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The correlation between cotinine levels in active smokers with color blindness

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ABSTRACT

Introduction: Color blindness can be congenital or acquired due to certain diseases. One of the causes of acquired color blindness is due to toxic optical neuropathy. Tobacco consumption, assumed to be one of the risk factors, has been proposed to be associated with toxic optical neuropathy. Active smokers are subjects who are susceptible to the toxic effects of tobacco. This study aimed to analyze the correlation between blood cotinine levels in active smokers with color blindness.

Methods: This study was an observational analysis of 33 smokers and 35 non-smokers samples. Cotinine levels were examined from blood samples, which were then examined by Calbiotech reagent. Farnsworth Munsell 15 Hue was used to examine color vision. Statistical analysis was done using Shapiro-Wilk for normality distribution data, Mann Whitney and Independent T-test comparing data between two groups, and Spearman correlation test.

Result: There was a significant difference between the mean color blind error score in the smoker group (4.83 ± 6.27) and the non-smoker group (0.24 ± 0.65). Similarly, a significant difference was found between the blood cotinine level of the smoker group (64.59 µg/ml) and the non-smoker group (0.44 µg/ml). There was a significant correlation between the color blind error score and blood cotinine levels in the total sample.

Conclusion: There was a correlation in the total sample between blood cotinine levels and a color-blind error score. The higher the blood cotinine level, the higher the color blind error score.

Keywords: Cotinine; smoker; color blindness.
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INTRODUCTION

Color blindness or dyschromatopsia is the decreased ability to see some colors or perceive their differences. It takes place when one or more of three types of color-sensitive cone cells or photoreceptors (red, green, and blue) do not perfectly gather or send the proper color signals to the optic nerve.[1,2] The prevalence of color blindness in Indonesia is 7.4%.[3] Color blindness can be congenital or acquired due to certain diseases. Inherited color blindness is not progressive and cannot be treated. Whereas acquired color blindness can be temporary or permanent and develops to become more severe if the disease or poisoning continues.[4]

One of the causes of acquired color blindness is due to toxic optical neuropathy. Toxic optic neuropathy is a condition characterized by bilateral symmetrical vision reduction without pain, the presence of a scotoma or visual field defect, and color vision deficit.[5,6] This situation is usually associated with exposure to toxic substances obtained at work, consumption of food or substances that contain toxic substances, or due to the use of systemic drugs.[7] Toxic optical neuropathy can be balanced between men and women and can be found in all ages and races.[8] Several risk factors have been proposed to be associated with toxic optical neuropathy that manifests with impaired color vision or color blindness, one of them being tobacco consumption.[9] Yet, the evidence is still unclear.

Active smokers mostly do tobacco consumption. Data from the Ministry of Health showed the prevalence of smokers in Indonesia at the age of 15 increased by 36.3% compared to the prevalence in 1995 at 27%. Indonesia has the third largest number of smokers worldwide, after China and India.[10] More than a thousand people under 18 are active smokers worldwide every day, which can cause health and socio-economic problems. Young smokers aged 20-30 are needed in important jobs such as in the military, civil work, and electronic industries that depend on good color vision.[11]

Nicotine is one of tobacco substances, which is the main ingredient in cigarettes. Nicotine (C10H14N2) is an alkaloid organic compound consisting of carbon, hydrogen, nitrogen, and a small portion of oxygen and sulfur. This chemical compound of alkaloids has a strong and stimulant effect on the human body. Nicotine has an addictive and psychoactive effect that causes effects of pleasure, reduced anxiety, tolerance, and physical attachment. After nicotine enters the body (blood flow), these substances will go to the brain and circulate throughout the body.[12] Nicotine is toxic to nerve tissue and increases systolic and diastolic blood pressure due to catecholamine hormone

stimulation. Heart rate and contraction of the heart muscle increase, the need for oxygen increases, blood flow in coronary vessels increases, and peripheral vasoconstriction occurs. Nicotine also increases LDL cholesterol and platelet aggregation.[13] Platelets will clot and clog narrow blood vessels, causing ischemia in the human body's tissues. The nicotine concentration is around 5% per 100 grams of tobacco weight. Cotinine is a nicotine metabolite whose concentration is much higher than the concentration of nicotine in the blood. Cotinine also has a longer half-life than nicotine, so cotinine concentrations are almost constant throughout the day compared to nicotine levels. Because of these pharmacokinetic properties, cotinine concentrations are often used as biomarkers of nicotine levels in the body.[14]

