The Relationship between theSeverity of *Obstructive Sleep Apnea* (OSA) and Tension-Type Headache Frequency

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Abstract

Background: *Obstructive Sleep Apnea* (OSA) is a condition where the upper airway obstruction periodically occurs while sleeping causing breathing to stop intermittently, either completely (apnea) or partially (hypopnea). Tension-Type Headache(TTH) is the most common headache and is defined as primary headache in the ICHD 3 classification. Patients with OSA have a higher possibilityof developing TTH than patients without OSA. The purpose of this study was to analyze the risk factors for the severity of OSA and to analyze the relationship between the severity of OSA and the frequency of tension-type headaches every month.

Research Methods: This research was an analytic observational study throughcross sectional design. The research subjects were OSA patients suffering from TTH in RSUP Dr. Kariadi, Semarang who met the inclusion and exclusion criteria. The inclusion criteria included OSA patients diagnosed using the STOP BANG questionnaire, patients suffering fromTTH usingthe ICHD 3 beta questionnaire, patients aged ≥ 18 years old, and patients/families who agreed to become the study participants by signing an informed consent. Exclusion criteria included patients with impaired consciousness, GCS <15, patients with language disorders (aphasia), patients with structural brain lesions such as: stroke, head trauma (which includes moderate head injury and severe head injury), brain infection, brain tumor, and *hydrocephalus normopressure* in the last 3 months as provenby history, physical examination, CT-scan image of the head or description (resume), patients diagnosed with other types of headaches, and patients with depression and anxiety. The study was conducted from April to December 2019. Patients' data were obtained through questionnaire filled by the patients. Polysomnography examination was performed to assess the severity of OSA. The research data were analysis using correlation test ofSpearman. The results were considered to be significant if the p-value <0.05

Research Result: Seventeen OSA patients at RSUP Dr. Kariadi, Semarang were involved in this research. There was a relationship between age (p = 0.017),BMI (p = 0.000), and neck circumference (p = 0.014) on the incidence of OSA. In addition, there was a relationship between the degree of OSA severity and the frequency of tension-type headaches per month(r = 0.62; p = 0.0 08).

Conclusion: There is a relationship between age, BMI, and neck circumference onOSA. There is a relationship between the severity of OSA and the frequency of tension-type headaches per month.

Keywords: *Obstructive sleep apnea (OSA), Tension-type headache (TTH), Degree of severity.*

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Introduction

Obstructive Sleep Apnea (OSA) is a common form of *Sleep Disordered Breathing* (SDB) which has been generally recognized and is associated with various

medical problems. It also has an impact on morbidity and mortality, so that it becomes a burden in public health services. This condition is characterized by repeated episodes of complete or partial collapse of the upper airway (especially the oropharyngeal tract) during sleep, with stopping/reduced airflow. [1-2] The diagnosis of OSA is made if the total frequency of decreased airflow associated with airway collapse or *apnea hypopnea index* (AHI) is more than 5 times per hour of sleep or is characterized by repeated episodes of apnea or hypopnea for at least 10 seconds while sleeping. This can lead to arousal periods (awakening or restlessness in sleep) and returning to sleep. AHI is obtained by conducting a polysomnographic examination. [3] Classification of the severity degree of OSA is based on the value of *Apnea-hypopnea index* (AHI) established by the American academy of sleeping medicine. It can be divided into mild (AHI 5-14), moderate (AHI 15-30), and severe (AHI> 30). [4] OSA as one of the causes of tension-type headache is often not well-diagnosed, thus complicating the management of headaches.We wereinterested in further research of OSA onthe frequency of tension-type headaches every month. The purpose of this study was to analyze the risk factors for the severity of OSA and to analyze the relationship between the severity of OSA and the frequency of tension-type headaches every month.

