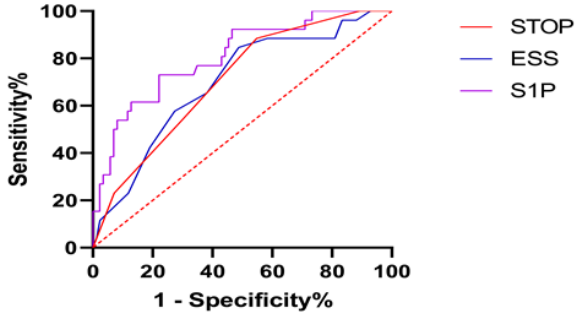

Figure 2: Receiver operating characteristic (ROC) curves for different predictive indexes in OSAS diagnosis.

Discussion

OSAS has been a major worldwide public health concern which results in great medical morbidity and mortality, especially in obese patients. However, most OSAS patients are not aware that they have OSAS because of the inconvenience and unavailability of PSG. Therefore, a reasonable biomarker for OSAS would be very helpful in OSAS screening. In the present study, it investigated the alternations of serum S1P in OSAS patients and the relationship of serum S1P with the OSAS severity. The results reveled that serum S1P was significantly decreased in OSAS patients and serum S1P was gradually downregulated consistent with OSAS severity. These findings suggest that serum S1P can be a novel biomarker in OSAS patients.

Bioactive sphingolipids, which mediate signaling in diverse cellular processes, are well known for their significant roles in health and disease [13-16]. More and more studies indicated the potential values of bioactive sphingolipids as therapeutic targets and diagnostic biomarker in diseases, such as acute lung injury [17], pneumonia [18] and cystic fibrosis [19]. S1P, one of bioactive sphingolipids, has recently emerged as an essential lipid mediator involved in regulating various cellular processes. Cumulative clinical studies certificated the important contribution of S1P in inflammation-related diseases, such

as hypertension [20], Alzheimer's disease (AD) [9], and septic shock [21]. Previous studies indicated that S1P plays a range of favorable roles in suppressing inflammation and enhancing endothelial integrity. A study conducted in COVID-19 patients demonstrated that serum S1P level was lower in COVID-19 patients compared to healthy controls, and serum S1P level was inversely associated with COVID-19 severity [22]. Liu et al. described that decreased serum S1P level could discriminate ischemic stroke from hemorrhagic stroke and controls and that serum S1P levels were associated with ischemic stroke severity [23]. Therefore, serum S1P may become a potential biomarker for inflammation-related diseases and can indicate disease severity. Persistent low-intensity systemic inflammation induced by intermittent hypoxia and oxidative stress is one of the main pathogenetic characteristics in OSAS patients [2, 24, 25]. Recent evidence suggested that low-intensity systemic inflammation in OSAS patients are partly responsible for OSAS-related metabolic and cardiovascular diseases [25, 26]. Many studies demonstrated elevated circulating inflammatory mediators including interleukin-6 (IL-6), interleukin 1β (IL-1β) and tumor necrosis factor-a (TNF-α) in OSAS patients and the positive correlations of proinflammatory mediators with OSAS severity [27-29]. Likewise, the counts of white blood cells (WBCs) were significantly elevated in OSAS patients. Inflammatory mediators the can reflect the systemic inflammation have been considered potential biomarker in OSAS patients. S1P is a significant inflammatory mediator which plays essential roles in neutrophil activation and recruitment [30,31], B-cell migration [32] and egress of lymphocytes into the circulation [33]. Several studies showed the protective effects of S1P in inflammation-related diseases, suggesting that S1P could be a potentially beneficial biomarker as an anti-inflammatory mediator. Hsu et al found S1P levels were inversely correlated with disease severity in patients with community-acquired pneumonia [34]. In the present study, it detected serum S1P in OSAS patients and control subjects. And the study found that serum S1P in OSAS patients is significantly decreased and serum S1P decreased in parallel with OSAS severity. To further clarify the relationship between serum S1P and OSAS severity, linear regression analysis was conducted. The study found that serum S1P level was negatively associated with AHI, and positively associated with LSaO2. Furthermore, the predictive power of serum S1P for OSAS was accessed with ROC curve test. Compared to ESS and STOP scores, serum S1P showed a better predictive capacity for OSAS. These results reveled the potential values of serum S1P in OSAS screening. Serum S1P may thus be a reliable biomarker indicative of OSAS occurrence and severity.

There are several limitations in this study. First, the sample size was relatively small, and all the subjects were from a single medical center. Further studies with larger population from multicenter are necessary to validate these findings. Second, all the subjects enrolled in the study are obese patients. These results may not be generalizable outside of this specific population. Further studies with normal BMI subjects are needed to confirm the association between serum S1P and OSAS. Fourthly, the present study investigated the alternations of serum S1P in OSAS patients. However, the mechanism leading to such alternations was not unclear. Further in vitro and in vivo research will thus be needed to clarify the mechanism.