The mechanism for the occurrence of color blindness in smokers until now has not been clearly explained. Some hypotheses regarding these mechanisms include decreasing antioxidants, increasing free radicals and lipid peroxidation, ischemia, hypoxia, and micro-infarcts that cause macular degeneration.[11] We hypothesized that smoking is associated with color blindness.

Several studies have shown an association between smoking, impaired color vision, and decreased contrast sensitivity.[15–18] Recent research by Han et al. showed a relationship between urine cotinine levels and visual impairment, which was seen in a decrease in visual acuity.[19] So, it is important to see the association between cotinine levels with color vision before a decrease in vision occurs. The study aimed to analyze the correlation between blood cotinine levels in active smokers with color blindness.

METHODS

This was an observational analytic study with a cross-sectional design at Diponegoro National Hospital Semarang. Blood cotinine levels were examined in the GAKI Laboratory of the Medical Faculty of Diponegoro University Semarang using Calbiotech reagents. The research time starting from sample examination to the presentation of research results was April to October 2018.

Sampling was carried out from April to June 2018 with consecutive sampling, which obtained a total number of 68 respondents, consisting of 33 smokers who had smoked for at least 1 year and 35 non-smokers who are active or passive. All respondents were male. Inclusion criteria consisted of ages 20-40 years, best visual correction ≥ 6/9, anterior and posterior segments of the eye within normal limits, and willingness to participate in the study. People with congenital color blindness or a family history of congenital color blindness, people with glaucoma and other retinal disorders, people with diabetes and hypertension, and those consuming alcohol and pregnant should not participate in this study. Sample size was calculated using a formula for hypothesis testing for the difference between two independent means, which obtained a minimum of 33 samples in each group.

Examination of color vision was conducted using Farnsworth Munsell 15 Hue. Subjects were instructed to place the loose cap in the tray closest in color to the last cap already in the tray. Scoring is accomplished by reading the numbers on the reverse side of the cap and recording the sequence selected by the patient on a copy of the score sheet. The score is obtained by adding up the difference in numbers whose sequence is not following normal color vision. Both eyes are examined one by one. Then the total score is obtained from the average score of both eyes. One examiner carries out this procedure. Blood cotinine levels were examined in the GAKI Laboratory of Medical Faculty of Diponegoro University Semarang from 3 ccs of antecubital venous blood, then centrifuged to obtain serum. Serum was then examined using Calbiotech reagents according to the ELISA (Enzyme-Linked Immunoassay) protocol with units of ng/ml.

The research data are processed and presented in the form of tables. The normality test of data distribution using Shapiro Wilk. The different tests used Independent T-test if the data was normal and Mann-Whitney if the data was not normal. The results of the normality test of the data obtained that color blindness error score data was not normal, so the Spearman correlation test was used.

The study was conducted after obtaining ethical clearance from the Health Research Ethics Commission of the Faculty of Medicine, Diponegoro University / Dr. Kariadi General Hospital Semarang with number 341 / EC / FK-RSDK / V / 2018.

RESULTS

Sixty-eight subjects were enrolled in the study, consisting of 33 (48.5%) smokers and 35 (51.5%) non-smokers. All respondents were male. Table 1 shows the baseline characteristics of all subjects. According to the Shapiro-Wilk test, the age data were abnormally distributed, so the Mann-Whitney test was used to analyze the difference. The result showed a p-value of 0.075, which meant there were no significant differences in the age between the smoker and non-smoker groups.

Meanwhile, color blindness error scores were abnormally distributed, while the blood cotinine levels data were normal. It was found that the average color blindness error score for smokers (4.83 ± 6.27) was significantly higher than for non-smokers (0.24 ± 0.65) ($p<0.001$). The difference between blood cotinine levels of smoker and non-smoker groups was also significantly different ($p<0.001$).