Material and Method

This research was an analytic observational study throughcross sectional. The research subjects were OSA patients suffering from TTH in RSUP Dr. Kariadi, Semarang who met the inclusion and exclusion criteria. The inclusion criteria includedpatients diagnosed with OSA using STOP BANG questionnaire, TTH patients diagnosed using ICHD 3 beta questionnaire, patients aged ≥ 18 years old, and patients/families who agreed to participate in the current research by signing an informed consent. Meanwhile, the exclusion criteria included patients with impaired consciousness, GCS <15 , patients with language disorders (aphasia), patients with structural brain lesions such as: stroke, head trauma (which includes moderate head injury and severe head injury), brain infection, brain tumor, and *hydrocephalus normopressure* in the last 3 months as provenby history, physical examination, CT-scan image of the head or description (resume), patients diagnosed with other types of headaches, and patients with depression and anxiety.

The research was conducted in the outpatient and inpatient installation of RSUP Dr. Kariadi Semarang, starting fromApril 2019 to December 2019. The study sample size was 17 patients. The size of the study subjects was determined by consecutive sampling, in whichpatients were selected throughinclusion and exclusion criteria from April 2019 to the completion of this research. Patient data were obtained through questionnaire filled by the patients. Polysomnography examination was performed to assess the severity of OSA. TTH frequency assessments used the ICHD 3 beta criteria, while TTH intensity used the VAS score. Data were analysis using the Spearmancorrelation test. The results were considered significant if the p-value <0.05

Results and Discussion

Based on Table 1, it can be seen that there wasa difference on the mean of the age betweenthe mild-moderate OSA group andthe severe OSA group (p = 0.017). There were more male participants than female participants in which the male participants were more involved in the mild-moderate OSA group and the number of female respondents was similar in the two OSA groups. In addition it was also known that most of the OSA subjects were at the age range of 50-59 years old (p = 1.00), and the relationship between OSA and TTH was significant (p <0.001). The current study also found that there were more male subjects than women (p = 1.00). [6] Previous research conducted in Norway found that most of the OSA age in TTH wereat the age range of 60-65 years old from a total of 431 samples, in which male participants were also dominating. [7] During the old age, there will be anatomical changes in the structure of the bones and muscles around the pharynx, lengthening the upper airway (pharynx) and thickening thefat around the pharynx which will result in decreased negative pressure reflex in maintaining patency of the upper airway. This is not different between men and women. [8-9] The study conducted by Bucks [10] also stated that as we get older, OSA increases.

Table 1 Characteristics of study subjects based on OSA severity

Variable	OSA Severity				P
	Mild - Moderate	%	Severe	%	
	AHI <30 (N)		AHI> 30 (N)		
Demographics					
Age	45.64 ± 13.65 (11)	64.71	54.83 ± 9.02 (6)	35.29	0.017
Gender					
Man	8	47.06	4	23.53	0.60
Women	3	17.65	2	11.76	
Total	11	64.71	6	34.29	
BMI					
Normoweight	4	23.5	0	00.0	0.000
Overweight	3	17.6	0	00.0	
Obese	4	23.5	6	35.3	
Neck circumference					
<40 cm	4	23.5	0	00.0	0, 0 14
≥ 40 cm	7	41.2	6	35.3	
Lifestyle					
Smoking history					
Yes Male	3	17.65	3	17.65	0.34
Female	0	17.65	0	17.65	
Total	3	0	3	0	
No	8	47.05	3	17.65	
Duration of smoking					
1-2 years	0	00.0	0	00.0	
3-4 years	0	00.0	0	00.0	
> 5 years	3	50.0	3	50.0	
History of alcohol consumption					
Yes Male	2	11.8	0	0	0.40
Female	0	0	0	0	
Total	2	11.8	0	0	
No	9	52.9	6	35.3	
Duration of alcohol consumption					
1-2 years	1	100.0	0	00.0	
3-4 years	1	100.0	0	00.0	
> 5 years	0	00.0	0	00.0	
Clinical					
History of hypertension					
Yes Male	4	23.53	2	11.76	0.37
Female	1	5.88	2	11.76	
Total	5	29.41	4	23.53	
No	6	35.30	2	11.76	
Duration of hypertension					
1-2 years					
Man	1	11.11	1	11.11	
Women	0	0	0	0	
Total	1	11.11	1	11.11	
3-4 years					
Man	2	22.22	0	0	
Women	0	0	2	22.22	
Total	2	22.22	2	22.22	
> 5 years					
Male	0	0	2	22.22	
Female	1	11.11	0	0	
Total	1	11.11	2	22.22	