Conclusion

The study showed that serum S1P was significantly lower in OSAS patients when compared with control subjects and was negatively correlated with the severity of OSAS. Furthermore, Serum S1P also has a reasonable specificity, sensitivity and positive predictive value in the diagnosis of OSAS. Thus, this findings suggest that S1P is a potential diagnostic biomarker for OSAS.

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Author's contribution

CZ designed the study and collected study-specifc data; CZ and JY analyzed the data; CZ wrote the manuscript; all authors revised and approved the manuscript.

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Availability of data and materials

Data will be made available on request.

Ethics approval and consent to participate

The study protocol was approved by the Research Ethics Committee of the Second Hospital of Anhui Medical University (No.YX2021-099(F1)).

Consent for publication

All authors consent for publication.

Competing of interests

The authors report no conflict of interest.

References

1. Le Tallec-Estève N, Rousseau C, Desrues B, Loréal O, Thibault R (2021) Transferrin saturation is independently associated with the severity of obstructive sleep apnea syndrome and hypoxia among obese subjects. Clinical nutrition (Edinburgh, Scotland) 40: 608-614.

2. Zou H, Yang W, Liu Y (2021) Correlation of serum myonectin concentrations with the presence and severity of obstructive sleep apnoea syndrome. Ann Clin Biochem 58:117-122.

3. Cai J, Lyu X, Huang P, Li S, Chen R, et al. (2022) Increased Levels of CHI3L1 and HA Are Associated With Higher Occurrence of Liver Damage in Patients With Obstructive Sleep Apnea. Front Med (Lausanne) 9: 854570.

4. Peres BU, Allen AJH, Shah A, Fox N, Laher I, et al. (2020) Obstructive Sleep Apnea and Circulating Biomarkers of Oxidative Stress: A Cross-Sectional Study. Antioxidants (Basel, Switzerland) 9.

5. Fakhouri EW, Weingarten JA, Singh SP, Shah P, Peterson SJ (2021) The Association of Nephroblastoma Overexpressed (NOV) and Endothelial Progenitor Cells with Oxidative Stress in Obstructive Sleep Apnea. Oxidative medicine and cellular longevity 2021: 7138800.

6. Chihara Y, Chin K, Aritake K, Harada Y, Toyama Y, et al. (2013) A urine biomarker for severe obstructive sleep apnoea patients: lipocalin-type prostaglandin D synthase. The European respiratory journal 42: 1563-1574.

7. Sunadome H, Matsumoto H, Tachikawa R, Matsumoto T, Tanizawa K, et al. (2020) Role of serum periostin in severe obstructive sleep apnea with albuminuria: an observational study. Respiratory research 21: 143.

8. Chew W, Wang W, Herr DR (2016) To fingolimod and beyond: The rich pipeline of drug candidates that target S1P signaling. Pharmacological research 113: 521-532.

9. Chua XY, Chai YL, Chew WS, Chong JR, Ang HL, et al. (2020) Immunomodulatory sphingosine-1-phosphates as plasma biomarkers of Alzheimer's disease and vascular cognitive impairment. Alzheimer's research & therapy 12: 122.

10. Ueda N (2022) A Rheostat of Ceramide and Sphingosine-1-Phosphate as a Determinant of Oxidative Stress-Mediated Kidney Injury. International journal of molecular sciences 23: 4010.

11. Raza Z, Saleem U, Naureen Z (2020) Sphingosine 1-phosphate signaling in ischemia and reperfusion injury. Prostaglandins & other lipid mediators 149: 106436.

12. Xiong Y, Hla T (2014) S1P control of endothelial integrity. Current topics in microbiology and immunology 378: 85-105.

13. Jiang J, Shi Y, Cao J, Lu Y, Sun G, et al. (2021) Role of ASM/Cer/TXNIP signaling module in the NLRP3 inflammasome activation. Lipids in health and disease 20: 19.

14. Bowler RP, Jacobson S, Cruickshank C, Hughes GJ, Siska C, et al. (2015) Plasma sphingolipids associated with chronic obstructive pulmonary disease phenotypes. American journal of respiratory and critical care medicine 191: 275-284.

15. Ma X, Chen L, He Y, Zhao L, Yu W, et al. (2022) Targeted lipidomics reveals phospholipids and lysophospholipids as biomarkers for evaluating community-acquired pneumonia. Annals of translational medicine 10: 395.

16. Yeganeh B, Lee J, Bilodeau C, Lok I, Ermini L, et al. (2019) Acid Sphingomyelinase Inhibition Attenuates Cell Death in Mechanically Ventilated Newborn Rat Lung. American journal of respiratory and critical care medicine 199: 760-772.