Spearman correlation analysis was used to assess the correlation between color blindness score and cotine level. The result showed a significantly strong correlation coefficient (r=0,93) between blood cotinine level and color blindness scores (Table 3). Figure 1 depicts the correlation between the two variables, and the angle of the bar indicates a positive correlation. The higher the blood cotinine level, the higher the color blindness error score.

DISCUSSION

The mean color blindness error scores for smokers were significantly higher than for non-smokers in our study. This finding is similar to Ar et al., who reported that the median total error score of the Farnsworth-Munsell 100 Hue Test or color blindness test was significantly (p=0.004) higher in the smoker group (65; range 12-221) than the non-smoker group (50.50; range 6-206).[11] The study by Fernandes et

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Table 1. Baseline characteristics of subject (n= 68).

Variable	Mean ± SD/ Median (min-max)	Frequency (n)	Percentage (%)
Gender			
- Male	-	68	100
- female		0	0
Age (years)			
- Smoker	23.61 ± 5.36 / 21.00 (20 – 39)	33	48.5
- Non-smoker	21.54 ± 2.64 / 21.00 (20 – 33)	35	51.5
Duration of smoking (years)	7.21 ± 6.61/ 5 (1 – 26)	33	100
Number of cigarettes/day	13.00 ± 4.66 / 12 (3 – 24)	33	100

Table 2. Comparison of Color Blindness Error Score and Blood Cotinine Level between Smoker and Non-smoker Group.

Variable	Group		p-value
	Non-smoker	Smoker	
Color blindness error score	0.24 ± 0.65	4.83 ± 6.27	<0.001*
Blood cotinine level	0.44 ± 0.13	31.59 ± 43.02	<0.001**

Note : *significant at p <0,05 by mann whitney; **significant at p <0,05 by independent t-test.

Table 3. The correlation between color blindness error score and blood cotinine level.

Variable	Mean ± SD	p	r	Explanation
Color blindness error score	2.47 ± 4.93	<0.001***	0.93	Significant, positive, moderate
Cotinine level	31.57 ± 43.90			

Note:***significant at p <0,05 by correlation of spearman's

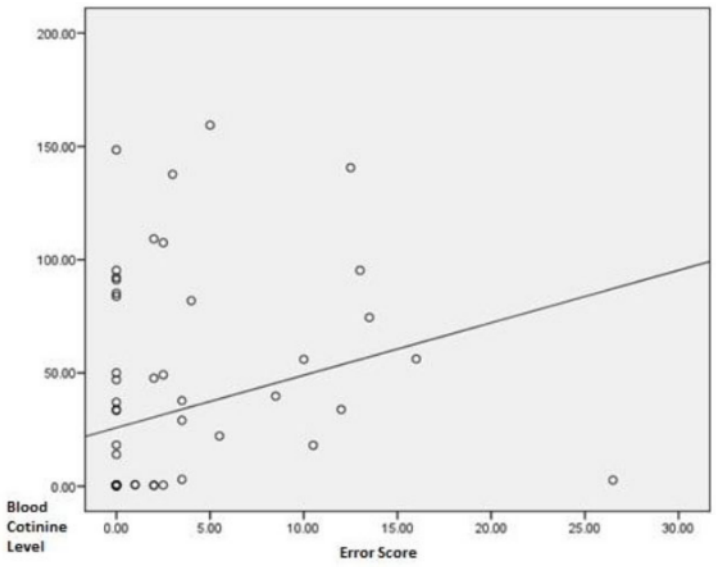

Figure 1. The correlation between blood cotinine levels and color blindness error scores in the total sample is a Diffuse diagram.

al. used the Lanthony D-15 test for color blindness and analyzed it quantitatively in the Color Confusion Index. The result showed significantly higher color confusion indexes in smokers compared to non-smokers.[16]

In this study, smokers' mean blood cotinine levels were significantly higher than of non-smokers. A significant difference was also observed between the groups. This finding is similar to a study by Ghazi et al. where there was a significant (p=0.015) difference between the smoker group (3.57 ± 2.77) and the non-smoker group (2.06 ± 1.63) in saliva cotinine level.[20]