Table 1 also shows that the two OSA groups had more obese BMI than normoweight and overweight BMI. Furthermore, subjects with obese BMI were more in the severe OSA group than the mild-moderate OSA group. According to a study conducted by Magdalena in Poland, based on the medical record data on 41 OSA patients, it was found that theincrease in BMI contributed to the severity of OSA (p = 0.000). [11] Increased BMI and obesity have the potential to increase the incidence of OSA. [12]

Subjects suffering from mild-moderate and severe OSA groups had more neck circumference of more than 40 cm than subjects with neck circumference of less than 40 cm. In a retrospective study conducted by Si Eun Kim in Korea, neck circumference was influenced by the degree of OSA severity (p <0.0001). [13] The increased risk of OSA in obesity is due to the addition of fat tissue, especially on the walls of the upper airway, causing narrowing the airway lumen diameter and fat deposits causing decreased airway muscle strength. The increase in fat tissue mass can be a predictor of OSA by measuring the neck circumference. [14-15]

On both OSA groups, it was knownthat the subjects who smoked between the mild – moderate OSA group and the severe OSA group were the same. In a study conducted by Wen at Lukang Christian Hospital, there was no significant relationshipbetween smoking and OSA after the adjustment to theage, sex and BMI (OR = 1.02, 95% CI: 0.66-1.57). [16] Other studies have suggested that smoking is a risk factor for OSA, but further research is needed to confirm these results. [17] In this study, smoking was not a risk factor.

Smoking can cause a decrease in eNOS activity, thus exacerbating OSA by reducing the production of nitric oxide. If this situation continues, there will be vasoconstriction in the smooth muscle of blood vessels, if it occurs long-term it can cause hypertension. In addition, smoking causes an inflammatory response that releases inflammatory mediators such as CRP and IL-6 and increases pro-inflammatory cytokines and attracts leukocytes to the endothelial surface at the start of the atherosclerosis process. [18-19]

There was no association between hypertension and the severity of OSA, where the subjects suffering from hypertension in the mild-moderate OSA group were more than the severe OSA group. Amongthe 3 subjects who smoked (> 5 years), it turned out that 2 people had hypertension (> 5 years) and suffered from severe OSA. A prospective cohort study conducted in Spain by José for 12.5 years regarding the relationship between hypertension and OSA found the incidence of OSA was related to hypertension and the incidence of hypertension increased as the severity of OSA (p <0.001) increased.They got a total of 705 OSA subjects, in which 656 subjects had previously suffered from hypertension and 49 new subjects were diagnosed at the time of examination. [20] Other studies suggest that there is a two-way relationship between hypertension and OSA. This relationship is also greatly influenced by age and gender. [21]

The history of alcohol consumption in this study wassmall because it fits the existing culture. In this study, alcohol had no effect. Several other studies suggested that alcohol consumption has the potential to worsen the incidence of OSA. [22] Other studies also stated that the effect of alcohol on OSA was inconsistent so that it could be different for each study result. [23] The results of the meta-analysis stated that alcohol consumption can increase OSA by 25% in low and middle-income countries [24]

Table 2 shows that there wasa strong positive correlation between the severity of OSA and the frequency of TTH (rho = 0.62; p = 0.008). This is consistent with a study conducted by Yu in Taiwan for 6 years with 4,759 OSA patients as subjects who gave significant results (p = 0.003). Yu's study also proved that patients with OSA experienced TTH (hazard ratio, 1.18; 95% CI, 1.06–1.31). [25] According to the research conducted by Alberti, headache on awakening in OSA patients wasmostly TTH (frequent 42.1%, chronic 15.8%). [26]This is consistent with the fact that OSA is a chronic process so that patients suffering from OSA are more likely to suffer from TTH. OSA will cause intermittent hypoxia which will affect NO levels thus causes pain with the occurrence of vasoconstriction in vascular smooth muscle so that ischemia can occur and NO can cause spasm in the skeletal muscles. If this continues, it will cause chronic pain through central sensitization. [27-29] This study reinforced by Alberti [30,]whostated that the severity degree of OSA affects the occurrence of headache by 74% and insomnia by 40%.