17. Kupsch S, Eggers LF, Spengler D, Gisch N, Goldmann T, et al. (2022) Characterization of phospholipid-modified lung surfactant in vitro and in a neonatal ARDS model reveals anti-inflammatory potential and surfactant lipidome signatures. European journal of pharmaceutical sciences: official journal of the European Federation for Pharmaceutical Sciences 175: 106216.

18. Torretta E, Garziano M, Poliseno M, Capitanio D, Biasin M, et al. (2021) Severity of COVID-19 Patients Predicted by Serum Sphingolipids Signature. International journal of molecular sciences 22.

19. Becker KA, Riethmüller J, Seitz AP, Gardner A, Boudreau R, et al. (2018) Sphingolipids as targets for inhalation treatment of cystic fibrosis. Advanced drug delivery reviews 133: 66-75.

20. Jujic A, Matthes F, Vanherle L, Petzka H, Orho-Melander M, et al. (2021) Plasma S1P (Sphingosine-1-Phosphate) Links to Hypertension and Biomarkers of Inflammation and Cardiovascular Disease: Findings From a Translational Investigation. Hypertension (Dallas, Tex : 1979) 78: 195-209.

21. Piotti A, Novelli D, Meessen JMTA, Ferlicca D, Coppolecchia S, et al. (2021) Endothelial damage in septic shock patients as evidenced by circulating syndecan-1, sphingosine-1-phosphate and soluble VE-cadherin: a substudy of ALBIOS. Critical care (London, England) 25: 113.

22. Marfia G, Navone S, Guarnaccia L, Campanella R, Mondoni M, et al. (2021) Decreased serum level of sphingosine-1-phosphate: a novel predictor of clinical severity in COVID-19. EMBO molecular medicine 13: e13424.

23. Liu J, Sugimoto K, Cao Y, Mori M, Guo L, et al. (2020) Serum Sphingosine 1-Phosphate (S1P): A Novel Diagnostic Biomarker in Early Acute Ischemic Stroke. Frontiers in neurology 11: 985.

24. Lin Q, Chen L, Yu Y, Liu K, Gao S (2014) Obstructive sleep apnea syndrome is associated with metabolic syndrome and inflammation. European archives of oto-rhino-laryngology : official journal of the European Federation of Oto-Rhino-Laryngological Societies (EUFOS) : affiliated with the German Society for Oto-Rhino-Laryngology - Head and Neck Surgery 271: 825-831.

25. Popadic V, Brajkovic M, Klasnja S, Milic N, Rajovic N, et al. (2022) Correlation of Dyslipidemia and Inflammation With Obstructive Sleep Apnea Severity. Frontiers in pharmacology 13: 897279.

26. Kheirandish-Gozal L, Gozal D (2019) Obstructive Sleep Apnea and Inflammation: Proof of Concept Based on Two Illustrative Cytokines. International journal of molecular sciences 20.

27. Cao Y, Song Y, Ning P, Zhang L, Wu S, et al. (2020) Association between tumor necrosis factor alpha and obstructive sleep apnea in adults: a meta-analysis update. BMC pulmonary medicine 20: 215.

28. Imani MM, Sadeghi M, Khazaie H, Emami M, Sadeghi Bahmani D, et al. (2020) Evaluation of Serum and Plasma Interleukin-6 Levels in Obstructive Sleep Apnea Syndrome: A Meta-Analysis and Meta-Regression. Frontiers in immunology 11: 1343.

29. Tang T, Zhou X, Huang H, Huang QD (2017) Relationship between IL-1β polymorphisms and obstructive sleep apnea syndrome. European review for medical and pharmacological sciences 21: 3120-3128.

30. Florey O, Haskard D (2009) Sphingosine 1-phosphate enhances Fc gamma receptor-mediated neutrophil activation and recruitment under flow conditions. Journal of immunology (Baltimore, Md : 1950) 183: 2330-2336.

31. Ratajczak M, Borkowska S, Ratajczak J (2013) An emerging link in stem cell mobilization between activation of the complement cascade and the chemotactic gradient of sphingosine-1-phosphate. Prostaglandins & other lipid mediators 122-129.

32. Cinamon G, Matloubian M, Lesneski MJ, Xu Y, Low C, et al. (2004) Sphingosine 1-phosphate receptor 1 promotes B cell localization in the splenic marginal zone. Nature immunology 5: 713-720.

33. Pappu R, Schwab SR, Cornelissen I, Pereira JP, Regard JB, et al. (2007) Promotion of lymphocyte egress into blood and lymph by distinct sources of sphingosine-1-phosphate. Science (New York, NY) 316: 295-298.

34. Hsu SC, Chang JH, Hsu YP, Bai KJ, Huang SK, et al. (2019) Circulating sphingosine-1-phosphate as a prognostic biomarker for community-acquired pneumonia. Plos one 14: e0216963.

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