A study by Han et al. showed that urinary cotinine level was associated with an increased risk of incident Visual Impairment in men and women (p <0.05), where visual acuity impairment was seen.[19] In our study, we investigated the relationship between smoking, represented by blood cotinine level as an objective marker with visual impairment, and assessed as the error score of the color blindness test. This study showed a significant (p<0.001) correlation between the error score of color blindness and blood cotinine levels. It is different from another study by Fernandes et al. that there was no correlation between Fagerström Test for Nicotine Dependence (FTND) with Color Confusion Index using the Lanthony D-15 test.[16] This is because FTND is a subjective instrument to evaluate smoking status.

Previous research showed that color blindness could occur in smokers who consume more than 20 cigarettes daily.[17] In previous studies, it was also mentioned that color blindness can occur in smokers

who have smoked at least 20 cigarettes a day for ten years.[18] The average duration of smoking in this study was 7.21 years, and the average number of cigarettes consumed per day was 13.

This study has several limitations, namely the minimum number of samples; this was because sampling was done in the Faculty of Medicine and Diponegoro National Hospital, and the average age was relatively young so there were not many chronic smokers who have been smoking for more than 10 years and more than 20 cigarettes consumed every day. The second limitation is the intellectual level of the cases; all of the participants were chosen from the university personnel with same intellectual level that causes variations in the duration and number of cigarettes that are almost the same.

This study has implications for extending our understanding of the detrimental effects of smoking, suggesting that the visual system can be affected. In addition, this data suggests research into visual processing impairments (e.g., reduced contrast sensitivity or color discrimination) in clinical populations.

Further study with a large population sample and other study designs such as case control or prospective cohort to find out more accurately about the correlation between cotinine level and color blindness in smokers and non-smokers.

CONCLUSION

There was a significant correlation in the total sample between blood cotinine levels and the score of color blindness, where the higher the blood cotinine level, the higher the score for color blindness. Prospective studies should evaluate early vision disorders using objective instruments such as electrophysiologic examination.

DISCLOSURES

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Conflict of Interest

There is no conflict of interest.

Author Contribution

RP contributed to the study concept and design. RP, M, EKSL, and MH provision of study material or patients. RAA contributed to administrative support. M, EKSL, and MH contributed to data collection and assembly. RP and RAA contributed to data analysis and interpretation. All authors contributed to manuscript writing and reviewing. All authors read and approved the final draft.

Ethics Approval

The study was conducted after obtaining ethical clearance from the Health Research Ethics Commission of the Faculty of Medicine, Diponegoro University / Dr. Kariadi General Hospital Semarang with number 341 / EC / FK-RSDK / V / 2018.