Table 2. Relationship between OSA severity and frequency of tension-type headaches every month

TTH frequency	OSA Severity				rho	p
	Mild-Moderate (AHI <30)	%	Severe (AHI ≥ 30)	%		
Infrequent (<1 day / month)	4	23.5	0	00.0	0.62	* 0.008
Frequent (<15 days / month)	6	35.3	2	11.8		
Chronic (≥15 days / month)	1	5,9	4	23.5		
Total	11	64.7	6	35.3		

** Spearman Correlation*

Conclusion

Risk factors which are related to the incidence of OSA include age, BMI, and neck circumferences. This study also proved that there wasa relationship between the severity of OSA and the frequency of tension-type headaches per month.

Ethical Clearance : The study has obtained ethical clearanceapproval from the Ethics Commission of the Faculty of Medicine, Universitas Diponegoro/RSUP dr. Kariadi Semarang with number: 397/EC/KEPK-RSDK/2019

Conflict of Interest: Nil

Source of Fund: Independent.

References

1. Antariksa B. Patogenesis, diagnostik dan skrining OSA (obstructive sleep apnea). Jurnal Respirologi Indonesia. 2010;30(1).
2. Spicuzza L, Caruso D, Di Maria G. Obstructive sleep apnoea syndrome and its management. Therapeutic advances in chronic disease. 2015 Sep;6(5):273-85.
3. Cahyono A, Hermani B, Mangunkusumo E, Perdana RS. Hubungan obstructive sleep apnea dengan penyakit sistem kardiovaskuler. Oto Rhino Laryngologica Indonesiana. 2011 Jun 1;41(1):37-45.
4. Hudgel DW. Sleep apnea severity classification—revisited. Sleep. 2016 May 1;39(5):1165-6.
5. Eckert DJ, White DP, Jordan AS, Malhotra A, Wellman A. Defining phenotypic causes of obstructive sleep apnea. Identification of novel therapeutic targets. American journal of respiratory and critical care medicine. 2013 Oct 15;188(8):996-1004.
6. Chiu YC, Hu HY, Lee FP, Huang HM. Tension-type headache associated with obstructive sleep apnea: a nationwide population-based study. The journal of headache and pain. 2015 Dec;16(1):1
7. Kristiansen HA, Kværner KJ, Akre H, Øverland B, Russell MB. Tension-type headache and sleep apnea in the general population. The journal of headache and pain. 2011 Feb 1;12(1):63-9.
8. Malhotra A, Huang Y, Fogel R, Lazic S, Pillar G, Jakab M, Kikinis R, White DP. Aging influences on pharyngeal anatomy and physiology: the predisposition to pharyngeal collapse. The American journal of medicine. 2006 Jan 1;119(1):72-e9.
9. Glasser M, Bailey N, McMillan A, Goff E, Morrell MJ. Sleep apnoea in older people. Breathe. 2011 Mar 1;7(3):248-56.
10. Bucks RS, Olaithe M, Rosenzweig I, Morrell MJ. Reviewing the relationship between OSA and cognition: W here do we go from here?. Respirology. 2017 Oct;22(7):1253-61.
11. Dobrowolska-Zarzycka M, Dunin-Wilczynska

I, Mitura I, Szymanska J. BMI in patients with obstructive sleep apnea. Current Issues in Pharmacy and Medical Sciences. 2015 Dec 1;28(4):244-6.

12. Romero-Corral A, Caples SM, Lopez-Jimenez F, Somers VK. Interactions between obesity and obstructive sleep apnea: implications for treatment. Chest. 2010 Mar 1;137(3):711-9.
13. Kim SE, Park BS, Park SH, Shin KJ, Ha SY, Park J, Park KM. Predictors for presence and severity of obstructive sleep apnea in snoring patients: significance of neck circumference. Journal of Sleep Medicine. 2015 Dec 31;12(2):34-8.
14. Saint Martin M, Roche F, Thomas T, Collet P, Barthélémy JC, Sforza E. Association of body fat composition and obstructive sleep apnea in the elderly: A longitudinal study. Obesity. 2015;23(7):1511–6.
15. Ahbab S, Ataoğlu HE, Tuna M, Karasulu L, Çetin F, Temiz LÜ, Yenigün M. Neck circumference, metabolic syndrome and obstructive sleep apnea syndrome; evaluation of possible linkage. Medical science monitor: international medical journal of experimental and clinical research. 2013;19:111.
16. Hsu WY, Chiu NY, Chang CC, Chang TG, Lane HY. The association between cigarette smoking and obstructive sleep apnea. Tobacco induced diseases. 2019;17.
17. Lin YN, Li QY, Zhang XJ. Interaction between smoking and obstructive sleep apnea: not just participants. Chinese medical journal. 2012 Sep 1;125(17):3150-6.
18. Ambrose JA, Barua RS. The pathophysiology of cigarette smoking and cardiovascular disease: an update. Journal of the American college of cardiology. 2004 May 19;43(10):1731-7.
19. Barua RS, Ambrose JA, Srivastava S, DeVoe MC, Eales-Reynolds LJ. Reactive oxygen species are involved in smoking-induced dysfunction of nitric oxide biosynthesis and upregulation of endothelial nitric oxide synthase: an in vitro demonstration in human coronary artery endothelial cells. Circulation. 2003 May 13;107(18):2342-7.
20. Marin JM, Agusti A, Villar I, Forner M, Nieto D, Carrizo SJ, Barbé F, Vicente E, Wei Y, Nieto FJ, Jelic S. Association between treated and untreated obstructive sleep apnea and risk of hypertension. Jama. 2012 May 23;307(20):2169-76.
21. Torres G, Sánchez-de-la-Torre M, Barbé F. Relationship between OSA and hypertension. Chest. 2015 Sep 1;148(3):824-32.
22. Kolla BP, Foroughi M, Saeidifard F, Chakravorty S, Wang Z, Mansukhani MP. The impact of alcohol on breathing parameters during sleep: a systematic review and meta-analysis. Sleep medicine reviews. 2018 Dec 1;42:59-67.
23. Scanlan MF, Roebuck T, Little PJ, Naughton MT. Effect of moderate alcohol upon obstructive sleep apnoea. European Respiratory Journal. 2000 Nov 1;16(5):909-13.
24. Simou E, Britton J, Leonardi-Bee J. Alcohol and the risk of sleep apnoea: a systematic review and meta-analysis. Sleep medicine. 2018 Feb 1;42:38-46.
25. Chiu YC, Hu HY, Lee FP, Huang HM. Tension-type headache associated with obstructive sleep apnea: a nationwide population-based study. The journal of headache and pain. 2015 Dec;16(1):1-7.
26. Alberti A, Mazzotta G, Gallinella E, Sarchielli P. Headache characteristics in obstructive sleep apnea syndrome and insomnia. Acta neurologica scandinavica. 2005 May;111(5):309-16.
27. Feigin VL, Abajobir AA, Abate KH, Abd-Allah F, Abdulle AM, Abera SF, Abyu GY, Ahmed MB, Aichour AN, Aichour I, Aichour MT. Global, regional, and national burden of neurological disorders during 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. The Lancet Neurology. 2017 Nov 1;16(11):877-97.
28. Ashina S, Bendtsen L, Ashina M. Pathophysiology of tension-type headache. Current pain and headache reports. 2005 Dec;9(6):415-22.
29. Olesen J. The role of nitric oxide (NO) in migraine, tension-type headache and cluster headache. Pharmacology & therapeutics. 2008 Nov 1;120(2):157-71.
30. Alberti A, Mazzotta G, Gallinella E, Sarchielli P. Headache characteristics in obstructive sleep apnea syndrome and insomnia. Acta neurologica scandinavica. 2005 May;111(5):309-16.