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REFERENCES

1. Smail HO, Ismael EM, Ali SA. Prevalence of Color Blindness among Students of four basic schools in Koya City. J Adv Lab Res Biol. 2019;6(4):154–7. Available from: https://e-journal.sospublication.co.in/index.php/jalrb/article/view/292
2. Riordan-Eva P, Augsburger JJ, editors. Vaughan & Asbury's : General Ophthalmology. 19th ed. New York: McGraw-Hill; 2017.
3. Health Research and Development Agency of the Ministry of Health of the Republic of Indonesia. Basic Health Research (Riskesdas) 2007. 2008; Available from: http://labdata.litbang.kemkes.go.id/images/download/laporan/RKD/2007/lap_rkd07.pdf
4. Mashige KP, Van Staden DB. Prevalence of congenital colour vision deficiency among Black school children in Durban, South Africa. BMC Res Notes. 2019;12(1):10–4. Available from: https://doi.org/10.1186/s13104-019-4374-1
5. Phillips KC, Clarke-Farr PC. Ethambutol toxic optic neuropathy: A case report and review. African Vis Eye Heal [Internet]. 2018;77(1):1–3. Available from: https://doi.org/10.4102/aveh.v77i1.419
6. Bhatti MT, Biousse V, Bose S, Danesh-Mayer H V., Levin LA, Phillips PH, et al., editors. 2020-2021 Basic and Clinical Science Course : 5. Neuro-Ophthalmology. San Fransisco: American Academy of Ophthalmology; 2017.
7. Nowomiejska K, Kiszka A, Maciejewski R, Jünemann A, Rejdak R. Central scotoma in tobacco-alcohol toxic optic neuropathy measured with semi-automated kinetic perimetry. Cutan Ocul Toxicol. 2018;37(4):319–23. Available from: https://doi.org/10.1080/15569527.2018.1459666
8. Chiotoroiu SM, Noaghi M, Stefaniu GI, Secureanu FA, Purcarea VL, Zemba M. Tobacco-alcohol optic neuropathy--clinical challenges in diagnosis. J Med Life. 2014;7(4):472–6. Available from: pmcid: PMC4316121
9. Kanwar D, Wasay M. Gutka Associated Optic Neuropathy. Pakistan J Neurol Sci. 2021;16(1):5–7. Available from: https://ecommons.aku.edu/pjns/vol16/iss1/5
10. Ministry of health of Republic Indonesia. The government strives to reduce the number of beginner smokers. Jakarta; 2017 [cited 2018 Mar 15]. Available from: https://www.kemkes.go.id/article/view/17060200002/pemerintah-upayakan-pengurangan-jumlah-perokok-pemula-.html
11. Arda H, Mirza GE, Polat OA, Karakucuk S, Oner A, Gumus K. Effects of chronic smoking on color vision in young subjects. Int J Ophthalmol. 2015;8(1):77–80. Available from: https://doi.org/10.3980/j.issn.2222-3959.2015.01.14
12. McEwan M, Azzopardi D, Gale N, Camacho OM, Hardie G, Fearon IM, et al. A Randomised Study to Investigate the Nicotine Pharmacokinetics of Oral Nicotine Pouches and a Combustible Cigarette. Eur J Drug Metab Pharmacokinet. 2022;47(2):211–21. Available from: https://doi.org/10.1007/s13318-021-00742-9
13. Marques P, Piqueras L, Sanz MJ. An updated overview of e-cigarette impact on human health. Respir Res. 2021;22(1):1–14. Available from: https://doi.org/10.1186/s12931-021-01737-5
14. Sharma P, Sane N, Anand SD, Marimutthu, Benegal V. Assessment of cotinine in urine and saliva of smokers, passive smokers, and non-smokers: Method validation using liquid chromatography and mass spectrometry. Indian J Psychiatry. 2018;59(4):271–6. Available from: 10.4103/psychiatry.IndianJPsychiatry_61_18
15. Díez-Ajenjo MA, García-Carabal M, Luque-Cobija MJ, García-Domene MC. Blue-yellow deficiencies in young moderate smokers. J Optom. 2021;14(2):199–205. Available from: https://doi.org/10.1016/j.optom.2020.06.006
16. Acquired Color Vision Defects in Chronic Heavy Smoking. J Addict Prev. 2017;5(1):1–4. Available from: 10.13188/2330-2178.1000037
17. Fernandes TM de P, Almeida NL, dos Santos NA. Comparison of color discrimination in chronic heavy smokers and healthy subjects. F1000Research. 2017;6(0):85. Available from: 10.12688/f1000research.10714.1
18. Fernandes TMDP, Almeida NL De, Santos NA Dos. Effects of smoking and smoking abstinence on spatial vision in chronic heavy smokers. Sci Rep. 2017;7(1):1–7. Available from: http://dx.doi.org/10.1038/s41598-017-01877-z
19. Han SY, Chang Y, Shin H, Choi CY, Ryu S. Smoking, urinary cotinine levels and incidence of visual impairment. Sci Rep. 2021;11(1):1–10. Available from: https://doi.org/10.1038/s41598-020-79865-z
20. Ghazi A, Pakfetrat A, Hashemy SI, Boroomand F, Javan-Rashid A. Evaluation of Antioxidant Capacity and Cotinine Levels of Saliva in Male Smokers and Non-smokers. Addict Heal. 2020;12(4):244–50. Available from: 10.22122/AHJ.V12I4.278

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